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4th Joint AIC-SILS Conference



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Presentation of 4th Joint AIC - SILS Conference.

Doriano Lamba,^a Federico Boscherini,^b Angela Altomare,^c Cinzia Giannini.^c

Dear Participants,

Despite its historic scale and intensity, the COVID-19 pandemic and the Ukraine crisis did not refrain us to finalize in presence the fourth Joint AIC-SILS Conference in Trieste, 12-15 September 2022.

The event returned to take place in Trieste nineteen years after the first one, held in July 2003.

On behalf of the Organizing Committee, we are very much thankful to the members of the Conference Steering and Scientific Committees in supporting and helping us in shaping an exciting and multidisciplinary scientific program.

The Conference hosted 13 micro-symposia, which included multidisciplinary aspects on:

Modern Integrative Structural Biology; Understanding Advanced Functional Materials Through Operando Studies; Italy@EuXFEL; Frontiers in Mineralogy and Inorganic Geochemistry; Experimental Design & Analysis of Data; Crystallographic and Spectroscopic Advanced Tools Applied to Pharmaceuticals, Materials at Extreme Conditions: X-ray Crystallography and Beyond; Bright Radiation Sources and Novel Software Applications; Current Approaches in Structural Biology; Investigating Molecular Crystals: Methods and Application; Interplay between Crystal Growth and Advanced Characterizations for Materials Development; Nanostructured Materials; Science & Society: from Dissemination to Communication.

We hope that the selected topics provided you with a wealth of information and paved the way for new research collaborations.

It is fair to say that the conference has been a success!

Nearly 200 attendees have contributed in so many ways to turn this event into a smoothly running meeting with many very insightful contributions: 4 plenary lectures, 25 keynote lectures, 42 oral and 25 flash communications, 27 E-posters, 3 commercial presentations and a vibrant atmosphere for discussion and networking.

The Conference has greatly benefited from the support of institutional Patronages and from the commitment, generosity and interest of the sponsors Highlights of the Conference have been:

- "Mineralogy 2022" a global-scale initiative established under UNESCO sponsorship to celebrate the importance of mineralogy among the basic sciences;
- The Round Table Discussion on "Horizon-Europe and the Future of Research Infrastructures: Next Generation of Scientific Instrumentation, Tools and Methods".

A particular emphasis has been placed on gender balance and on student and early-career research participation.

The Mario Nardelli AIC 2022 prize has been awarded ex-aequo to Paolo Pio Mazzeo, University of Parma, and to Marco Taddei, University of Pisa. The SILS Young Scientist 2022 prize has been awarded to Alberta Terzi, Institute of Crystallography - CNR, Bari and the SILS "Carlo Lamberti" 2022 best PhD prize to Mariele Romano, Ludwig Maximilian University, München. Rosaria Bruno, University of Calabria, Alessandro Grinzato, University of Padova and Daniela Mauro, University of Pisa were the recipients of the Fiorenzo Mazzi AIC 2022 prize for the best PhD thesis.

Lisa Baratelli, Tommaso Battiston and Luca Sironi, all from the University of Milano, were the recipients of the Fiorenzo Mazzi AIC 2022 prize for the best MSc thesis.

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† 4th Joint AIC-SILS Conference, (Trieste) 12-15/09/2022

AIC and SILS generously provided 10 and 2 travel grants and complimentary registrations respectively to assist early-career investigators, post-docs and undergraduate students to attend the Conference.

Eldico Scientific presented to Matteo Melegari, University of Parma the prize for the best E-poster; CCDC presented ex-aequo to Francesca Menescardi, University of Genova, and to Davide Salusso, University of Torino the prize for the best flash contribution.

Meetings of the AIC Biological Macromolecule and AIC Young Crystallographer groups as well as the AIC and SILS Annual General Assemblies took place during the Conference.

The web master Guido Righini has designed the set-up of the contents of the web site and has succeeded in building a logical structure with user-friendly registration procedure and the total program including all abstracts online. Nicola Corriero and Teresa Sibillano have composed the Abstract Book.

The “green” crew of Luisa Barba, Angelo Chiatto, Giuseppe Chita, Andrea Caporale, Alberto Cassetta, Sonia Covaceuzach and Alessandro Pesaresi from the Institute of Crystallography - CNR, Trieste and, Rita de Zorzi and Neal Hickey from the Department of Chemical and Pharmaceutical Sciences, University of Trieste, are thanked and complimented for their enormous effort and effective contribution to welcoming and helping participants with registration and logistics.

We owe much gratitude to Silvano Geremia and Francesco Princivalle for selecting the Teatrino Basaglia situated in the Saint John Park, Trieste and the Department of Chemical and Pharmaceutical Sciences of the University of Trieste as the venues of the Conference. The staff of the social cooperative “La Collina”, the Posto delle Fragole and Nuovo Savron have taken care of professional technical excellence and high-quality catering.

The pleasant performance by the Ricmanje Orchestra Wind Quintet enlivened the Welcome Party with the unmistakable atmosphere of the Mitteleuropa music.

The Conference Gala Dinner took place at the historical Café Tommaseo. Finally, yet importantly, we are honored to pass the baton to the Organizers of the 2023 SILS Annual meeting to be held in Roma and of the 50° AIC congress to be held in Bologna, to whom we wish good work!

To all those who contributed to the success story of the fourth Joint AIC-SILS conference: Thank you for all your excellent work!

Doriano Lamba – Chair of the Organizing Committee

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Scientific Programme

MS-01 **Modern Integrative Structural Biology**

Chairs: S. Mangani, B. Vallone

The complexity of the chemistry occurring in living organisms involves interactions between large numbers of a variety of molecules. In order to achieve a better understanding, at the structural level, of the processes occurring in the crowded environment of cells there is need to exploit the capabilities of different experimental techniques. Modern Integrative Structural Biology addresses this subject and involves cross-links of data coming from X-ray crystallography, cryo-electron microscopy/tomography, computational methods, NMR, XAS, SAXS and other spectroscopies to produce structural models of biological systems.

The microsposium aims to highlight updated scientific results obtained by such integrated approaches.

MS - 02 **Understanding Advanced Functional Materials Through Operando Studies**

Chairs: E. Borfecchia, S. Galli

The microsposium will focus on in situ/operando studies aimed at disclosing the structural and physico-chemical properties of advanced materials and at tracking their response in controlled environments relevant to the target functional application. An emphasis will be given to cutting-edge diffraction methods applied under non ambient conditions and synchrotron-based X-ray spectroscopies exploiting in situ/operando setups, as well as to their possible combination and integration within multi-technique approaches. The microsposium is envisaged to encompass a broad range of high-impact research fields, including, e.g., (photo/electro-) catalysis, gas adsorption and separation, energy storage and conversion.

MS - 03 **Italy@EuXFEL**

Chairs: C. Masciovecchio, S. Pascarelli

The European X-Ray Free-Electron Laser (EuXFEL) provides the international user community hard and soft x-ray flashes with unprecedented characteristics, enabling new experiments in a variety of scientific fields ranging from condensed matter physics to chemistry and from geophysics to biosciences. In 2020, in synergy with SILS, EuXFEL initiated an effort to better organize its scientific exploitation by Italy and a first very successful "Italy@EuXFEL 2020" workshop demonstrated the interest by the scientific Italian community to take advantage of the unique features of EuXFEL. At this MS, first results in particular from Italian users will be presented, and discussions will focus on how to foster tighter links between EuXFEL and potential Italian users.

MS - 04 **Frontiers in Mineralogy and Inorganic Geochemistry**

Chairs: D. Belmonte, G. Giuli

This microsposium deals with state of the art techniques (using either laboratory facilities or synchrotron light sources) aimed at studying structure, chemistry, reactivity, thermodynamic and physical properties of minerals, glasses, melts and fluids of interest in Earth Science and technological applications.

We encourage submission of contributions reporting advanced experimental and/or numerical approaches aimed at studying mineralogical and geochemical aspects related to both Earth Science and advanced technology.

MS - 05 **Experimental Design & Analysis of Data**

Chairs: A. Di Cicco, M. Milanesio

The recent evolution of both sources and detectors allowed improving the data quality and signaling to noise ratio at XFEL, synchrotron and laboratory X-ray sources. X-ray diffraction and spectroscopy techniques can now be carried out routinely at high resolution with a time frame of seconds or even much less with a high degree of automation in sample manipulation and experiment execution. New experimental possibilities and new challenges are emerging. Innovative methods, complementary to traditional ones, are necessary to face "the X-ray big data" analysis and propose efficient solutions. The microsposium is focused on the new avenues of both methods and data analysis in X-ray diffraction and spectroscopies of the XXI century.

MS - 06 **Crystallographic and Spectroscopic Advanced Tools Applied to Pharmaceuticals**

Chairs: F. Gozzo, M. Saviano

This microsposium is intended to be the opportunity for academic and industrial scientists to exchange on the main challenges faced in the pharmaceutical world and the advanced methodology available for the characterization of pharmaceutical compounds. The microsposium welcomes contributions dealing with the many aspects related to the advantages offered by the combination of different characterization methods applied to pharmaceuticals.

MS - 07 Materials at Extreme Conditions: X-ray Crystallography and Beyond

Chairs: G. Aquilanti, D. Comboni

In the last decades, experiments at non-ambient conditions have greatly benefited from the improvement of large-scale facilities, which allow investigating and manipulating matter at extreme PT conditions. Experiments performed at non-ambient conditions are devoted to unveil the interplay between structure, physical properties, reactivity and the deformation mechanisms of various materials, expanding our knowledge regarding the evolution of planets and providing critical information to tailor the future new cutting-edge materials. This microsposium aims to be the stage for scientists who wish to show the results of their research performed under extreme conditions using a variety of analytical techniques.

MS - 08 Bright Radiation Sources and Novel Software Applications

Chairs: C. Cuocci, F. Stellato

AIC and SILS societies collect scientists exploiting high intensity photons and electron beams to study a wealth of crystalline and non-crystalline systems. The microsposium dedicated to “Bright Radiation Sources and Novel Software Applications” acts as a bridge connecting the two sides of the research.

On the one hand, the microsposium collects contributions about the brightest present and future radiation sources, keeping an eye on the new experiments they will allow. On the other hand, it hosts talks describing the most recent software developments that allow an increasingly efficient information extraction from the experimental measurements.

MS - 09 Current Approaches in Structural Biology

Chairs: M. Cianci, S. Fermani

In the last decades, structural biology has experienced a tremendous growth. The ensemble of low- and high-resolution techniques now available offers the possibility of studying complex macromolecular structures at an unprecedented resolution. Historically, X-ray crystallography was the preferred method for structure determination; however, alternative/complementary approaches are further increasing our capability to explore previously intractable molecules. This microsposium is focused on the current strategies (single or in combination) used to study both the structure and the dynamics of proteins and protein complexes which are relevant for biomedical and biotechnological applications.

MS -10 Investigating Molecular Crystals: Methods and Applications

Chairs: A. Forni, E. Priola

This Microsposium welcomes contributions from both fundamental and applicative research on solid-state molecular systems, where knowledge of the crystal structure, possibly combined with information obtained from quantum mechanical calculations, is vital to understand properties, processes and reactivity. Examples include, but are not limited to, quantum crystallography studies on molecular properties and intermolecular interactions, structure/properties investigations on emissive and non-linear optical materials, crystal engineering of functional materials.

MS - 11 Interplay between Crystal Growth and Advanced Characterizations for Materials Development

Chairs: F. Boscherini, P. Prete

To go beyond a trial and error approach for the optimization of functional properties of modern materials a close connection between the development of novel methods for crystal growth and use of refined tools for their experimental characterization is essential. The goal of this interplay is to gain a physical understanding at the atomic level of materials properties. In this symposium we aim to highlight recent results in these two strongly connected and challenging areas of materials science.

MS - 12 Nanostructured Materials

Chairs: A. Cedola, P. Scardi

The study of materials at the nanoscale is now an integral part of various research disciplines, which go far beyond materials science and concern all the physical, chemical and life sciences. Diffraction and imaging techniques, in particular those based on X-rays, are among the most widespread tools both in basic research and in the development of applications of nanostructured materials. The microsymposium aims to collect the state of the art in crystallography and X-ray analysis applications in this lively and ongoing field of research.

MS - 13 Science & Society: from Dissemination to Communication

Chairs: P. D'Angelo, M. Morana

Crystallography and synchrotron radiation are fascinating topics that play a major role in a wide range of disciplines, shedding light on materials, minerals, and biomolecules. However, the general public is mostly unaware of this contribution. This microsymposium aims to promote dissemination and outreach of these themes, highlighting the importance of science communication in many different aspects of everyday life, including the ongoing COVID-19 pandemic. At the same time, we want to stimulate the discussion about the interplay between science and society in terms of inclusion, representation and diversity.



Quantum imaging with X-rays.

Sharon Shwartz.^a

Quantum optics has been very fruitful and led to many seminal achievements in fostering quantum technologies in a variety of fields including imaging and spectroscopy.¹ However, the focus of quantum optics is on the optical range of the electromagnetic spectrum. The extension of concepts of quantum optics into the x-ray range can lead to remarkable applications with enhanced performances with respect to the present methodologies that are used in x-rays science and technology.² Recently, the properties of the strong time-energy correlations of photons produced by the process of spontaneous parametric down conversion (SPDC) have been extended to the x-ray regime to demonstrate the ability to improve the visibility and the SNR of an image with a small number of photons in an environment with a noise level that is higher than the signal by many orders of magnitude.³ Another quantum imaging modality called ghost imaging has been reported as well.⁴ More recently, the observation of the interaction of a single photon with a beam splitter has been observed⁵ and extension of other quantum effects such as the Hong-Ou-Mandel effect to sub-attosecond sub-Angstrom optical path metrology with x-rays have been proposed.⁶ Ghost imaging with SPDC of x-rays into visible radiation has been discussed for the high-resolution imaging.⁷ Thereby, opening the possibility for future application of x-ray imaging and phase sensing applications with low radiation dose.

In my talk I will review the recent progress toward quantum x-ray imaging and discuss the potential advantages of using quantum technologies for x-ray sensing.

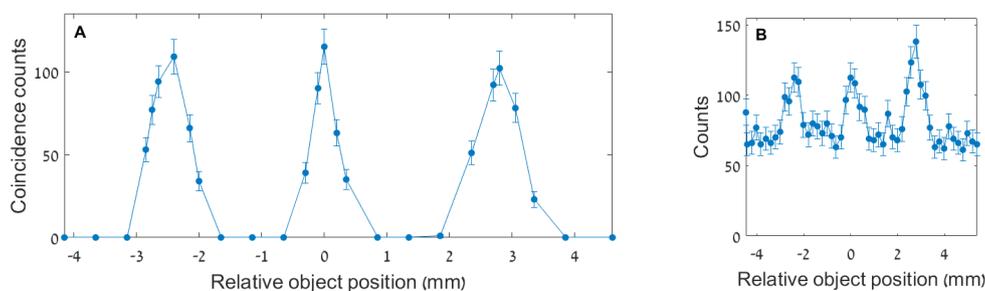


Fig. 1 Example for x-ray quantum imaging: Reconstruction of the image of the triple slit object by (A) quantum enhanced x-ray detection. (B) Classical imaging of the same object for comparison. In each of the panels the horizontal axis represents the relative position of the object and the vertical axis represents the number of events that are detected.

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† plenary lecture at 4th Joint AIC-SILS Conference, (Trieste) 12-15/09/2022

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High Pressure Phase Transitions in Molecular Crystals.

Simon Parsons.^a

In the organic solid state, high pressure to 10 GPa leads to compression of intermolecular interactions and phase transitions. Pressure is therefore a very useful means for studying polymorphism in molecular solids. We have investigated hydrogen-bonded materials (*e.g.* amino acids) as well as very simple compounds (*e.g.* pyridine), and the talk will show how experimental structures of organic solids can be interpreted using semi-empirical and *ab initio* volume and energy calculations to develop an understanding of phase stability. Volume minimisation is the dominant driving force in almost all high-pressure phase transitions, although the relief of unfavourably compressed contacts can also play a role. Analysis of volume changes are therefore critical in the interpretation of phase transitions at high pressure, and we have developed a Monte Carlo algorithm for calculation of occupied (“network”) and unoccupied (“void”) space in crystal structures.¹ The variation of the volumes of the voids and the network of intermolecular contacts with pressure sensitively reveals discontinuities associated with first and second order phase transitions, providing insight into the effect of compression. The method is shown to be especially useful for the correlation of high-pressure crystallographic and spectroscopic data, illustrated for naphthalene, where a phase transition previously detected by vibrational spectroscopy, and debated in the literature for over 80 years, has been revealed unambiguously in crystallographic data for the first time.

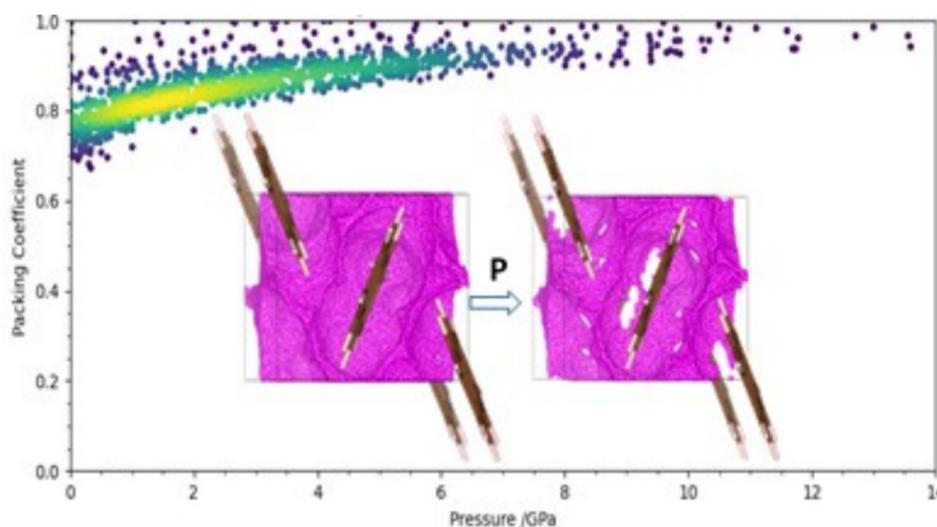


Fig. 1 Variation of packing coefficient with pressure. Inset: loss of interstitial void space in naphthalene at high pressure.

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† plenary lecture at 4th Joint AIC-SILS Conference, (Trieste) 12-15/09/2022



Nanoscience & Nanotechnology Powering the Digitization of Our World.

Heike Riel.^a

For decades Moore's law has been the driving force of semiconductor technology and miniaturization has resulted in microprocessors with billions of transistors thus enabling today's information technology. The past 20 years exemplified this trend, with nanotechnology research spearheading the extension of Moore's Law past prophecies of its demise. Heroic engineering and scaling efforts have propelled the development of successive generations of technology for the acquisition, processing, and storage of digital information reaching now the 3nm and 2nm-technology node. Reducing the power consumption and increasing the performance as well as density will remain the driving force for future innovation. Therefore, the precise control and characterization of nanoscale materials and devices will increase in importance.

Beyond scaling and digital computing completely new computing paradigms are explored and developed such as quantum computing and specialized hardware for AI including non-von Neumann architectures. Despite the continued computational advances, there are still many important and relevant problems that are intractable to classical computers but could be addressed by Quantum Computers. Quantum computing systems are built from the bottom up and are reaching today the limits of what can be classically simulated. Significant advances have been recently achieved that enabled to scale superconducting qubits to a 127-qubit processor and increase quality and speed to improve the performance of quantum computation.

In this presentation I will discuss developments in nanoscale science and technology that have transformed the digital world over the past two decades and looks into the future how today's nanotechnology discoveries are likely to impact the next 20 years. The talk will include a brief overview of our activities in the field of new computing paradigms of AI hardware technologies and quantum computing.

^a IBM Research, Zurich, Swiss

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Macromolecular Crystallography – Quo vadis?

Thomas R. Schneider.^a

Macromolecular Crystallography with X-rays (MX) had its beginnings in the 50's and 60's of the last century. Since then, the method has become ever more powerful by enormous technological progress in the production of samples, growth of crystals, production of X-rays, instrumentation for data collection, computer programs, and data bases. MX has produced the major fraction of the high-resolution structural information on biological macromolecules available to us today.

With the recent resolution revolution in cryo-electron microscopy and the latest breakthroughs in protein structure prediction, the landscape of methods supporting structural biology is changing. I will discuss this changing landscape and expose current and future opportunities in static and time-resolved macromolecular crystallography, in particular with respect to its use in the field of structural enzymology.

^a EMBL Hamburg Unit, Germany

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Crystal Engineering for storage and release of molecular active ingredients.

Paolo P. Mazzeo,^{a,*} Michele Prencipe,^a Fabio Montisci,^a Fabio Fornari,^a Federica Bianchi,^a Maria Careri,^a Paolo Pelagatti,^a Alessia Bacchi.^a

The ever-increasing attention on environmental problems and sustainability has highlighted several issues related to the use of conventional pesticides in the agricultural industry and the use of more effective food preservatives for the development of active packaging against food waste. In the search for natural antimicrobial and insecticide alternatives, essential oils and their active components have emerged as promising candidates, although they suffer from some drawbacks related to their physical properties. We exploited different crystal engineering approaches to stabilize the active components of the essential oils into the solid-state, either trapping them into flexible metal organic frameworks via crystalline sponge methods^{1,2} or designing novel cocrystals with the final aim of controlling their release into the environment.³⁻⁵ Wherever possible, and particularly for cocrystals, mechanochemical syntheses were preferred to wet reaction strategies. Providing “greener” and potentially less-expensive strategies than traditional solution methods, mechanochemistry was dubbed by the International Union for Pure and Applied Chemistry (IUPAC) as one of the 10 chemical innovations that will change our world. An excursus on different case studies will be provided with an hint into the mechanistic description of the mechanochemical synthesis via time-resolved in situ monitoring X-ray powder diffraction (TRIS-XRPD).^{5,6}

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The quest for ordered porosity in zirconium phosphonates: blood, sweat and tears (and powder X-ray diffraction).

Marco Taddei.^a

The chemistry of metal phosphonates has a long history, started in 1978 when the first examples of zirconium phosphonates were reported.¹ From the structural point of view, metal phosphonates often adopt dense layered or pillared-layered arrangements, with the organic moieties residing in the interlayer region, hardly accessible to potential guest species. In fact, most metal phosphonates are non-porous materials. When porosity is present, it is usually the result of a disordered assembly of the structure and lacks the specificity desirable for many applications, such as gas sorption/separation and catalysis²

The advent of metal-organic frameworks (MOFs), a class of porous and crystalline organic-inorganic materials, has sparked huge research interest, thanks to their high surface areas and well-defined pore size distribution. Most MOFs are based on carboxylate or N-heterocyclic linkers, and phosphonate-based MOFs only represent a rather small fraction of the thousands of MOF structures reported over the last 20 years.² Yet, the exceptional stability and insolubility of metal phosphonates are attractive features for practical employment.

This contribution is concerned with the challenging development of zirconium phosphonates possessing ordered porosity, starting from the design and synthesis of suitable polyphosphonic linkers to escape the ubiquitous dense layered motif, through the identification of the synthetic conditions to obtain sufficiently (micro)crystalline products, and ending with the ab initio determination of crystal structures from powder X-ray diffraction data.³

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Metal-Organic Frameworks as advanced porous materials for gas separation and water remediation.

Rosaria Bruno.^a

The removal of contaminants from air and aquatic systems must be a priority research topic to re-establish ecosystem balance and secure a more sustainable future. In this context metal-organic frameworks (MOFs) have revealed them as excellent platforms for the removal of harmful species from both air and water. MOFs show great potential for applications in the area of environmental sustainability because their channels can be pre- or post-synthetically fine-tuned, in terms of size, shape, and functionality, resulting in a fascinating controlled host-guest chemistry. In addition, unlike other porous materials, MOFs allow for the use of X-ray crystallography to observe what happens within their channels. Single crystal X-ray diffraction leads to structural resolution that allows to understand and rationalize the adsorption mechanisms that conduct to an efficient capture or separation of hazardous species.

In this work, MOF-based technologies are reported unveiling successful developments achieved in the adsorptive removal of inorganic or organic contaminants. A new emerging class of porous materials, which are the mixed component metal-organic frameworks known as multivariate-MOFs (MTV-MOFs), have been also studied. In these MTV-MOFs heterogeneity and complexity are installed at the service of application performances. The modular nature of MTV-MOFs opens substantial possibilities in the field of water remediation, as it makes possible to tailor their porosity with two or more different and cooperative functional groups, capable of acting synergistically to capture contaminants of very different nature at once.

In-situ studies on single crystal X-ray diffraction by synchrotron radiation revealed the nature of the interactions of gases with MOF active sites. These results were used then to prepare rubbery mixed matrix membranes (MMMs) with MOFs as filler and new MMMs for liquid or gas phase capture/separation were produced and tested.

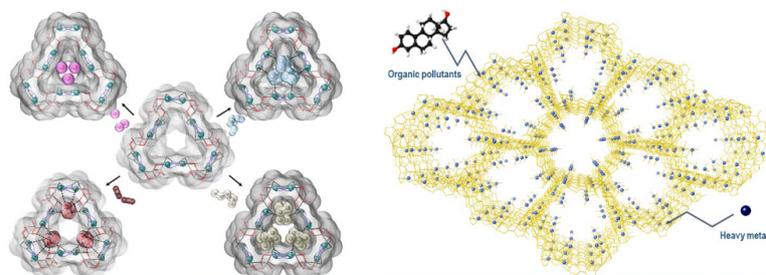


Fig. 1 Metal organic Framework for gas capture and water remediation.

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Applications of Cryo-Electron Microscopy in Structural Biology.

Alessandro Grinzato.^{a,b}

For many years, cryo-electron microscopy (Cryo-EM) was used only to determine low-resolution density maps of large proteins structure. However, thanks to recent technological developments, the resolution achievable with Cryo-EM reaches the same values as those obtained with X-Ray crystallography. Moreover, Cryo-EM can study flexible and functionally active macromolecules, which are impossible to study using X-Ray crystallography. Below are presented the structures of four different protein complexes which, due to their flexible and heterogeneous nature, could not be solved without the aid of cryo-EM

Campylobacter jejuni serine protease HtrACj is implicated in bacterial virulence, stress response, proliferation, migration, and cell fate. We took a cryo-EM approach to understand how its unique architecture is responsible for a remarkable structural and functional plasticity that allows cells to respond to misfolded or mislocalized polypeptides rapidly. The 3D reconstruction pictures HtrACj as a dodecamer built of four trimers. The contact between the trimers is loose, which explains the dodecameric assembly's flexibility and mobility. Such flexibility allows the opening of the dodecamer to expose the proteolytically active site of the protease.

Tetanus neurotoxin (TeNT) is the bacterial protein toxin that causes tetanus. Although a vaccine exists for tetanus, it remains a health concern owing to the observations of decreasing anti-TeNT antibodies-load in human serum after the vaccination, implying the need to look for other therapeutics. Therefore, we explored the possibility of neutralizing TeNT using human-derived fabs. The structure of the TeNT-Fabs complex shows the relative movement of the toxin domains and the Fab bounding. Identifying new TeNT epitopes will help in antibody design to block the insurgents of tetanus.

Photosystem II-LHCII is a protein complex of the thylakoid membrane involved in photosynthesis and is formed by one or more LHCII trimers that bind in a stable (S) or moderate (M) manner to the PSII dimeric core (C2). To study the PSII-LHCII light acclimation, we collected two different datasets of PSII-LHCII grown in low and high-light conditions, which led respectively to a map of the stacked (C2S2M2)₂, (C2S2M)₂, and (C2S2)₂ conformation, confirming that M trimers decrease with the increasing of light exposure. Furthermore, all these maps show the presence of flexible connections between the two PSII-LHCII and a different rotational offset between the two PSII-LHCII of the stacked conformation around the membrane plane's normal vector, responsible for modifying their interaction and energetic connectivity.

Potato virus X (PVX) is a flexible filamentous plant virus from the Alphaflexviridae family that infects herbaceous plants. While PVX has a detrimental impact on the global potato economy, PVX can be genetically engineered to be used as a scaffold for nanotechnology or nanomedicine applications. The 2.2 Å resolution map, obtained using helical reconstruction, provides near-atomic details of the interaction between its coat-protein and the genomic RNA, thereby opening the avenue to the design of antiviral compounds. Furthermore, the structure of the virus particle shows that the N-terminal region is flexible and exposed to the solvent, suitable for the transport and delivery of epitopes.

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Crystal-chemistry of the secondary minerals of the thallium-rich pyrite ores from the Apuan Alps (Tuscany, Italy).

Daniela Mauro.^{a,b}

The mineralogy of secondary assemblages deriving from the alteration of pyrite ore deposits from the southern sector of the Apuan Alps (Tuscany, Italy) has been investigated. Twenty-five mineral species have been identified so far; among them, eight, showing interesting crystal-chemical features, were fully characterized using X-ray diffraction, chemical analyses, and spectroscopic techniques.¹ The structural description of some previously known minerals (epsonite, wilcoxite, coquimbite, khademite, alum-(K), and voltaite) allowed to improve our knowledge about H-bond systems in sulfates and to assess their role in hosting potentially toxic elements. Moreover, this study permitted the identification of two new mineral species, giacovazzoite, $K_5Fe_3^{3+}O(SO_4)_6(H_2O)_9 \cdot H_2O$, from the Monte Arsiccio mine, and bohuslavite, $Fe_4^{3+}(PO_4)_3(SO_4)(OH)(H_2O)_{10} \cdot nH_2O$ ($5 < n < 24$), from the Buca della Vena mine.^{2,3}

Giacovazzoite (Figure 1) is the natural counterpart of the β -Maus' Salt. It is monoclinic, space group $P2_1/c$, with $a = 9.48$, $b = 18.44$, $c = 18.05$ Å, $\beta = 92.6^\circ$, $V = 3153.6$ Å³. Its crystal structure is characterized by a heteropolyhedral $[Fe_3^{3+}O(SO_4)_6(H_2O)_3]^{5-}$ cluster and by an interstitial complex with composition $[K_5(H_2O)_7]^{5+}$. The heteropolyhedral cluster is known in other minerals (metavoltine, scordariite, carlsonite) as well as in some synthetic compounds.

Bohuslavite (Figure 1) is triclinic pseudo-hexagonal, space group $P\bar{1}$, with unit-cell parameters $a = 13.38$, $b = 13.34$, $c = 10.86$ Å, $\alpha = 92.8$, $\beta = 91.0$, $\gamma = 119.9^\circ$, $V = 1675.7$ Å³. This mineral can be considered a new kind of microporous compound, with heteropolyhedral layers with composition $[Fe_4^{3+}(PO_4)_3O(OH)(H_2O)_{10}]$, decorated on both sides by SO_4 groups. Additional H_2O groups are hosted in channels running along c as well as in the interlayers.

This work stressed the complexity of sulfates, improving the knowledge of their systematics.

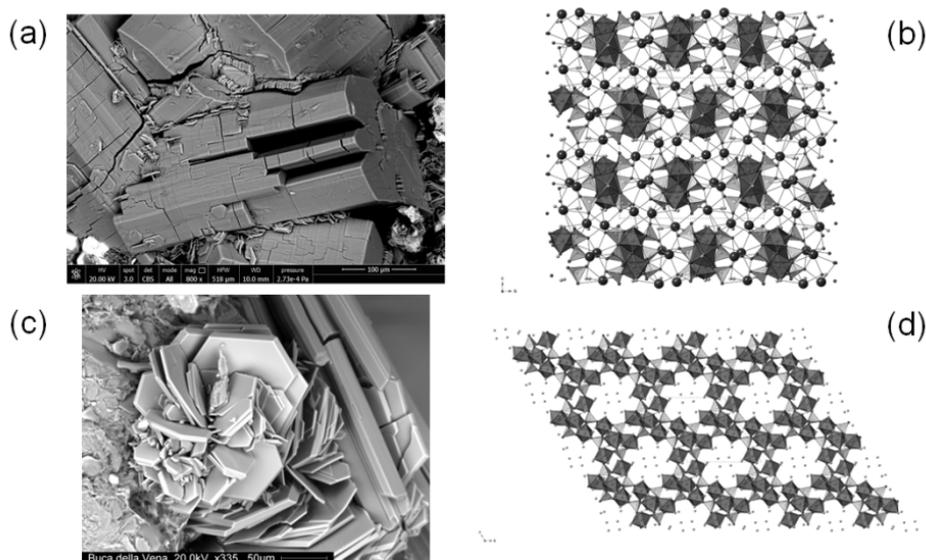


Fig. 1 Giacovazzoite (a,b) and bohuslavite (c,d): crystal morphologies and crystal structures.

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Crystal chemical study of arsenates and vanadates of the brackebuschite supergroup from Valletta mine, Canosio, Val Maira (CN).

Lisa Baratelli,^{a,*} Fernando Cámara Artigas.^a

The aim of this study is the crystal chemical description of arsenates and vanadates of the brackebuschite supergroup, belonging to Valletta mine, in Canosio municipality (CN), Piedmont, Italy, through structure and composition determination.

The Valletta mine is type locality of three new species of the brackebuschite supergroup: canosioite $Ba_2Fe^{3+}(AsO_4)_2(OH)$, grandaite $Sr_2Al(AsO_4)_2(OH)$ and lombardoite $Ba_2Mn^{3+}(AsO_4)_2(OH)$. As-rich minerals probably form by precipitation from hydrothermal fluids in an oxidizing environment. They are concentrated in quartz or calcite-rhodochrosite veins, often associated with baryte, or along the fault planes. They are present in orange-brownish and submillimetric crystalline aggregates.

Minerals of the brackebuschite supergroup have general formula $A_2M_3+(TO_4)_2(OH)$, in which:

- A = Pb, Ba, Sr, Ca;
- M = Al, Fe^{3+} , Mn^{3+} (Zn, Cu if an hexavalent is present in the T site);
- T = V, As, P (S, Si).

The crystal structure can be described as composed of infinite chains of sharing edge octahedra [M3+O6] which extends along the [010] direction. The octahedra chains are connected to each other by two tetrahedra sites [T5+O4] or (OH)- groups or a water molecule.

Minerals of the brackebuschite supergroup were characterized by:

- transmission optical microscopy, for the description of thin sections and the measurements of the optical properties;
- scanning electron microprobe (SEM) with EDS and WDS;
- single crystal X-ray diffraction;
- Raman spectroscopy.

Following the analyses it was possible to identify a new lombardoite polytype and a new mineralogical phase of the brackebuschite supergroup; it was called aldomarinoite, in honour of Aldo Marino, researcher and collector, and discoverer of the Valletta mine. Aldomarinoite has chemical formula $Sr_2Mn^{3+}(AsO_4)_2(OH)$ and has recently been approved by IMA (International Mineralogical Association).

The results of this study show that there is a relation between the Raman shifts and the chemical composition of the analysed minerals which would allow identifying different species in terms of peaks position variation in the Raman spectra. This was possible because of the understanding of structural variations obtained through structure refinements.

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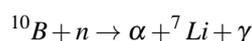
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Thermal and compressional behavior of the natural borate kurnakovite, $(MgB_3O_3(OH)_5 \cdot 5H_2O)$.

Tommaso Battiston^a

Natural borates are minerals of relevant economic interest, as they represent the main source of boron (*i.e.* since 2014, in the Critical Raw Material list for the Europe's economy). The peculiar properties of boron opened several routes of applications in a large variety of industrial sectors, including glass, ceramics, electronics, metallurgy, textile, cosmetics and chemistry.¹ Moreover, boron also finds applications as a fundamental constituent of neutron radiation-shielding materials, which are used in nuclear energy plants, as well as in facilities for scientific research or medical applications.² The high capability of borates to act as neutron-shielding materials is due to the isotope ^{10}B , representing about 20% of natural boron, having a high cross section (3840 barns) for thermal neutrons, leading to the following reactions:



In this light, kurnakovite $(MgB_3O_3(OH)_5 \cdot 5H_2O)$, $a = 8.308(7)$ $b = 10.599(2)$ $c = 6.442(3)$ $\alpha = 98.85(3)$ $\beta = 109.09(6)$ $\gamma = 105.57(4)$, space group = $P\bar{1}$ was selected as a promising natural candidate in neutron radiation-shielding materials, based on Portland or Sorel cements.³ Moreover, the absence of Na prevents the occurrence of alkali-silica reactions, which can decrease the durability and the mechanical strength of Portland cements.⁴

In this study, the thermal and compressional behaviour of kurnakovite was investigated (up to 13.65(5) GPa and in a T range 100(2) – 393(2) K) by means *in-situ* single-crystal synchrotron X-ray diffraction experiments, performed at the XRD1 beamline at Elettra (Trieste, Italy) and at P2.02 beamline at PETRA-III (Hamburg, Germany). The bulk thermal expansion coefficient was calculated based on the non-ambient T data, yielding to the value of $\alpha_v = 5.18(1) \cdot 10^{-5} K^{-1}$. The crystal structure showed the first evidence of collapse at $T > 393$ K and completely amorphized at 423 K, posing questions on the potential application as matrix-aggregates in radiation-shielding concretes.⁴ The refined bulk modulus of kurnakovite resulted to be $K_{V0} = 35(3) GPa^{-1}$. A reconstructive phase transition was observed in the range 9.23(5) – 11.11(5) GPa [4]. The high- P polymorph, kurnakovite-II, is still triclinic with a unit cell volume three times larger with respect to kurnakovite [4]. As observed in other borates (*e.g.* ulexite and colemanite,^{5,6} only a fraction of trigonal-planar B increases its coordination to tetrahedral by bonding with a H_2O -oxygen atom.⁴

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Combined Experimental and Computational Studies on Molecular Recognition among D-Glucose Molecules.

Luca Sironi,^{a,*} Silvia Rizzato,^{a,b} Leonardo Lo Prestia.^b

D-glucose ($C_6H_{12}O_6$) is a strategic chemical for the agri-food and pharmaceutical industries, with a market that is expected to grow in next years. Two anhydrous $P2_12_12_1$ crystal forms, differing in the anomeric (α/β) configuration, plus one hydrated form, are known to date.¹ Due to the presence of a high number of $-OH$ groups with almost null rotational barriers, many low-energy structures are predicted for both anomers in computational studies.² Thus, the reasons for the observed conformational monomorphism in glucose are unclear. In this work (Figure 1), an extensive crystallization screening was carried out, which led to the discovery of a new acetonitrile solvate of the β anomer that was crystallized at room temperature. Through high resolution (0.46 Å) single crystal X-ray diffraction experiments at $T = 90(1)$ K, the most common α form was characterized, demonstrating a possible anomeric disorder, never reported before. The experimental charge density study of the crystalline anomer α was obtained from the high-resolution dataset, quantifying the relative strength of hydrogen bonds in the crystal.³ Finally, Molecular Dynamics simulations of the crystal, liquid and solution states were carried out with the MicMoS⁴ and GROMACS⁵ suite of programs at different temperatures. These complemented the static, space-time average picture of standard crystallographic methods with the analysis of the equilibrium dynamics in condensed phase, allowing us to shed new light on the nature of the cohesive forces in D-glucose.

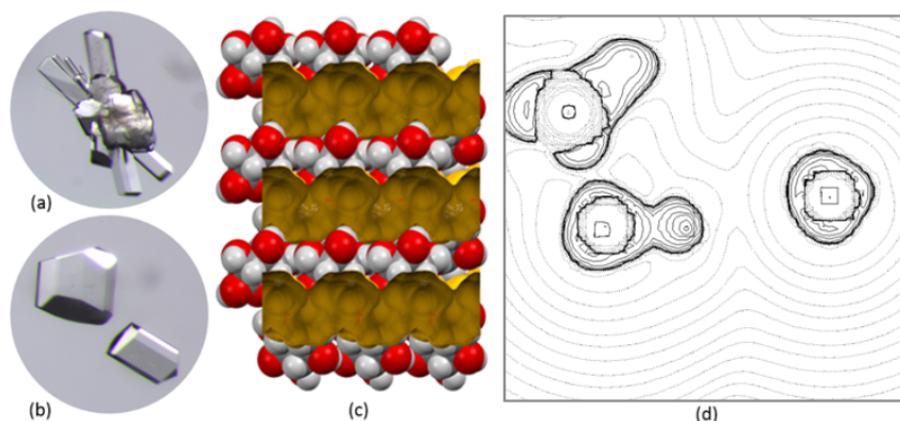


Fig. 1 (a) α D-glucose single crystals obtained from EtOH:pentane. (b) Same, from EtOH:hexane. (c) Crystal structure of the newly discovered β D-glucose CH₃CN solvate, with the space occupied by the solvent shown as brown cavities. (d) Negative charge density Laplacian ($-\nabla^2\rho$) in the region of one hydrogen bond. Solid lines highlight regions of charge concentration.

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The health seen through collagen network: from disease to regeneration.

Alberta Terzi,^{a,*} Teresa Sibillano,^a Davide Altamura,^a Liberato De Caro,^a Dritan Siliqi,^a Anna Moliterni,^a Rocco Lassandro,^a Cinzia Giannini.^a

In the last decades the extracellular matrix (ECM) has aroused growing interest thanks to its pivotal bio-physical interaction with cells, modelling the structure and function of tissues in relation to physiologic and pathologic stimuli. It is a complex fibrous network made by different components, but the main fibril-forming protein is type I collagen. Thanks to its tissue-specific morphology, its hierarchical structure and the functional domains, it supplies bio-physical support to cells attachment, tissue growth and re-modeling. From the molecular order, up to supramolecular scale, type I collagen is organized in triple helices assembled in fibrils and fibers, in accordance with a liquid crystalline arrangement at nanoscale, a quasi hexagonal packing observed in corneal tissue.¹ In order to study collagen arrangement and to deeply understand the role of its alteration at both atomic and nanoscale in pathology, we combined scanning small (SAXS) and wide angle (WAXS) X ray scattering microscopies, inspecting the structural features in the tissue over an extended area. For instance, mapping abdominal and popliteal aortic aneurysms biopsies by scanning X-ray microscopy led to the detection and co-localization of the nanometric structure of type I collagen, myofilament and elastin, organic components of the tissues. It were also identified pathological micro calcifications, whose crystalline phases have been identified.² Multiscale scanning microscopies were also employed for the structural characterization of intra- and inter-molecular features of type I collagen in diabetes minimal models for the study of the effect of glycation. In particular X-ray scattering (SAXS/WAXS) analyses conducted on decellularized bovine pericardia biotissues, soaked with different sugars (D-glucose, D-galactose, D-ribose) at increasing concentrations (0, 2.5, 5, 10, 20 and 40 mg/ml), and incubated at 37°C for 3, 14, 30 and 90 days, allowed to identify the sites of glycation and speed of glycation due to glucose/galactose and ribose.³⁻⁵ Moreover the study of type I collagen by X-ray diffraction techniques have also demonstrated to be a useful tool in regenerative medicine. Indeed, its biocompatibility, activity and degradability, made collagen attractive as biomaterial for implantable medical devices. It was extracted from different collagen-rich tissues of distinct animal species by chemical and/or enzymatic processes and each biomaterial fabrication steps could modify the physiologic sub and supramolecular features of the protein, leading to different biomaterials. WAXS and SAXS techniques have revealed how manufacturing protocols deeply affect the structural characteristic of the biomaterial itself, and therefore its function, becoming fundamental tools to screen the suitable protocols, according to the tissue to regenerate.⁶⁻⁸

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A multi-technique hierarchical X-ray phase-based approach for the characterization and quantification of the effects of novel radiotherapies.

Mariele Romano,^{a,b,*} Paola Coan.^{a,c}

Cancer is the first or second leading cause of premature deaths worldwide with an overall rapidly growing burden.¹ Standard cancer therapies include surgery, chemotherapy and radiotherapy (RT) and often a combination of the three is applied to improve the probability of tumour control. Follow up techniques, able to monitor and investigate the effects of therapies, are important for surveying the efficacy of conventionally applied treatments. They are also key for evaluating the curing capabilities and the eventual onset of acute or late adverse effects of new therapies. In this framework, this research project proposed the X-ray Phase Contrast Imaging - Computed Tomography (XPCI-CT) technique² to study and quantify the effects of novel RTs, namely Microbeam and Minibeam Radiation therapy (MRT³ and MB⁴), and to compare them to the standard Broad Beam (BB) induced effects on brain and lungs in pre-clinical settings. MRT and MB deliver an array of highly collimated micrometric spatially fractionated X-ray beamlets issued from a synchrotron radiation source. To visualize with high sensitivity the effects of the treatment along and outside their path, a high-resolution and a full-organ imaging approach is necessary. XPCI-CT was here suggested and proven as a powerful imaging technique able to determine and quantify the effects of the radiation on normal and tumour-bearing tissues.^{5,6} Moreover, it is shown as an effective technique to complement, with 3D information, the histology findings in the follow-up of the RT treatments. Using a multi-scale and multi-technique X-ray-based approach, we analysed the effects of RT delivery on healthy and glioblastoma multiforme-bearing rat brains as well as on healthy rat lungs. *Ex-vivo* XPCI-CT datasets acquired with isotropic voxel sizes down to $0.65^3 \mu\text{m}^3$ could distinguish, with high sensitivity, the idiopathic effects of MRT, MB and BB therapies. Histology, immunohistochemistry, synchrotron Small and Wide-Angle X-ray Scattering and X-ray Fluorescence experiments were also carried out to accurately interpret and complement the XPCI-CT findings as well as to obtain a detailed structural and chemical characterization of the pathological and treatment-effect features. Overall, this multi-technique approach provided the recognition and differentiation of brain and lungs anatomical details down to the cellular level and identification of microscopic cancerous cell-clusters far from the main lesion. For brains, it was possible to discriminate tissue necrosis, tumour oedema, micrometric MRT-transsections as well as high-density calcifications, identified, for the first time, as hydroxyapatite crystals with the coexistence of Fe deposits.⁵ In lungs, radiation induced fibrosis and collagen noduli are visible. The former can be visualized as thickening of alveolar walls, expansion of alveolar spaces and destruction of their normal structures, which are replaced by irregular, abnormal air spaces and large areas of scarring.⁶ The 3D nature of XPCI datasets was finally exploited to quantify the radio-induced pulmonary and brain lesions. This multi-technique approach appears to be well suited for investigating cancer development and radiotherapy effects on both the studied biological targets. In the future, other types of tumours and target organs will be considered and the method will be also tested for image-guidance during radiotherapy in preclinical research.

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Molecular Crosstalk between Fate Determination and Orientation in Epithelial Cell Divisions.

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Keywords: cell division, self-renewal, molecular motors, multivalent interactions

In multicellular organisms, oriented cell divisions are fundamental for morphogenesis and homeostasis.¹ Division orientation is orchestrated by the microtubule-based motor dynein, which sustains all mitotic spindle functions. During cell division, cortical force generators connect epithelial polarity sites with astral microtubules, allowing dynein movements to orient the mitotic spindle meanwhile astral microtubules depolymerize. Complexes of the LGN and NuMA proteins, that are fundamental components of force generators, are recruited to the cortex by G α i-subunits of heterotrimeric G-proteins. They associate with dynein/dynactin and activate the motor activity pulling on astral microtubules. I will present the structure of NuMA:LGN hetero-hexamers, and discuss their role in promoting by multivalent interactions the assembly of active cortical dynein/dynactin motors required to oriented divisions in polarized cells. I will also describe the bipartite interaction interface between NuMA and the light intermediate chain (LIC) of eukaryotic dynein, supporting the notion that NuMA acts as a dynein-activating adaptor in the mitotic processes of spindle organization and positioning. Collectively this work elucidates the basis for the structural organization of essential spindle orientation motors.

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Structural Characterization of a post-mortem Amyloid Fibril from a Cat Kidney.

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Amyloidosis are systemic diseases characterized by deposition of misfolded proteins into cross- β amyloids in multiple organs in humans and animals. During chronic inflammation, serum amyloid A protein (SAA) levels increases, which result in AA amyloidosis. There is an extreme disease prevalence in captive animals, e.g. 70% in captive cheetah and 57-73% in domestic short hair cats kept in shelters,¹ and therefore a prion-like mechanism in amyloid formation has been proposed to explain the horizontal transmission of the disease.

Herein, we present the 3.3 Å resolution cryo-EM structure of fibrils from renal tissue of a cat affected by severe AA amyloidosis in a shelter (Fig. 1).² The fibril is assembled from two twisted proto-filaments, each comprising 76 residues. Amyloid fold and fibril assembly differ from previously reported human and mouse ex vivo AA amyloid structures. Almost identical fibril sequences and similar disease prevalence in related captive cheetah suggest that the structure reported here may depict the prion agent responsible for the high AA amyloidosis prevalence in these two related felids

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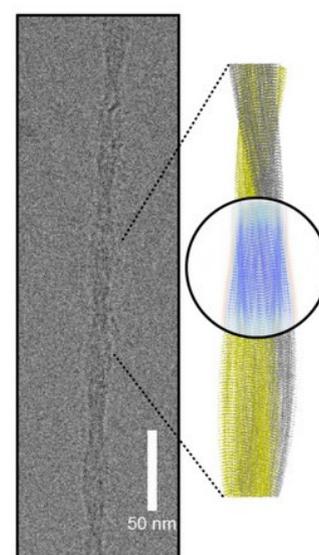


Fig. 1 Cryo-EM image of a single fibril with the reconstructed map and model

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Titolo.

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The human genetic variant BDNF (V66M) represents the first example of neurotrophin family member that has been linked to psychiatric disorders. In order to elucidate structural differences that account for the effects in cognitive function, this hproBDNF polymorph was expressed, refolded, purified and compared directly to the WT variant for the first time for differences in their 3D structures by DSF, limited proteolysis, FT-IR and SAXS measurements in solution. Our complementary studies revealed a deep impact of V66M polymorphism on hproBDNF conformations in solution. Although the mean conformation in solution appears to be more compact in the V66M variant, overall, we demonstrated a large increase in flexibility in solution upon V66M mutation. Thus, considering that plasticity in IDR is crucial for protein function, the observed alterations may be related to the functional alterations in hproBDNF binding to its receptors p75NTR, sortilin, HAP1 and SorCS2. These effects can provoke altered intracellular neuronal trafficking and/or affect proBDNF physiological functions, leading to many brain-associated diseases and conditions such as cognitive impairment and anxiety. The structural alterations highlighted in the present study may pave the way to the development of drug discovery strategies to provide greater therapeutic responses and of novel pharmacologic strategy in human populations with this common polymorphism, ultimately guiding personalized medicine for neuropsychiatric disorders.¹

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C-terminus of the histone-lysine N-methyltransferase NSD3 characterized by small-angle X-ray scattering.

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Nuclear receptor binding SET domain (NSD) proteins, a family of three histone lysine methyltransferases, are considered decisive for suppressing currently lethal cancer diseases.¹ Aside from the well characterized catalytic SET domain, NSD have multiple potential chromatin-binding motifs that are clinically relevant, such as the proline-tryptophan-tryptophan-proline (PWWP), the plant homeodomain (PHD) and the adjacent Cys-His-rich domain (C5HCH) located at the C terminus. The crystal structure of the individual domains is available and has allowed initiating drug-designing of potential inhibitors, but the analysis of the intra-domain features and the characterization of mutual domain conformations has been hindered by the intrinsic flexibility of larger constructs. We have obtained the first structural characterization of the NSD3 C-terminal region comprising PWWP2, SET and PHD4 domains, by using solution small-angle X-ray scattering (SAXS). The challenging task of modelling flexible systems has been faced by complementing SAXS data on two multiple-domain NSD3 constructs with size-exclusion chromatography and advanced computational modelling. Structural models predicted by state-of-the-art homology modelling based on machine learning have been validated in direct space, by comparison with the SAXS-derived molecular envelope, and in reciprocal space, by reproducing the experimental SAXS profile. Selected models have been refined by molecular dynamics simulations, where the *ab initio* molecular envelope calculated from SAXS data represents an additional potential. The role of S-adenosyl methionine and histone H3 peptide ARTKQTARKSTGGKAPGGC in determining the geometrical features of the interdomain conformation has been also elucidated, finding a dramatic effect of the first ligand in shrinking the SET-PHD4 region. This study shows how SAXS data can be used in synergy with advanced computational modelling technique to achieve a detailed structural characterization that sheds light on how NSD3 domains are interconnected in the C-terminus.

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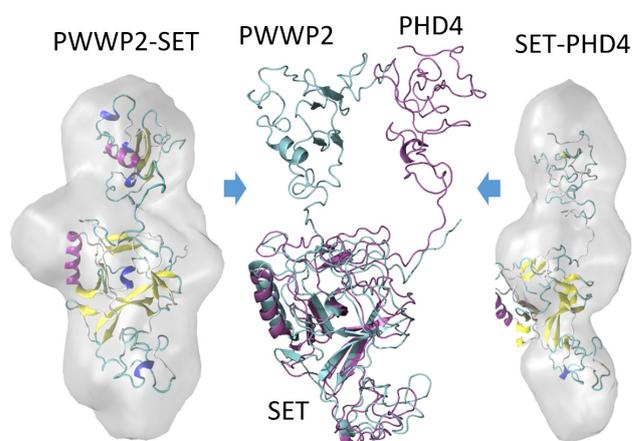


Fig. 1 Structural model of the NSD3 C-terminal region comprising PWWP2, SET and PHD4 domains (center), obtained by modelling SAXS data on the constructs PWWP2-SET and SET-PHD4.

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Directional explosion. A hybrid simulation study.

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Single particle imaging (SPI) using X-ray pulses has become increasingly attainable with the advent of high-intensity free electron lasers. SPI overcomes the need of a crystalline sample, but the extreme intensity of the X-ray pulse causes severe radiation damage to the molecule, leading to coulombic explosion.¹ Diffraction patterns are thus obtained from separate exposures of identical molecules, each in their own random orientation. Hence, a single diffraction pattern reflects a single view of the particle. The unknown orientation of the particle renders its 3D reconstruction problematic, complicated and expensive – in terms of large sample consumption and beam-time required. If additional information about the orientation of the protein in the instant of X-ray exposure could be recorded, it would be beneficial for the algorithms that find the relation between the diffraction images.

One way to control proteins orientation prior to the interaction with the X-ray pulses is to make them interact with external electric field.² Unfortunately, in some cases, the field can be destructive for the protein structures, as positively and negatively charged moieties will be pulled in opposite directions, potentially leading to unfolding and therefore to artefacts on the reconstructed images. It has also been proposed that by measuring the directions of the ejected ions from the Coulomb explosion of the protein, the orientation of the protein could be determined a posteriori.³ In our previous simulation study, it has been shown how the sulphur atoms from a lysozyme protein tend to follow similar trajectories in 150 independent simulations. Since lysozyme is a rather small protein, and most of the sulphurs are closed to the surface of the protein, it is hard to draw any conclusions of how well defined the trajectories of atoms heavier than N, C and O from a larger protein would be. To test if the findings from the simulations agrees with what happens in an experiment, one needs to design an experiment to test this aspect. In such experiment it is necessary to know how the distance from the surface of the protein affects the direction of the ion path. In the present study we are addressing this specific question. By placing a sulphur atom at different distances from a water surfaces, and measure sulphur trajectories we aim at understanding how close to the surface of a biomolecule an atom can be to give reliable orientation information. To this end, we developed a hybrid simulation approach employing a combination of non-local thermodynamic equilibrium and extensive classical molecular dynamics simulations. Based on our findings, we conclude that explosion data can aid spatial orientation in SPI experiments and could substantially improve the capabilities of the SPI technique.

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Structural insights into the hYAP-hTEAD4 protein-protein interaction: an emerging target in cancer treatment.

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The Hippo pathway is a signaling network, regulating cell growth, proliferation, and apoptosis, involved in tissue homeostasis and organ size control. A central role in this pathway is played by the Yes-Associated Protein (YAP), a DNA transcription co-activator without an intrinsic DNA binding domain. Upon activation of the Hippo pathway, a core kinase-cascade mediates the intracellular signaling, leading to phosphorylation and subsequent degradation of YAP. In its hypo-phosphorylated status, YAP moves inside the nucleus where it interacts with various DNA-binding partners. In mammalian cells, YAP primarily binds all four Transcriptional Enhancer Associate Domains (TEAD1-4).¹ TEAD transcription factors can induce gene transcription only upon interaction with YAP [2]. This protein-protein interaction (PPI) is essential for expressing Hippo pathway-downstream genes, modulating cell proliferation and apoptosis.² All human TEADs (hTEADs) have an acylation binding site, physiologically occupied by palmitic/myristic acid; even so, the functional role of acylation is yet not fully understood.³ Dysregulation of the Hippo pathway is associated with tumorigenesis, thus targeting the YAP:TEAD interaction is an emerging, attractive therapeutic strategy in the oncology field.⁴ The development of new modulators of this PPI is challenging, indeed very few YAP:TEAD4 inhibitors have been reported so far.⁵ A relevant problem is the poor structural information available on this complex, limited to the characterization of the C-terminal YAP-Binding Domain of hTEAD4 (hTEAD4-YBD) in complex with a 40mer peptide, a fragment of the TEAD-Binding Domain of human YAP (hYAP-TBD). Aiming to expand the current structural understanding on this PPI, we developed reliable protocols for co-expression and co-purification of hTEAD4-YBD in complex with hYAP-TBD (L-complex) and with two shorter fragments, including 70 and 90 residues (S and M complex, respectively). All three complexes were crystallized but, despite optimization, crystals showed only poor diffraction in preliminary X-ray crystallographic analyses. Meaningful improvements were achieved by the microseeding technique, allowing to obtain diffraction quality crystals for both the S and L complexes. The structure of the S complex was determined to 2.5 Å resolution, in the trigonal space group $P3_121$ with unit cell parameters $a,b=164.58$ Å and $c=258.61$ Å, whereas the L complex was obtained to 3.1 Å resolution. The crystal ASU consists of 12 heterodimers, showing new structural insights on hYAP:hTEAD4 PPIs. Recently, we further expanded the study of this complex to the characterization of hTEAD4-YBD in complex with full length hYAP (XL complex). We set up a production protocol and preliminary structural characterization through bioSAXS, cryo-EM and X-ray crystallography are currently ongoing. Our results expand the current knowledge on the downstream effectors of the Hippo pathway, providing novel information to design hYAP:hTEAD4 PPI modulators.

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Understanding the Structure-Properties Relationship in Nanocatalysts for CO_2 Electroreduction using Time-Resolved XAS and Advanced Data Analysis.

Janis Timoshenko,^{a,*} Beatriz Roldan Cuenya.^a

Electrochemical CO_2 reduction to valuable chemical feedstocks and fuels, powered by the energy from renewable sources, is an attractive possibility for the CO_2 minimization in the atmosphere (e.g., at industrial sites where concentrated CO_2 is available) but a suitable catalyst is needed. Currently Cu-based catalysts are the only ones that can convert CO_2 with significant yield to energy dense C_{2+} products, such as ethylene and ethanol. Nonetheless, the distribution of possible reaction products for CO_2 reduction reaction (CO_2RR) over Cu catalysts is broad, and the selectivity of the catalyst is hard to control. Atomistic details of the CO_2RR and the nature of active states also remain debated due to the coexistence and transformations under reaction conditions of multiple copper species. To address these questions, X-ray absorption fine structure spectroscopy (XAFS) has been used for decades.¹ Nonetheless, new exciting possibilities are enabled by the recent development in the instrumentation and data analysis approaches. The former allow now *operando* quick XAFS (QXAFS) studies with subsecond time resolution. Thus, the evolution of the catalyst structure and composition under realistic working conditions can be directly tracked for the first time. Moreover, QXAFS method provides also a direct insight into the catalyst dynamics under non-equilibrium reaction conditions, which have been recently proposed as an attractive way to steer the catalyst functionality by dynamically controlling the catalyst's surface composition and structure.² On the other hand, the breakthrough developments in data science provide now the possibility to employ machine learning methods for the interpretation of XAFS data, allowing quick analysis of disordered, heterogeneous structures of working electrocatalysts.³⁻⁵

Here we demonstrate the potential of QXAFS method and machine learning-based data analysis on an example of studies of Cu-based catalysts under potentiostatic and dynamic (pulsed) CO_2RR conditions. In particular, our approach allows us to explain the different selectivity trends for shape-selected Cu_2O nanocubes (NCs) exposed to pulsed CO_2RR with different pulse durations,² to understand the dynamics of NCs oxidation state under pulsed and static CO_2RR in gas-fed cell at high current densities,⁶ and to track the fast alloying/dealloying processes and their link to oxidation/reduction processes in Zn-decorated Cu_2O NCs.⁵ The compelling evidences about the nature of the catalyst active states, obtained from *operando* time-resolved XAFS coupled with advanced data analysis approaches allow us to decouple the contributions of different species coexisting in working catalysts to the CO_2RR selectivity, and provide guidelines for the further optimization of catalytic systems and reaction protocols.

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Characterization of metal-organic frameworks with synchrotron and neutron sources for catalytic applications.

Marco Ranocchiari.^a

The chemical-flexibility, tunable pore size and chemical and structural stability of MOFs can be used to design active sites at the molecular level and to produce heterogeneous catalysts, which can be characterized with atomic precision.^{1,2} In this contribution, we show how advanced characterization at synchrotron sources can be used to reveal the mechanism of formation of UiO-66 under microwave irradiation conditions. The synthesis of UiO-66 was monitored with in-situ X-ray diffraction at the material science beamline at the Swiss Light Source revealing the influence of modulators and aging in the yield and crystallite size of the material.³

In addition, we present how X-ray and neutron sources can help identify active sites in catalysis and the structure of adsorbed species. We developed a catalytic methodology that uses such metal complexes to catalyze Suzuki-Miyaura cross coupling reactions in unprecedented mild conditions, at a low temperature of 40 °C and with a mild organic base such as triethylamine and characterized the relation between active site and selectivity.⁴ The use of a MOF-immobilized catalysts results in a ten-fold reduction of the metal and ligand contamination in the reaction products. We also show how MOFs with MOF-74 and UMCM-1 topologies push Co-catalyzed hydroformylation into kinetic regimes not available under standard conditions. The micropores of MOFs increase the olefins density beyond neat conditions and partially prevent the adsorption of syngas allowing branched selectivity up to 90% using olefins with no directing groups, which is not achievable with existing Co catalysts.⁵ Neutron diffraction revealed the structure of the adsorbed alkenes.

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Operando and ex-situ PXRD Study of Ni-doped Manganese Hexacyanoferrate Cathode Material in Aqueous Zn-ion Battery System.

Mariam Maisuradze,^{a,*} Min Li,^a Mattia Gaboardi,^b Jasper Rikkert Plaisier,^b Marco Giorgetti.^a

Operando experiments are essential in the field of battery research as they avoid the typical drawbacks of ex situ experiments, such as sample transfer or relaxation reactions, that may occur after opening the electric circuit; alongside the availability of providing sample behaviour under the normal operating conditions in single test cell experiments, avoiding the uncontrolled differences between the cells.¹ Aqueous rechargeable Zinc-ion batteries (ARZIBs) are one of the most promising post lithium-ion battery candidates and Prussian blue analogues (PBAs) are widely considered as cathode materials for them, due to their large ionic channels and redox-active sites.² Our study material is manganese hexacyanoferrate (MnHCF). For the improvement of its performance Ni-doping technique is applied, mostly for the relaxation of the Jahn-Teller distortion and therefore improving the long-time stability.³

Here the experimental results of 10% Ni doped MnHCF will be highlighted in AZIB system with 3M ZnSO₄ electrolyte and Zn metal anode. PXRD studies were performed in MCX beamline in Elettra synchrotron facility. For operando experiment EL-CELL was used in reflection mode with CCD detector.

Generally, during the cycling process some structural changes or the new phase formation might occur inside the cathode material. The structural exchange of Mn with Zn in AZIB system based on XAS analysis has been reported before in pure MnHCF material.⁴ According to our operando and ex-situ PXRD measurements the same phenomena were observed for Ni-doped material. The lattice parameter has changed and the additional peaks have appeared even during the resting mode, just by electrode being exposed to the electrolyte. Changes continued to occur during the consecutive charge and discharge process. The appearance of additional peaks both in operando and ex-situ samples proves the new phase formation inside the material. During the discharge process the PXRD patterns showed only partial reversibility of the structure.⁵

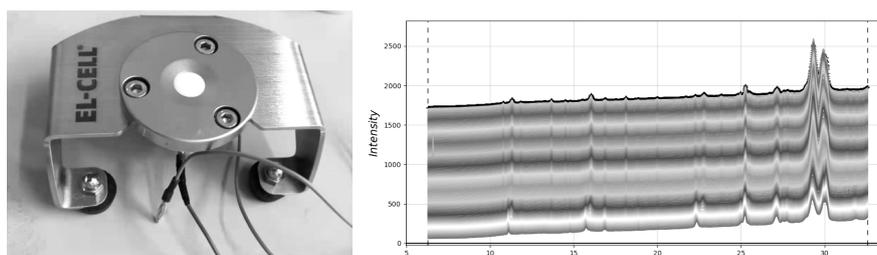


Fig. 1 El-cell (left) and operando PXRD pattern of Ni-doped MnHCF (right).

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On the mechanism of cocrystal mechanochemical reaction via low melting eutectic: a time resolved in-situ monitoring investigation.

Paolo P. Mazzeo,^{a,*} Michele Prencipe,^a Torvid Feiler,^b Matteo Masino,^a Franziska Emmerling,^b Alessia Bacchi.^a

Cocrystals, namely crystalline compounds made of different chemical entities, are typically synthesized in bulk via mechanochemistry. Whereas the macroscopic aspects of grinding are becoming clear,¹ the fundamental principles that underlie mechanochemical cocrystallisation at the microscopic level remain poorly understood.

Time-resolved in situ (TRIS) monitoring approaches have opened the door to exceptional detail regarding mechanochemical reactions.²⁻⁴ We here report a clear example of cocrystallisation between two solid cofomers that proceeds through the formation of a metastable low melting binary eutectic phase. The overall cocrystallisation process has been monitored by TRIS-XRPD with a customized ball milling setup and low-energy synchrotron beam. The reaction is complete in less than 5 seconds and the metastable formation of the amorphous-like phase is clearly spotted thanks to a fast data acquisition time of 500 ms.⁵

An insight on the details of the TRIS-XRPD data analysis for the real-time structure and microstructure investigation, generally applicable to all chemistry, will be also provided.⁴

The binary system and the low melting eutectic phase were further characterized via DSC, HSM, and VT-XRPD.

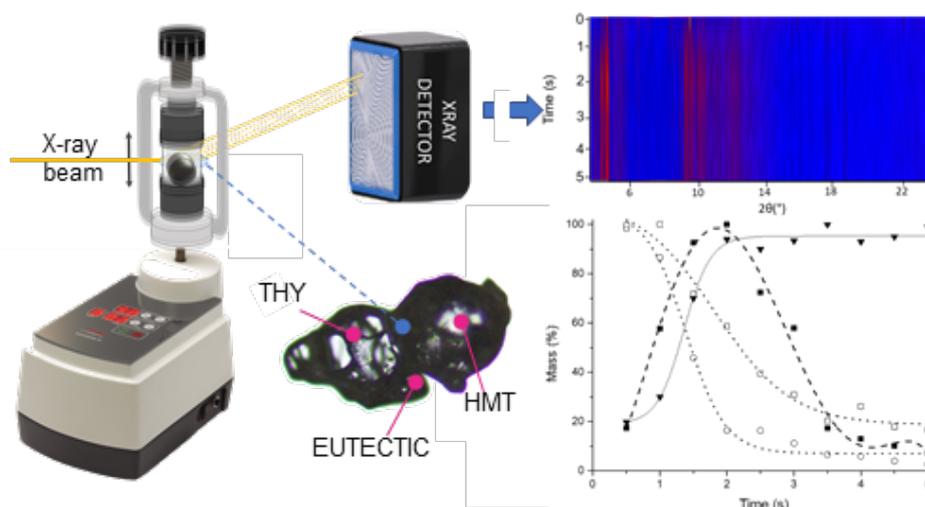


Fig. 1 Schematic representation of the TRIS-XRPD setup and the Rietveld Refinement output.

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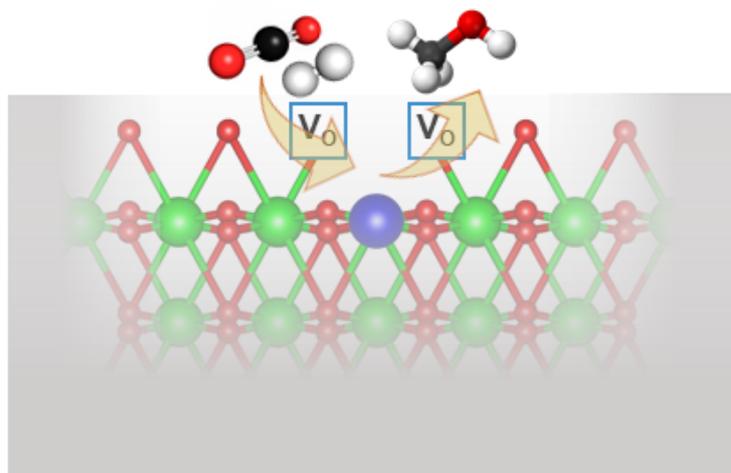
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MZrOx (M = Zn, Ga) catalysts for CO₂ hydrogenation reaction: exploiting XAS and PXRD to understand catalyst's structure, activity and stability.

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In the panorama of CO₂ hydrogenation catalysts, the COZMOS project (<https://www.aspire2050.eu/cozmos>) is investigating MZrO_{2-x} (M : Zn,Ga) as potential catalysts for CO₂-to-methanol conversion. Aliovalent elements ZrO₂ doping has been largely exploited to improve catalyst's properties through oxygen vacancies (V_o) formation. However, whilst great efforts have been done to improve catalyst performances, very little research investigated how and where the V_o active site was generated during doping. In this contribution, through Powder X-Ray Diffraction (PXRD) and X-Ray Absorption Spectroscopy (XAS) we unveil as two MZrO_{2-x} catalysts having similar catalytic properties are structurally very different. Single phase PXRD patterns are observed for both materials and, as largely accepted, they describe the catalysts as a MZrO_{2-x} solid solutions. Nevertheless, a detailed in-situ - XAS analysis at Zn/Ga/Zr K-edges unveils as: I) ZnZrOx catalyst consists of ZnO nanoclusters embedded in a ZrO₂ matrix having catalytic active site at the ZnO/VO/ZrO₂ interface and II) Ga substitutionally replaces Zr forming a xGaZr(1-x)ZrZr(2-x/2)OO solid solution where Ga tetrahedral/octahedral coordination changes under reducing conditions increasing the active sites Ga-VO-Zr concentrations. The different structural nature of the two catalysts drastically affects their reactivity and stability. Indeed, whilst any evident differences are observed for GaZrOx after reaction, ZnO/ZrO₂ reports significant variations of Zn total concentration and local environment. By in-situ PXRD and ex-situ XAS we observe as during H₂ activation ZnO cluster dimension increases favouring Zn sublimation, globally causing a drastic loss of active ZnO/ZrO₂ interface and reducing tetragonal ZrO₂ polymorph stability.



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Hg(II)-Bispidine 1D Coordination Polymers: three different topologies and their dynamic behavior in solvent adsorption and exchange processes.

Martina Lippi,^{a,*} Andrea Murelli,^b Patrizia Rossi,^a Paola Paoli,^a Massimo Cametti.^b

The wide development of Coordination Polymers (CPs) has raised large interest in solid-state and material chemistry. Build upon the combination of organic ligands and metal salts, or clusters, CPs represent functional materials for many useful applications, such as storage, adsorption, sensing and catalysis.¹ Besides the presence of an intrinsic porosity, the possibility to control the final structural arrangement can be of real advantage to develop materials with specific features suitable for specific applications. Moreover, dynamic structural properties can be considered advantageous for adsorption purpose, especially in the case of 1D CPs whose entire architecture does not always warrant for porous structures, preferably required for this intent. Indeed, there are several works revealing solvent exchange and selective adsorption ability of 1D CPs, often controlled by their intrinsic crystal flexibility.² From our recent studies a new class of ligands based on bispidine molecules has been employed for the synthesis of novel 1D Mn(II)-CPs with interesting tunable adsorption properties.^{3,4} Herein, the work describes the development of novel 1D solvated CPs made upon the self-assembly between a further bispidine ligand **L3** and $HgCl_2$ in presence of different solvents such as 1,2- and 1,3-dichlorobenzene, toluene, MeCN, EtOH and MeOH (Figure 1). The dynamic attitude of these systems in response to chemical and physical stimuli was studied by means of X-ray analysis.⁵ In particular, CPs in forms of single crystals and microcrystalline powder were produced depending on the reaction conditions (fast and slow crystallization, solid-state grinding). Five good quality single crystals were obtained showing the formation of different topologies of 1D CPs: two zig-zag, a ribbon-like and a more uncommon poly-catenane structures (Figure 1). Microcrystalline powders were synthesized, characterized by XRD and tested for solvent adsorption and exchange experiments as well as thermal treatments. Zig-zag structures showed much more stability if compared to the behavior of poly-catenane which undergoes a change of topology after chemical stimuli. Results showed different CPs response in relation to their different topologies, confirming the close connection between the structural assembly of CPs and their dynamic behavior.

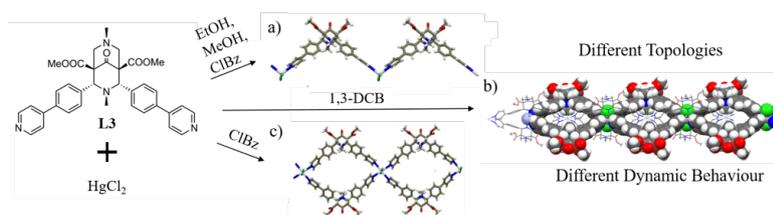


Fig. 1 Self-assembly between **L3**, $HgCl_2$ and different solvents leading to three different CPs topologies.

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Megahertz-rate Ultrafast X-ray Scattering and Holographic Imaging at the European XFEL.

Matteo Pancaldi,^{a,b}

During 2019, the novel DSSC 2D imaging detector¹ was commissioned at the Spectroscopy and Coherent Scattering (SCS) instrument of the European X-ray Free-Electron Laser (EuXFEL).² To fully exploit the high repetition rate provided at EuXFEL (up to 2.25 MHz), the DSSC detector was designed to be the fastest one-megapixel camera available worldwide, providing single-photon sensitivity in the soft X-ray regime. As a test-bed for operation at megahertz rates, time-resolved magnetic X-ray scattering and holographic imaging experiments in solid state samples were chosen as representative.³ Indeed, these two types of measurements allow to assess fundamental features of a 2D detector for X-ray science. For example, a high dynamic range is needed for recording the tiny variations in magnetic scattering induced by a laser pump, and holography requires measurements characterized by a high signal-to-noise ratio in order to provide well-defined image reconstructions. During this talk, we will present the obtained results, which were validated by measurements performed at other facilities (BESSY II, SOLEIL, MBI).

As potential future application for high-repetition rate scattering and imaging experiments at free-electron lasers, we propose the use of light beams possessing orbital angular momentum (OAM), which are rapidly becoming a way for probing condensed-matter systems, even in the X-ray regime.⁴ The wavefronts of such beams are characterized by an azimuthal angular dependence of the electric field phase, associated with an OAM topological charge $l \neq 0$.

In this framework, OAM beams allow for novel kinds of dichroism experiments, paving the way for new spectroscopic tools in the fields of orbital physics and magnetism.⁵ In particular, it has been demonstrated that, after the scattering of an OAM beam from magnetic structures featuring a non-uniform magnetization (like magnetic vortices), the far field intensity profile encodes the vortex symmetries in a way that depends on the sign and value of l , giving rise to magnetic helicoidal dichroism.⁶

On the other hand, for imaging purposes, the use of OAM beams can help in overcoming the Rayleigh criterion limit, so enhancing the theoretical resolution with respect to gaussian illumination ($l = 0$).⁷ This feature has been recently tested at the DiProI beamline of the FERMI free-electron laser⁸ by performing ptychographic experiments with a standard sample. As predicted, the ptychographic reconstructions with OAM beams showed a higher image resolution, and the retrieved illumination functions proved to be very sensitive to optical aberrations, providing the basis for new characterization and diagnostic tools.

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Ultra-fast structural dynamics in materials at extreme conditions.

Valerio Cerantola,^{a,*} Zuzana Konopkova,^a Rachel Husband,^b Karen Appel,^a Erik Brambrink,^a Johannes Kaa,^a Anand Dwivedi,^a Carsten Baehtz Sebastian Göde,^a Hauke Höppner,^{c,b} Alejandro Laso Garcia,^{c,b} Jona Mainberger,^b Mikako Makita,^a Motoaki Nakatsutsumi,^a Alexander Pelka,^{c,b} Thomas R. Preston,^a Jan-Patrick Schwinkendorf,^a Cornelius Strohm,^b Toma Toncian,^{c,b} Lennart Wollenweber,^a Sakura Pascarelli,^a Ulf Zastrau.^a

Planetary science is witnessing a revolution with the discovery of hundreds of extra-solar planets orbiting nearby stars¹ Characterising such astrophysical objects requires the knowledge of physical properties of their main constituents at multi-Mbar pressures and few-eV temperatures (1 eV = 10605 K). The precondition is the establishment of phase diagrams of these materials, in order to identify and characterize structural changes, phase transitions, metallization, and dissociation processes. Physical and chemical changes induced by the application of high pressures and temperatures can occur in a wide range of different time scales, thus capturing their nature and underlying mechanisms requires the use of adapted tools, capable to catch happening phenomena in static and dynamic regimes. Also, it was shown that materials structural response to pressure increase might be different under static or dynamic compression loads i.e.²

Since the opening in 2019, HED Instrument at the European XFEL has persistently upgraded and today offers standard platforms for static and dynamic compression studies, at timescales spreading between minutes and seconds to micro- or nanoseconds. X-ray diffraction and emission spectroscopy are routinely coupled to diamond anvil cells (static and dynamic, dDAC) in a different range of sample environments. Relevant studies comprehend the synthesis of metastable iron hydrides, phase diagram of water, dynamic compression of high-Z compressible gases like Krypton, the spin states and electronic transitions in iron sulfates, carbonates, and melts and many more. Shock-compression will be also available by the end of 2022 and will be coupled initially to x-ray diffraction and large area detectors. The presentation will focus on our most recent and interesting results. An outlook towards the future will elucidate ongoing projects and expected outcome.

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First high energy and temporal resolution pump-probe RIXS at the EuXFEL.

L. Adriano,^a A. Alic,^b D.R. Baykusheva,^m R. Carley,^a G.S. Chiuzaian,^b M.P.M. Dean,^c O. Duros,^b A. Foelisch,^d M. Foerst,^e B.K. Freelon,^f N. Gerasimova,^a G. Ghiringhelli,^g X. Jiang,ⁱ D. Jost,ⁱ M. Kusch,^d T. Laarman,^j V. Lebedev,^k W.S. Lee,ⁱ C.Y. Liu,^d L. Martinelli,^{g,*} L. Mercadier,^a G. Merzoni,^{a,g} M. Minola,^l M. Mitrano,^m S. Molodtsov,^a C.S. Pathiraja,^f S. Parchenko,^a J.N. Ranhili Pelige,^f Y. Peng,^h Q. Qiu,^h T. Schmitt,ⁿ J. Sears,^c A. Scherz,^a S. Sreenkatan Nair Lalithambika,^j S. Techert,^j M. Teichmann,^a S.F.R. TenHuisen,^m B. van Kuiken,^a Z. Yin,^a J. Schlappa.^a

High-resolution Resonant Inelastic X-ray scattering (RIXS) and ultrafast pump-probe techniques using optical or THz radiation have nowadays reached a prominent role for the investigation of strongly correlated materials.

At the intersection of the two worlds, the development of a high energy and high temporal resolution RIXS instrument at the SCS beamline of the European XFEL is a cornerstone in the field of x-ray techniques. After the successful commissioning of the User Consortium Heisenberg RIXS (hRIXS) spectrometer in May 2021, we have recently carried out first pump-probe (pp) RIXS experiments. As a test case, we selected the prototypical cuprate parent compound La_2CuO_4 (LCO) and NiO, pumped with an optical laser above the Mott gap. The pp-RIXS measurements at the Cu L3 and Ni L3 edges were performed with a 113 kHz pulse repetition rate, reaching a temporal resolution of ≈ 100 fs and an energy resolution of ≈ 93 meV and ≈ 80 meV for the Cu and Ni L_3 edges, respectively. Exploiting full control over laser power and delay between optical and x-ray pulses, we acquired spectra changing the pump delay between 0.1 ps and 5 ps, and the laser fluence on the sample from $1mJ/cm^2$ up to $35mJ/cm^2$.

We observed strong changes in the orbital and charge-transfer excitations driven by the optical pumping in both samples, clearly scaling with the laser fluence and with a sub-ps dynamics. The results of this first high-resolution ppRIXS commissioning represent a major success and opens the route to ppRIXS studies on strongly correlated materials at the European XFEL.

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Microsecond dynamics in complex liquids with MHz XPCS.

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Complex liquids are a broad family of materials that cover key roles in several aspects of everyday life, from biological processes that can take place only in such environments to industrial applications that sees complex liquids either as a final product or as a fundamental manufacturing step. From a physicist perspective most of the more interesting phenomena take place at inter-particle distances, which for proteins and nanoparticles correspond to few nanometers, accessible only via X-ray based techniques. Moreover, such processes are often connected to diffusion mechanisms, which for water-based systems implies timescales of the order of few microseconds. These time and spatial constraints pose a real challenge to current 3rd generation synchrotron sources, limiting experiments only to a handful of complex experiments on prototypical systems.¹

The MHz repetition rate of the European XFEL matches perfectly with these timescales making it an ideal choice for this kind of experiments. Here we report the results from MHz X-ray Photon Correlation Spectroscopy (XPCS) experiments performed at the instruments MID and SPB/SFX,^{2,3} showing how it is possible to execute measurements both on prototypical charge-stabilized silica in water and on radiation-sensitive core (silica) – shell (PNIPAm) nanoparticles. Moreover, we can show that tuning the pulse intensity and repetition rate it is possible to control the radiation-induced heating of the system without necessarily damaging it, which, combined with the capabilities of the XPCS techniques, opens the way to the study of out of equilibrium dynamics.

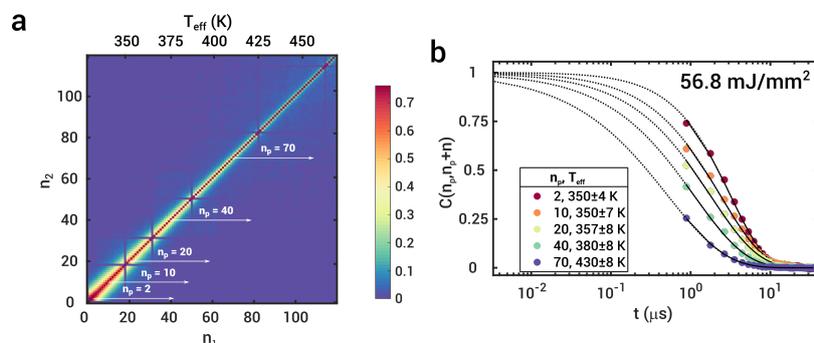


Fig. 1 Example of an out of equilibrium measurement on a colloidal system. The two times correlation matrix (a) shows a clear speeding up of the dynamics with increasing number of pulses. This acceleration can be quantified selecting portions of the matrix, highlighted by the white arrows in figure (a), and plotted in figure (b). Figure adapted from².

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Crystal Chemistry of Natural REE-Phosphates and Arsenates and their (T,P)-Behavior.

Paolo Lotti.^a

Rare Earth Elements (REE, i.e. lanthanides, Y and Sc) are nowadays fundamental components in many technological applications. For their strategic importance and supply risk, REE have been included in the EU list of the so-called “critical raw materials”.¹ This has recently fostered the study of REE minerals, aiming at a deeper understanding of their crystal chemistry, formation and accumulation processes. This contribution focusses on the crystal-chemical features and (T,P)-behavior of REE phosphates and arsenates from Mt. Cervandone (Western Alps, Italy), where REE minerals are common constituents of Alpine quartz-bearing hydrothermal veins, cross-cutting pegmatitic dykes intruded in leucocratic gneisses of the metamorphic basement.

The mineral species under study are the isostructural monazite-(Ce) (ideally $CePO_4$) and gasparite-(Ce) ($CeAsO_4$), Sp. Gr. $P2_1/n$, hosting the larger Light REE, and the isostructural xenotime-(Y) (YPO_4) and chernovite-(Y) ($YAsO_4$), Sp. Gr. $I4_1/amd$, hosting the larger Heavy REE. They define two solid solutions characterized by the monoclinic monazite-type and the tetragonal zircon-type structures, respectively. Chemical data obtained by WDS electron microprobe analysis show that an almost complete solid solution occurs along the xenotime-cherovite tetragonal series, with Y being the dominant cation in the 8-coordinated A site followed by the HREE, whereas a strong depletion in LREE is observed. The latter populate the 9-coordinated A site in the monoclinic structure of monazite and gasparite, for which an apparent miscibility gap is observed among the end members, differently to what observed in samples from other localities.² Single-crystal XRD analyses on samples with different crystal chemistry pointed out the prevailing control exerted by the composition of the tetrahedra (P vs. As) on the size and distortion of the structural units and, in turn, of the unit cell volume, independently from the REE composition of the A site. *In situ* single-crystal and powder synchrotron XRD experiments have been performed at high-T (Elettra, Trieste), high-P (ESRF, Grenoble; PETRA-III, Hamburg) and combined HPHT (PETRA). The interplay among the crystal chemical and structural features control the bulk response of the investigated REE₂O₄ phases to external thermal and compressional stimuli. The results showed that the monazite-type structure is more compressible and expandable than the tetragonal zircon-type, whereas, among the zircon-type minerals, chernovite is more compressible than xenotime, but at high temperature xenotime shows the higher thermal expansion coefficient. *In situ* HPHT XRD experiments have been performed for the first time on monazite and chernovite: monazite was found to be stable within the investigated range ($T < 500$ °C and $P < 20$ GPa), whereas chernovite, which at ambient-T undergoes a phase transition to a scheelite-type polymorph at $P > 8-12$ GPa, at $250 \leq T$ (°C) ≤ 500 preserves the zircon-type tetragonal structure at $P < 20$ GPa, even though with signs of structural destabilization above 12-15 GPa. A comparison with the thermo-elastic parameters reported in the literature for synthetic end members (see e.g.^{2,3}) suggests that further studies on complex multi-component natural solid solutions are needed for a thorough comprehension of the structure-related properties in these minerals.

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Elastic vs. Visco-plastic Rheology of Stressed Host-Inclusion Mineral Systems under non-Ambient Conditions: Insights from in situ Raman Spectroscopy.

Nicola Campomenosi,^{a,*} Ross J. Angel,^b Matteo Alvaro,^c Boriانا Mihailova.^a

Mineral inclusions at ambient conditions often show residual pressures (P_{inc}) significantly different from the external one. This is the result of the contrast in the thermo-elastic properties between the inclusion and its surrounding host, which can be used to back calculate the pressure (P) and temperature (T) conditions of inclusion entrapment during metamorphic processes. This is the underlying concept of elastic thermobarometry, a method exclusively relying on the elastic behaviour of the system.¹

We have studied zircon-in-garnet (ZiG) systems by in-situ Raman spectroscopy at high temperature and ambient pressure to explore the elastic and non-elastic rheology of the system when the inclusion passes from the compression to tensile stress with respect to a free crystal at the same external conditions.

Upon heating non-elastic relaxation takes place immediately after the zircon inclusion experiences a given tensile residual stress with respect to a free crystal at the same external conditions. However, the inclusion develops a new compressive elastic stress on subsequent cooling without relaxation within the same T range it occurred upon heating. Consequently, P_{inc} at room T is significantly different from the original one. We conclude that ZiG resetting within the time scale of laboratory experiments occurs because, under tensile stress conditions, the resistance to plastic (rate-independent) deformation decreases significantly with respect to compression.

An important geological implication is that elastic thermobarometry using ZiG systems is only reliable when applied to low-P high-T rocks where the cooling path after inclusion entrapment passes quickly into the compression domain of the inclusion.² On the other hand, high-pressure rocks exhumed along quasi-isothermal paths take zircon inclusions into the tensile domain where they are reset until significant cooling starts at low pressures. ZiG systems in UHP rocks therefore often indicate pressures on clockwise exhumation paths instead of the conditions of original entrapment.³

Finally, we emphasize how these results open the avenue for new and promising experimental approaches to study host-inclusion rheology beyond elasticity.

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***Ab initio* thermodynamics of MgSiO₃ protoenstatite at high temperatures conditions.**

Mattia La Fortezza,^{a,*} Francesca Menescardi,^a Donato Belmonte.^{a,b}

Protoenstatite (PEn) is one of the high temperature forms of $MgSiO_3$ pyroxenes, having stability range from 1200 to 1600 K at ambient pressure. Its importance has been recognized by many authors, in fact PEn is regarded as a precursor phase of low-clinoenstatite (LP-CEn)/orthoenstatite (OEn) intergrowths in some cometary samples¹ and in calcium-aluminum-rich inclusions (CAIs) from CV3 chondrites.² The presence of a high temperature PEn precursor in planetary materials implies that its formation must have occurred close to solar nebula conditions by equilibrium condensation via a reaction between forsterite and gaseous SiO₃³ or, alternatively, as a result of reheating process after primary condensation.² Despite its role as a precursor mineral phase in the solar system, very little is known about the thermodynamics and phase relations of PEn with other $MgSiO_3$ polymorphs. This is due for the most part to its unquenchable nature, meaning that even if PEn can be synthesized at high temperature conditions, it doesn't preserve as a metastable phase at ambient conditions since it very rapidly reverts either to OEn or LP-CEn.⁴ The impossibility to perform measurements on samples of PEn prevents to obtain information on its thermodynamic properties, which are in turn fundamental for the investigation of phase equilibria. In that sense, *ab initio* calculations based on quantum-mechanical theory are one of the most reliable methods available to obtain information on thermodynamics and phase relations of minerals at planetary conditions. We present a DFT based *ab initio* B3LYP computational study on $MgSiO_3$ protoenstatite thermodynamics. All the relevant thermophysical and thermodynamic properties of PEn (e.g. heat capacity, vibrational entropy, thermal expansion, EoS) have been calculated in the framework of the quasi-harmonic approximation (QHA) by a full phonon dispersion calculation. This allowed to obtain original insights into protoenstatite thermodynamics and enabled to retrieve a complete set of physically consistent thermodynamic properties, that are in excellent agreement with the very few experimental data currently available.

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High Pressure Single-crystal Synchrotron XRD diffraction of natural pyrochlores.

Sabrina Nazzareni,^{a,*} Marco Merlini,^b Sula Milani,^b Paolo Lotti,^b Joseph Boby.^c

Accessory minerals are able to incorporate trace-elements whose content is affected by factors that include lattice strain, melt polymerization and the water content of the melt. Most of High Field Strength Elements (HFSE) including rare earth elements (REE), yttrium, niobium, and tantalum are used in a vast array of devices such as lasers, electronic screens, permanent magnets, battery alloys, and ceramics. The worldwide demand of HFSE supply raised constantly in recent time. In this framework, understanding the physical and chemical properties of REE- and REE-bearing minerals becomes critically important as, based on the available data, they are still far to be fully understood.

In particular, in order to understand the structural factors governing REE incorporation in host lattices and REE partition coefficients, is crucial to investigate the structural role of REE in crystalline structures of accessory REE-minerals.

In order to increase the available data on the physical and chemical properties of REE-minerals we studied the HP structural variation of natural pyrochlore by performing XRD data collections at increasing pressures in hydrostatic mode up to around 10 GPa at the XPRESS beamline (Elettra).

Pyrochlore-group minerals are among the most common HFSE-bearing minerals, they have a cubic structure (sp.gr. F-3d) characterised by a [8]-fold and a [6]-fold cations sites where HFSE can enter by a complex substitutions scheme. Na, Ca, Ba, Y, Ce (and other REE) may be hosted in the A site, whereas the B site may host Ta, Nb, Ti. The X and Y sites can host OH, F, H–2O and vacancies.

We selected natural Na-pyrochlore from the Agua de Pau syenites (Azores islands, Portugal) particularly rich in Ba. The pyrochlore crystal was tested for crystallinity by single-crystal in-house XRD at the Dept of Physics and Geology (Perugia University) before the HP experiment. The selected crystal is cubic, sp. gr. F-3d, with lattice parameter $a = 10.3568(3) \text{ \AA}$ and a volume of $1110.91(6) \text{ \AA}^3$.

For the HP experiment we used a DAC assemblage prepared with a stainless steel gasket indented to $81 \mu\text{m}$ thick with a hole of $150 \mu\text{m}$, and $600 \mu\text{m}$ culets diamonds. A mix of methanol:ethanol 4:1 was used as pressure transmitting medium. As pressure calibrant a ruby chip was loaded in the DAC. Pressure was measured before and after each data collection. Data collections were carried out by $\pm 35^\circ$ ω -rotation scan, angular step 1° and 5 sec scan time. We collected diffraction data at 16 pressure points up to ca. 9 GPa. Each collection data were processed by the CrysAlis software (Rigaku) to obtain the cell parameters and to extract the intensity for the refinements.

Pyrochlore crystal remained crystalline up to 9 GPa. A discontinuity in the lattice parameters and volume P -trends between 6 and 7 GPa suggests a phase transition.

We will present the bulk elastic parameters and structure modification up to the phase transition.

How the entering of REE correlates with physical properties like bulk modulus could help to better understand the pyrochlore cation partitioning at high pressure.

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The Cu-Fe-Ni-Co Sulphide Ore Deposits of the Monte Ramazzo-Lagoscuoro Mines..

Sirio Consani,^{a,*} Donato Belmonte,^b Roberto Cabella,^b Cristina Carbone.^b

The Cu-Fe-Ni-Co sulphide ore deposits hosted in ophiolitic rocks of the Sestri-Voltaggio Zone (Genova, North-West Italy) have a great interest due to the several new minerals discovered here and for the processes which are recorded from such mineralisations. Sulphides in the Monte Ramazzo-Lagoscuoro mines occur in stockwork-vein and seafloor stratiform orebodies associated with serpentinised mantle peridotites and serpentinite breccias.¹ The primary mineralisation records several stages of evolution due to geological processes happened both before and after orogenesis. Fluid-rock interaction, hydrothermal mobilisation, and multi-stage alteration processes led to sulphide reconcentration and recrystallisation along tectonic structures. Moreover, metal reworking and formation of secondary phases, such as (Ni,Co)-bearing oxy-hydroxydes, carbonates, and silicates took place. The mineral assemblage occurring in the Monte Ramazzo-Lagoscuoro ore deposit is quite different from other hydrothermal sulphide mineralisation described so far in ophiolites from the Eastern Liguria, where (Ni,Co)-enrichment occurs mostly in pyrite and/or accessory minerals like millerite, siegenite, and pentlandite.²⁻⁴ The aim of the present work was to fully understand and unravel the several stages of evolution recorded by the sulphide mineralisation. In order to achieve this goal, we applied a multi-analytical approach (Optical Microscope, Scanning Electron Microscope, and Powder X-ray Diffraction). Our observations allowed us to understand that the primary sulphide ore deposits were composed of pentlandite and first generation pyrrhotite. During the phase of cooling, first generation hexagonal pyrrhotite evolved in a monoclinic pyrrhotite, a more stable phase at this T condition.⁵ Ni- and Co-rich pentlandite transformed to violarite ($NiFe_2S_4$) and second generation pyrrhotite. Another alteration stage of the sulphide ore led to the formation of first generation magnetite and valleriite ($2[(Fe,Cu)S]_{1.53}[(Mg,Al)(OH)_2]$). Finally, during the orogenesis the Sestri-Voltaggio Zone underwent pumpellyite-actinolite facies metamorphism.⁶ This peculiar moment led to the formation of second generation magnetite and andraditic garnet, probably related to hydrothermal fluid circulation.

Further data are needed in order to unravel the fate of Co and Ni during the different evolution stages. The relationships between the Cu-Fe-Ni-Co primary mineralisation and secondary phases would shed a light on the effect of hydrothermal fluids in Ni vs. Co selective mobilisation and enrichment.

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Molecular dynamics strategies to determine the melting curve of CaO.

Francesca Menescardi,^{a,*} Davide Ceresoli,^b Donato Belmonte.^a

The thermodynamic properties of multicomponent liquids at high pressure and temperature (HP-HT) are of paramount importance to elucidate the melting and crystallization phase relations in geological systems. High-pressure melting experiments suffer from uncertainties of hundreds of K and rarely predict the ultimate nature of melting.¹ *Ab initio* molecular dynamics (AIMD) gave useful insights on the structure-energy properties of solid and liquid phases up to very HP-HT conditions, but the calculated melting temperature (T_m) depends critically on the simulation protocol and the computational cost increases proportionally with the number of atoms to process.

In this work we focus on the melting curve of CaO, not only because it is a key phase in material and geological sciences, but also because the thermodynamic properties of the liquid phase are still controversial due to the very high melting point of the crystal.^{1,2} The simplicity of its phase diagram makes it a good candidate for AIMD simulations. However, AIMD simulations are expensive, while classic MD with empirical potentials allows to employ different strategies at a reasonably low computational cost.

We simulate the melting process of CaO with classic molecular dynamics, by the means of the LAMMPS code.³ We tested three different methods, which gave insights both on the melting temperature of the crystal and on the enthalpy of fusion (ΔH_f).

The two-phase solid-liquid coexistence method consists of running a solid-liquid interface at constant enthalpy.^{4,5} The melting temperature is determined as the average equilibrium temperature. The void-nucleated method exploits holes in the crystal structure to initiate the melting process, thus decreasing the unrealistic high melting point resulting from homogeneous heating simulations by introducing a defect.⁶ Finally, to calculate the enthalpy of fusion, the temperature of the crystal is increased up until the solid melts, and then the temperature is lowered again until the liquid phase recrystallizes. The difference in energy between the liquid and the solid curves at the melting point represents the enthalpy of fusion, ΔH_f .⁶

The values of T_m and ΔH_f obtained with these methods by the means of classic MD on CaO are found to be consistent with experimental data available in literature.^{7,8}

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Combining experimental and statistical tools for a comprehensive approach to cultural heritage.

Ilaria Carlomagno.^a

X-rays, thanks to the elemental selectivity coupled with the non-destructiveness, are well known for the investigation of structural and chemical properties of historical artefacts. Synchrotron radiation sources provide high-intensity X-ray beams, with the additional benefit of energy tunability, which is crucial to fully exploit the elemental sensitivity of X-rays. This talk presents several methodological case studies on samples relevant for cultural heritage. In these studies, X-rays techniques such as X-Ray Fluorescence (XRF) and X-ray Absorption Near Edge Spectroscopy (XANES) were employed not only for a chemical analysis of the artefacts but also to assess the nature of the surface contaminants.

XRF data is commonly used to evaluate the surface distribution of the elements and/or to provide quantitative analysis of the chemical content of a given specimen. Lately, a preliminary data treatment using a t-SNE algorithm has been proposed to compare the pixels in each XRF map on the basis of their spectral similarities. Upon this comparison, the pixels being the most representative of the clean specimen can be discriminated from the ones being most affected by the contamination of successive deposits due to the burial periods. This preliminary selection, operated before the quantitative analysis, ensures the minimisation of the contaminants contribution, and the identification of different phases, enhancing the accuracy of the results.

Quantitative analyses carried out after this preliminary treatment can highlight small fluctuations in the samples composition and assess the presence of trace elements. Such details can be used as proxies to grasp further information of historical relevance (e.g. fineness of coins as a function of the time of coinage, for devaluation dynamics; different composition of inks to assess the artistic knowledge in ancient times).

The areas corresponding to the pixels discarded for the quantification of the clean specimen composition, can be used to investigate the nature of the debris accumulated on the surface of the samples. In artefacts found underground, soil is likely to accumulate in the hollow areas. As the relative abundance of Fe oxides in soil depends on environmental conditions, the fraction of Fe oxides can then be used as an indicator for the provenance of the accumulated soil. From XANES spectra collected in the hollow regions, oxides can be easily identified and quantified, yielding information on the fate of the artefacts over the centuries.

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Synchrotron *in situ* Experimentation, Big data, and New Tools for Fast Data Processing and Analysis.

Dmitry Chernyshov.^a

Synchrotron *in-situ* or *operando* experiments assume large volumes of experimental information to be collected, visualised, processed and analysed; those volumes increase with advent of new detectors and upgrade of the synchrotron sources. In many cases the data have to be treated during operando experiment to tune physical-chemical processes of interest and optimize the information outcome. Fast and efficient algorithms for automated processing and analysis of big scattering data are discussed and illustrated with powder and single crystal diffraction data collected at BM01 station of Swiss-Norwegian Beam Lines at the European Synchrotron Radiation Facility.

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Relativistic effects in EXAFS: overview and application to gold.

Nodoka Hara,^{a,*} Georghii Tchoudinov,^a Calogero R. Natoli,^b Adriano Filipponi,^c Andrea Di Cicco.^a

Current XAFS (X-ray Absorption Fine Structure) data-analysis is based on accurate multiple-scattering (MS) calculations, usually carried out solving the non-relativistic Schrödinger equation for complex effective optical muffin-tin potentials describing the scattering of the atoms. The introduction of relativistic effects in extended XAFS (EXAFS) multiple-scattering calculations has been described in several previous papers¹⁻⁴ and shown to be important for heavy atoms. However, few examples of applications and detailed studies of relativistic effects were given so far. In this work, we have performed a systematic investigation of relativistic corrections in systems of increasing atomic number, using a reliable simulation scheme based on the incorporation of a pseudo-Schrödinger equation^{4,5} effectively replacing the Dirac relativistic form and incorporated in the GnXAS package for data-analysis.^{6,7} Calculations have been put to a test in 12 different pure-element condensed-state systems, with the atomic number ranging from $Z = 10$ for crystalline Ne to $Z = 90$ for crystalline Th. The importance of accounting for relativistic effects has been highlighted for elements with $Z > 60$, as ones for which relativistic corrections for amplitudes of calculated XAFS MS signals exceed 10%. The impact of relativistic effects for calculated higher-order XAFS signal has been also evaluated for L_3 and K edges, showing a slight increase of relativistic corrections for the L_3 spectra. The present accuracy of XAFS simulations have been studied comparing the results obtained for structural refinements of the L_3 edge of crystalline Au in a wide temperature range from 80 K to the melting point.

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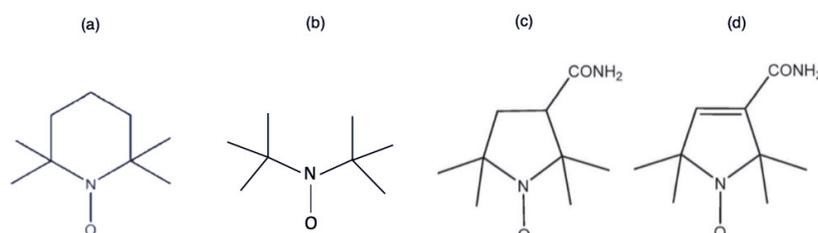


Spectroscopic investigations of nitroxide persistent organic radicals. Future perspectives in view of Elettra 2.0: the MOST beamline.

Roberta Totani,^{a,*} Ivan Ljubic,^b Sascha Mehl,^c Matteo Jugovac,^c Cesare Grazioli,^d Federico Galdenzi,^e Monica de Simone,^e Polina Sheverdyayeva,^a Paolo Moras,^a Tsud Nataliya,^f Marcello Coreno.^a

Nitroxide free radicals (NRs), such as (2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO, Fig.1a), are organic radicals stabilized by the delocalization of their unpaired electron between N and O atoms as well as by screening of the paramagnetic center by bulky substituents¹ They are employed in catalysis² and, in chemical synthesis, as initiators in radical-chain polymerization and redox reactions.³ Moreover, the magnetic moment of their unpaired electrons makes them suitable for quantum computing, spintronics and molecular magnetism.⁴

We will show the synchrotron radiation investigations performed on TEMPO and three of its analogues, i.e., Di-tert-butyl nitroxide (DTBN), nit8 and nit9 (Fig.1) in gas phase and as thin films, with the support of Density Functional Theory (DFT) calculations. In gas phase,⁵ we exploited X-ray Absorption Spectroscopy (XAS) and Resonant Photoemission Spectroscopy (ResPES), to determine N and O atomic contributions to the resonant valence band structures. This elucidated the role of the Single Occupied Molecular Orbital in the photoexcited molecules. Afterwards, we grew molecular films of TEMPO and nit9 on Au(111) and Cu(111) in ultra-high vacuum (UHV) and we performed X-ray Photoemission Spectroscopy (XPS) and XAS. To the best of our knowledge, this was the first time NRs molecular films were achieved under well-controlled UHV conditions. In the films the molecular properties are preserved on Au(111) and consistently modified on Cu(111). Moreover, while the amide functional group is not influencing the behavior of the isolated photoexcited molecules in gas phase, it plays a fundamental role in the molecular films. Indeed, its presence can prevent NRs undergoing a complete decomposition of the nitroxide paramagnetic center upon adsorption on the more reactive Cu surface.



The obtained results mark a step forward towards the full comprehension not only of through-bond effects in the isolated molecules but also of the through-space effects in the adsorbate systems and are an important proof of principle in view of the realization of organic radical-based devices.

In the end, we would like to spend few words about the conceptual design of MOST (Molecular and Optical Science Technology), the new beamline of Elettra 2.0, replacing the existing GasPhase and Circular Polarization (CiPo) beamlines. MOST innovative optical layout will employ state-of-the-art technologies, to allow a full exploitation of the

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improved performances of Elettra 2.0. The higher flux of the new source will permit the spectroscopic characterization of a large variety of highly reactive gaseous species, up to now hampered by the low density of the target. Together with the implementation of a more performing electron analyzer, it will help, for example, the realization of ResPES experiments on the most common C, N and O K-edges, affected by a poor statistics and a low count rate on the current beamlines.

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Material density and effective atomic number maps of soft tissues via synchrotron radiation spectral CT.

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Spectral computed tomography (CT) systems for probing tissue attenuation at different energy levels offer added information to tissue characterization and can help in resolving the ambiguity created when different tissue produce very similar gray levels at a single energy range. Attenuation maps measured at different energy can be used to perform material decomposition and/or compute material characteristic quantities such as material density and effective atomic number. Material decomposition is a procedure in which spectral data is represented in the basis of two known materials and often serves as an intermediate step for ρ/Z_{eff} mapping. The clinical relevance of ρ/Z_{eff} mapping has been demonstrated in terms of better tissue distinction¹ material-specific imaging (e.g., iodine, bone, or calcium), and treatment planning in particle radiation therapy.² To this day many algorithms were developed to extract this information from spectral datasets obtained by monochromatic and polychromatic X-ray sources.

In our previous work, we developed two different algorithms to perform material decomposition³ and an approach to compute ρ and Z_{eff} from said decomposition. The results of this approach are shown in Fig. 1. In the present work, we compared several approaches also published by different authors⁴ to extract material density and effective atomic numbers from the spectral CT dataset of various soft tissues obtained at SYRMEP beamline at Elettra Sincrotrone Trieste. The comparison study is performed to find an optimal solution to the state-of-the-art synchrotron radiation breast CT setup currently developed in Trieste. The algorithms were evaluated based on the SNR and the accuracy of extracted ρ and Z_{eff} values.

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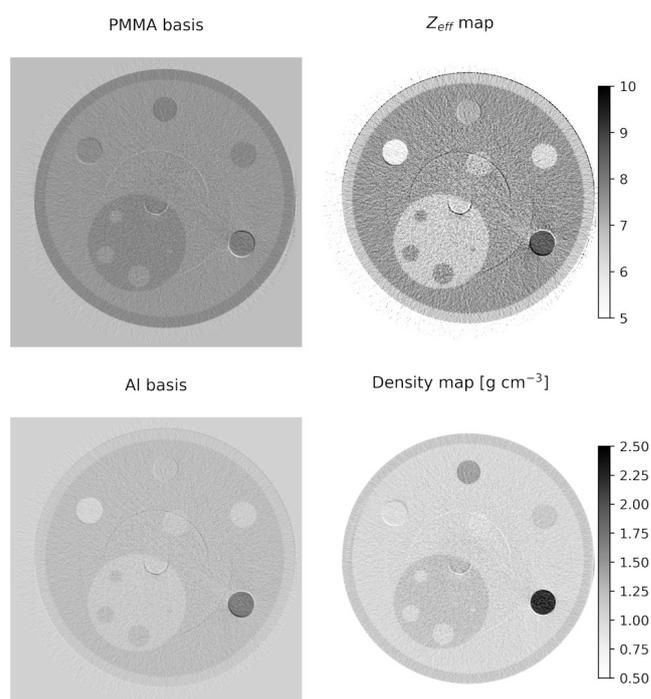


Fig. 1 Spectral CT data decomposed in PMMA-Aluminum basis and extracted ρ/Z_{eff} maps

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Principal component scores projection on a barycentric coordinate system for a quantification in polycrystalline mixtures XRPD data without crystal structure data.

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X-ray diffraction from powders is one of the most widespread techniques for the qualitative and quantitative analysis of polycrystalline mixtures and solid materials in general. In many cases, traditional methods fail to overcome intrinsic problems of the samples being analyzed (enhanced micro absorption and preferred orientations) or even just sample preparation (little sample, not homogeneous, little ground). Moreover, most traditional quantification methods require the knowledge of the crystal structure or at least pure phase XRPD profile only. In the last decade, several solutions based on multivariate statistical analysis have taken hold, on principal component analysis (PCA).¹ This technique can limit the contribution of the experimental error contained in the data, to extract efficiently the useful information. However, PCA-based quantification passes through the construction of regression models, as happens for traditional methods based on internal standards. A novel method is proposed for the quantification of components in polycrystalline mixtures by X-ray diffraction data from powders, in principle without any a priori knowledge about crystal structure and/or pure phase profile. The method is based on a coordinate change proposed by Cornell in his book "Experiments with Mixtures"² and is virtually scalable for polycrystalline systems with any number of components. The mathematical methods are accompanied by two case studies recently published^{3,4} to provide tangible examples of how the coordinate change method works in phase quantification. The results show that the developed method is fast and suitable for direct semi-quantitative analysis with no a priori structure information, which can be combined with a finer quantitative analysis, if necessary. The developed algorithm is presented in its form which has recently been integrated into RootProf⁵ a software dedicated to X-ray diffraction data analysis.

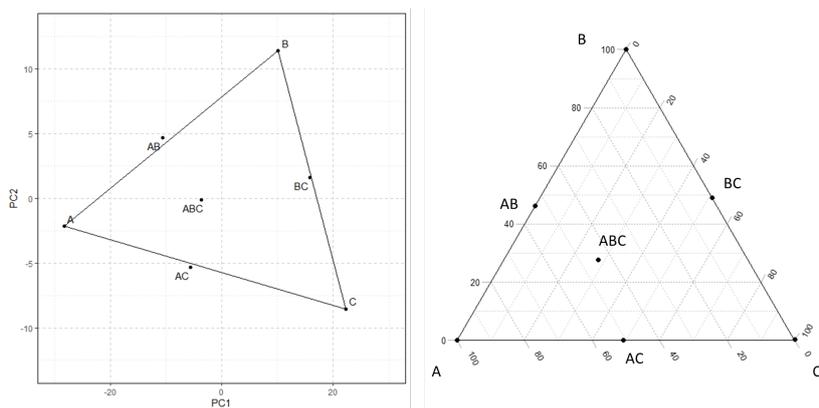


Fig. 1 Left: a set of samples as obtained after Principal Component Analysis on the score plot. Points are positioned in the shape of a triangle for a ternary system. Right: the same samples after the coordinate system change, from the independent coordinate system to the barycentric system.

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Structural Insights into TRPM Channels. A Long and Unexpected Journey.

Carmine Talarico,^{a,*} Sergii Palchevskiy,^b Mariusz Czarnocki-Cieciura,^b Marcin Nowotny,^b Giulio Vistoli,^c Andrea Rosario Beccari.^a

The Transient Receptor Potential Melastatin (TRPM) family belongs to the superfamily of TRPcation channels. These targets have increased their scientific interest so much that in 2021, David Julius and Ardem Patapoutian won the Nobel Prize in Physiology or Medicine "for their discoveries of receptors for temperature and touch."¹

This subfamily is composed of eight members that are involved in several biological functions covering from temperature sensing, inflammation, hormones secretion, and redox sensing.

In 1998, when TRPM1 was cloned, the functions, structure and pharmacology of this family were studied in depth. Thanks to cryo-EM technology and computer simulations, many complete and partial structures of TRPM2, TRPM4, TRPM8 and TRPM7 have been determined, allowing understanding of the mechanisms that are finely regulated by these complex protein structures.^{2,3}

Given the growing interest in TRP receptors and their ligands, combining *in silico* simulation and experimental data, we have focused our efforts on an M subfamily. In this work, we will show the results obtained from Cryo-EM experiments reporting the low-resolution structural reconstruction (Figure 1) of one of these interesting targets and the main differences among TRP subfamilies.

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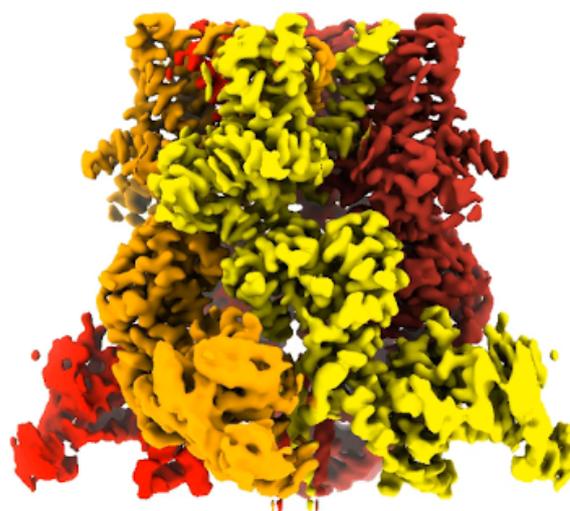


Fig. 1 Cryo-EM reconstruction of TRPM channel.

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Relevance of solid form's curriculum for drug product development: beyond polymorphism of drug substance.

Arnaud Grandeury.^a

Appropriate selection of the crystalline form of an Active Pharmaceutical Ingredient (API) is a key decision in developing patient-centered drug products as this influences the safety, efficacy and performance of the pharmaceutical product. On top of these considerations, it is aimed also to facilitate development of robust drug manufacturing processes while guarantying appropriate key quality criterion during the shelf life of the drug product¹.¹ Advanced characterization tools are needed to analyze the crystalline drug substance in formulated drug products, especially when multicomponent systems and low concentrations are involved. Laboratory and synchrotron-X-ray powder diffraction are seen as complementary techniques among the tools that involve different vibrational spectroscopic techniques and imaging technologies. This presentation will exhibit case studies which illustrate applications of recent improvements of these methods as well as unmet needs and efforts that are deployed to assess and mitigate risks when unpredictable event occurs.

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The “Form Selection Process” in the Pharmaceutical Industry: the importance of being Earnest.

Matteo Daldosso.^a

Active Pharmaceutical Ingredients (API) shows the tendency to get order and crystallize as solids in different structures (forms). This phenomenon is known as polymorphism.

In general, different polymorphs show different physicochemical characteristics and properties. Therefore, the selection of the API form for drug product (DP) development is more than critical because the API form itself has a great impact on the properties of the final DP: the form selection problem has ethic, therapeutics, commercial and economic implications.

A number of historical and real industrial examples are presented in order to show how the X-Rays Powder Diffraction (XRPD) is an essential technique for the determination and quantification of polymorphic (or pseudo-polymorphic) forms in a given API to effectively support the form selection process for Drug Product Development, coupled with orthogonal techniques.

In particular, in house quantitative XRPD methods and how discovering of late appearing polymorphs has influenced the downstream medicine development is presented.

We will underline the needs to open the standard industrial approach to techniques with higher resolution (like synchrotron XRPD) with the objective to create new culture in the industry. The question: ‘Which API form is suitable for pharmaceutical development?’ is a crucial point that must have a solid and earnest answer.

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The structural biology task force at Elettra to support drug discovery against Covid-19.

Paola Storici,^{a,*} Stefano Morasso,^{a,c} Elisa Costanzi,^{a,d} Nicola Demitri,^b Theo Battista,^{a,c} Barbara Giabbai,^a Annie Heroux.^b

At the beginning of 2020 the Covid-19 pandemic emergency caused by a newly identified coronavirus universally known as SARS-CoV2 spread out all over the world, changing irreversibly our life style and wellness. In response to the crisis, while everybody was caught off guard by the rapid diffusion of the viral infection and the alarming of death toll worldwide, the global structural biology community has experienced an unprecedented “call-to-arms” to shed light on every step of the viral replication.¹ All x-ray diffraction beamlines at synchrotrons focused their efforts on the 3D structure determinations of the druggable proteome of SARS-CoV2. The Protein Facility, and the XDR2 beamline at Elettra, jumped on the opportunity to be involved in a huge drug discovery project, financed by the EC H2020 emergency call to counter the SARS-CoV2 Coronavirus pandemic. The project Exscalate4Cov (E4C, <https://www.exscalate4cov.eu>), brought together 18 European institutions combining supercomputing resources and AI with state-of-art experimental facilities up through clinical validation. Goal of the project was to identify the most promising and safe in man drugs for immediate treatment of the infected population.

Elettra group has been part of the structural biology task force focusing on the 3D structure determination of the two SARS-CoV2 proteases: 3CLpro/Mpro and PLpro. We applied classical crystallographic techniques to validate the binding mode of several compounds coming from the virtual and biochemical High-Throughput Screening performed by the partnership.^{3,4} A number of repurposed and de-novo designed molecules were co-crystallized with Mpro and PLpro respectively. A large amount of crystals was screened and collected on XRD2 resulting in different ligand-bound and unbound structures. Here we will describe the complete workflow of Elettra’s activities; from protein production to crystal structure determinations. The highlighting will be on the most relevant results⁴ as well as on the strategies applied to maximize our knowledge when crystallisation did not prove to be on our side.

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Structural characterization of human Heat shock protein 90 N-terminal domain in complex with a potent 1,2,3-triazole based inhibitor.

Giusy Tassone,^{a,*} Samuele Maramai,^a Marco Mazzorana,^b Stefano Mangani,^a Cecilia Pozzi.^a

Heat shock protein 90 (Hsp90) is a ubiquitous molecular chaperone that stabilizes client proteins in a folded and functional state. Hsp90 uses ATP hydrolysis as a source of energy to perform its cellular activity.¹ Hsp90 is composed of two identical and symmetrical subunits and each monomer consists of three domains, the N-terminal (NTD), the middle (MD), and the C-terminal domain (CTD). The NTD contains the main structural elements generating the ATP binding site in which the ATP substrate is hydrolyzed.² Molecules preventing ATP hydrolysis act as Hsp90 inhibitors, blocking its chaperone activity, and subsequently leading to client protein degradation and cell death.² Human Hsp90 represents a validated target for developing new anticancer drugs due to its pivotal role in cell signaling and proliferation.³ In a previous work, a novel series of Hsp90 inhibitors based on a 1,4,5-trisubstituted 1,2,3-triazole have been developed through a multidisciplinary approach.⁴ In these molecules, the concomitant presence of a resorcinol-like moiety, an aryl group, and an alkyl amide in position 4 of the triazole ring represented essential features accounting for their potent inhibitory activity. The most promising inhibitor of the series, namely JMC31, showed Hsp90 binding in the single-digit nanomolar concentration in the fluorescence polarization (FP) assay. Furthermore, JMC31 displayed antiproliferative activity toward non-small cell lung carcinoma NCI-H460 with an IC₅₀ of 2.1 nM. In the present work, the structural characterization of the human Hsp90-NTD in complex with JMC31 has been performed through X-ray crystallography. The structure, solved by combining automatic techniques and manual rebuilding, has shown significant conformational changes in the area surrounding the catalytic site, to which JMC31 is bound if compared with ligand-free Hsp90-NTD and its complexes with ATP and ADP analogues.⁵ The structural information obtained from the complex of Hsp90-NTD with JMC31 has allowed us to evaluate the key structural determinants responsible for inhibitor binding.

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Prediction of hERG-Mediated Cardiotoxicity based on the integration of docking scores and protein-ligand interaction fingerprints.

Pietro Delre,^{a,*} Teresa Maria Creanza,^b Nicola Ancona,^b Giovanni Lentini,^c Michele Saviano,^d Giuseppe Felice Mangiatordi.^a

Drug-induced cardiotoxicity is a common side effect of drugs in clinical use or under post-market surveillance and is commonly due to off-target interactions with the cardiac Human-Ether-a-go-go-Related (*hERG*) potassium channel. Several ligand-based models were developed in the last years and are today used in the early stages of a drug discovery program for *in silico* safety assessment of drug candidates. We present the first structure-based classifiers able to discern *hERG* binders from nonbinders and based on the integration of docking scores and protein-ligand interaction fingerprints.¹ In particular, 396 models were trained and validated based on: (i) high-quality experimental bioactivity information returned by a curated dataset extracted from ChEMBL (version 25) and (ii) structural predictor data. Docking simulations were performed using two software programs (*i.e.*, GLIDE and GOLD) and four different *hERG* structural models, namely two recently published structures obtained by cryoelectron microscopy (PDB codes: 5VA1 and 7CN1) and two homology models selected for comparison. Remarkably, performances comparable to ligand-based classifiers in terms of area under the ROC curve ($AUC_{MAX} = 0.86 \pm 0.01$) and negative predictive values ($NPV_{MAX} = 0.81 \pm 0.01$) were returned by some models, thus supporting the robustness of the proposed computational workflow. From a more methodological point of view, the study represents the first example of successful integration of docking scores and protein-ligand interaction fingerprints (IFs) through a support vector machine (SVM) LASSO regularized strategy and highlights the importance of employing *hERG* structural models accounting for ligand-induced fit effects. Finally, the obtained data allowed us to select the best-performing protein conformation to be used in the future for structure-based predictions of *hERG*-related cardiotoxicity.

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Exploring Phase Diagrams, Structures and Properties with the Large Volume Press at the ESRF.

Wilson Crichton^a

The ESRF's large-volume press beamline, ID06LVP, has been in User operation for 10 years (e.g. Guignard & Crichton, 2015).¹ It complements the ESRF's already wide-ranging extreme conditions portfolio by offering, primarily, *in situ* angle-dispersive diffraction-based experimentation with a multi-anvil device that operates in one-and two-stage modes. Through use of independent anvils; both normal compression, with high degrees of triaxiality, and deformation data collections are possible. It operates with continuous acquisition in pressure, temperature, time space through use of a custom-built CdTe detector, allowing for rapid assessment of phase diagrams, reactions (and rates) and, under static conditions, sufficiently resolved data for structure solution and refinement. Ancillary techniques often supplement the primary diffraction measurements (conductivity, resistivity, ultrasound, imaging, &c); thus providing the complementarity of transport and physical properties measurements required by materials exploration in solid-state sciences. In this presentation, we highlight the evolution of the main design features of the instrument during this period of continuous User operation. We will give an overview of the current operational status as part of the ESRF's EBS and expectations for future technologies. During these, we will draw-upon data and examples from in-house testing and User operation to illustrate features and the typical uses from various fields of research.

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Role of crystal lattice in pressure induced electronic transitions: selected examples.

Boby Joseph.^a

Superconductivity is an amazing macroscopic quantum many body effect.¹ This phenomena continue to arouse the interest of material scientists, physicists and chemists due to a variety of systems which show such an effect and the intriguing nature of the structural effects on superconductivity. This makes the high-pressure structural studies of such systems an important field of research. At the high-pressure diffraction beamline, Xpress, of the Elettra synchrotron, recently we have been involved in such studies.^{2,3} One of the key information sought out from these studies is the role of structure in tuning the collective excitations and possible role of such collective excitations in acting as the “pairing glue” for the Cooper pair formation. Systematic high-pressure structural investigations coupled to transport or vibrational spectroscopy studies seems to be very effective.³⁻⁵ There are several emerging new systems where there is a strong connection between the structural properties and the interesting physical properties, where the high-pressure studies are found to provide interesting inputs³⁻⁷ – some examples in this direction will also be discussed.

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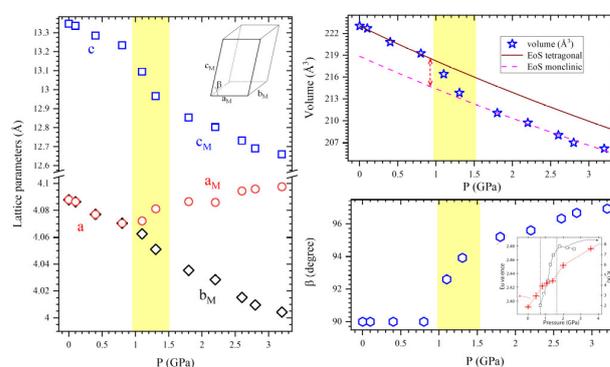


Fig. 1 Pressure evolution of the lattice parameters (a), unit cell volume (c) and the β angle (b) for $EuFBiS_2$.² The shaded area in each panel shows the region of phase coexistence marking the structural phase transition. Inset of panel (a) depicts the monoclinic unit cell. Inset in (c) presents the pressure dependence of the superconducting transition temperature together with the Eu valence.

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X-ray diffraction shines light on mineral inclusions: A natural high-pressure experiment.

Marta Morana,^{a,*} Joseph P. Gonzalez,^b Anna Barbaro,^b Giulia Mingardi,^b Federico G. Albarse,^c Ross J. Angel.^d

From a mineralogical, geological and geodynamical point of view, mineral inclusions trapped inside another minerals are a treasure trove of information that can shed light on processes occurring at depth in the Earth. Entrapped at depth and protected by their host minerals during their ascent to the surface, inclusions are rare and provide pristine samples of regions of the Earth otherwise inaccessible with direct exploration methods i.e. hundreds of km against tens of km the deepest borehole drilling. Information on the environment of growth and the pressure and temperature conditions of formation can only be retrieved by performing in situ non-destructive measurements on the enclosed inclusions to prevent any possible loss of precious information.

Two techniques are the most common in this type of studies: Raman spectroscopy and X-ray diffraction (XRD). From these measurements phase identification allows to determine the environment of growth, whereas elastic geobarometric calculations allow to calculate the conditions of pressure and temperature of the entrapment, i.e. at the depth of formation for the pair, from the strain in the inclusion and the equations of state of both minerals. Raman spectroscopy is a popular technique for characterising mineral inclusions, since it is quick and allows small portions of the sample to be probed. However, while phase identification for determining the environment of growth is quite straightforward, the relationship between the strains and the Raman peak position is not well established for several mineral phases. On the contrary, XRD directly measures the unit cell parameters and from their change with respect to a reference mineral is possible to calculate the strains acting on the inclusion trapped in the host at laboratory P and T.

We developed a methodology to calculate the strain from the Raman peaks, but it needed to be cross validated against direct measurements of the strains, such as the ones from XRD. Conventional laboratory set up do not allow us to measure inclusion smaller than 70 μm , because of the large X-ray absorption coefficient of the host minerals, and the 1-2 mm thickness required to preserve inclusion stress state. Unfortunately, inclusions of such dimensions are very rare in most natural rocks, so we extended our study using synchrotron light at the XPress beamline at Elettra (Basovizza, TS). Furthermore, XRD can be used to simultaneously extract a wide range of information. In fact, intensity data can be used for structural refinement for phase identification, allowing to infer the environment in which the host-inclusion system grew, and to characterize the structure of the entrapped mineral, which is under deviatoric stress, a condition very difficult to reproduce in a laboratory experiment in a controlled way. At the same time peak positions can be used determine the orientations matrices of both the host and the inclusion to enable modelling possible growth processes and scenarios.

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P-mediated crystal-fluid interaction in ERI and OFF topology.

Tommaso Battiston,^{a,*} Davide Comboni^b Francesco Pagliaro,^a Paolo Lotti,^a G. Diego Gatta.^a

The intrusion of molecules or ions into the structural voids of open-framework minerals (*i.e.* zeolites) was extensively investigated during last decades, due to the potential exploitability in creating new multifunctional materials or to boost industrial catalytic processes.^{1,2} These phenomena can have potential implications in Earth Sciences: zeolites are widely spread in the upper oceanic crust; therefore, they may play an important role as fluid carriers during the early stages of subduction, especially considering a potential over-hydration effect governed by the physical-chemical conditions of the subduction zones.

The present study describes the high-pressure behaviour and crystal-fluid interaction of two natural zeolites: of-fretite and erionite (OFF and ERI topologies). Both species are members of the ACB-6 family, sharing a similar framework sequence (AABAAC for ERI and AAB for OFF), which results in a quite common intergrowth in natural samples.³ Erionite, the most abundant in nature, was observed in the volcanoclastic deep-sea sediments collected in the framework of the Oceanic Drilling Program (ODP).⁴ Investigation were conducted by means of in-situ high-pressure single-crystal synchrotron X-ray diffraction, using a diamond anvil cell (DAC), at the ID15b beamline of ESRF (Grenoble, France) and P02.2 of PETRA-III (Hamburg, Germany). Samples were compressed using different hydrostatic *P*-transmitting fluids (PTFs), both non-penetrating (silicone oil and daphne oil 7575) and potentially penetrating (methanol:ethanol:water mixture 16:3:1, distilled H_2O and ethanol:water 1:1). Offretite was also investigated using Ne as PTF.

The *P* – *V* patterns show different trends with penetrating and non-penetrating PTFs, revealing the unambiguously occurrence of an intrusion of molecules within the structural nanocavities, and the magnitude of this phenomenon was surprisingly high in natural erionite. Results from the Ne experiment in offretite showed a similar trend to potentially penetrating PTFs, suggesting a *P*-induced adsorption of this noble gas within the structural voids. Thank to single crystal X-ray refinements, the deformation-mechanisms at the atomic scale, as well as the location of the new atomic sites, are here described.

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Structure determination of CaSiO_3 wollastonite polymorphs at HP/HT conditions by single crystal in-situ diffraction.

Benedetta Chrappan Soldavini,^{a,*} Marco Merlini,^a Sula Milani.^a

CaSiO_3 wollastonite and its polymorphs are very interesting since they represent the major pure calcium silicate in different geological settings. In the upper-crust, wollastonite and its common polytype parawollastonite (wollastonite 2M) are stable in specific metamorphic reaction zones (skarns), while the high-temperature ambient pressure polymorph pseudowollastonite is associated to Ca-rich paralavas and hornfels. At pressure above 3 GPa, the breyite-structured polymorph, stable over a wide range of temperatures and pressures, has been found in diamonds as one of the most abundant inclusions.¹

The structural evolution with pressure of wollastonite and breyite is characterized by several phase transitions to denser structure.² We report new data on high pressure structural and elastic properties on wollastonite 2M and pseudowollastonite, based on in-situ single crystal diffraction experiments at high-pressure and high- pressure/high-temperature conditions.

We used resistively heated Diamond Anvil Cell at XPRESS beamline (Elettra, Trieste). We performed multiple single crystal diffraction, exploiting the relatively large beam available at the beamline. In this way we have been able to collect simultaneously two sample crystals with different crystallographic orientation and two reference crystals, suitable both for increasing reciprocal space coverage for low symmetry samples, and for P and T determination, together with spectroscopic methods and direct temperature measurements by thermocouples.

The wollastonite 2M polymorph showed a phase transition to a triclinic structure above 8.5 GPa, while for the pseudowollastonite no phase transition was observed in the pressure range from 0 to 16 GPa, in contrast with previous literature data.³ The HP/HT data confirm the stability of the triclinic wollastonite polymorph at upper mantle conditions, and allow the determination of thermal equation of state parameters.

The identification of stable and metastable high-pressure polymorphs could be extremely useful also to interpret shock wave experiments on these systems.⁴

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Depth selective local coordination in amorphous $Co_xFe_yB_z$ thin films probed by XAFS under x-ray standing wave condition.

M. Abdolrahimi,^{a,*} M. Singh,^b K. V. Sarathlal,^b M. Gupta,^c V. Raghavendra Reddy,^c I. Carlomagno,^d G. Das,^d G. Aquilanti,^d C. Meneghini,^a A. Gupta.^b

Heterostructures consisting of $HM/Co_xFe_yB_z/HM$ (HM being heavy metals like Mo, Hf, Ta, W) may develop peculiar properties at the interfaces, such as interfacial Dzyaloshinskii–Moriya interaction (IDMI), Spin Hall effect (SHE), perpendicular magnetic anisotropy (PMA), which are valuable for low power spintronic developments.¹ IDMI is also responsible for chiral domain walls and skyrmions, which hold great potential for high density non-volatile memory devices. The local atomic coordination and perpendicular homogeneity in amorphous $Co_xFe_yB_z$ interlayer may significantly affect the interfacial interactions with the HM layers, and hence the functional properties of the system. In general, the atomic coordination of amorphous the $Co_xFe_yB_z$ layer significantly differs from *bulk* metallic glasses of similar composition because of the influence of HM interactions, deposition process, and eventual post deposition treatments. Elucidating the local structure and coordination at the atomic scale of the $Co_xFe_yB_z$ layer is relevant because atomic scale mechanisms intimately affect the functional properties of $HM/Co_xFe_yB_z/HM$ multilayers. The x-ray absorption fine structure (XAFS) spectroscopy, being a chemical selective probe for the local atomic structure, is especially suited to this aim, and, in the case of such multilayer structure, can be coupled with the x-ray standing wave (XSW) geometry to access depth selective information.² A recent experiment carried out at the XRF- Beamline (Elettra)³ has demonstrated differences between Fe and Co local atomic structure and significant vertical inhomogeneities in the $Co_xFe_yB_z$ with evident differences between the coordination of Fe and Co located close to the HM interfaces and in the center of the layer.

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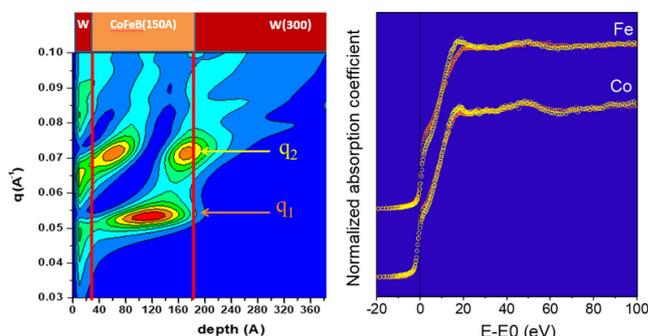


Fig. 1 Left panel: antinode position as a function of q in the $W/Co_xFe_yB_z/W$ multilayer. Right panels: Fe-K and Co-K XANES spectra measured at the q_1 (antinode at the layer center) and q_2 (antinodes at the layer interfaces).



Solid States NMR Spectroscopy with Quantum Espresso.

Davide Cerasoli.^a

Recent advances in the application of *first principles* calculations of NMR parameters to periodic systems^{1,2} and the steady increase of computational power, have become attractive in their use to support experimental measurement. Such calculations often play an important role in the emerging field of *NMR crystallography*, where NMR spectroscopy is combined with techniques such as diffraction, to aid structure determination.^{3,4}

In this talk I will introduce the capabilities of QE-GIPAW,⁵ which is based on the popular DFT package Quantum Espresso.⁶ After reviewing the underlying theory of the magnetic response of periodic systems, I will highlight how QE and QE-GIPAW can be used in a computational workflow, integrated with NMR/EPR simulation software like Simpson⁷ and EasySpin.⁸ I will present two case studies of the structure determination of purely inorganic and pharmaceutical crystal polymorphs, where the QE-GIPAW provided a correct assignment of the ¹H and ¹³C NMR shifts.

Finally, I will briefly illustrate the plans to provide a user friendly *cif-to-spectrum* workflow to be run in the cloud or on premises, thus avoiding the complication of installing and compiling the complete software stack.

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Ultrafast X-ray sources: an opportunity for science.

Emiliano Principi.^a

During the last decade X-ray sources experienced a remarkable technical progress that radically extended their achievable scientific horizons with significant impact in many disciplines. As a result, today X-ray sources are no longer intended only as stationary but also as ultrafast pulsed sources for experiments in the sub-picosecond time domain.

A prominent role in this revolution is definitely played by the free electron laser facilities that could undergo a further impressive upgrade with the forthcoming advent of the plasma acceleration technology like that envisaged by the EuPRAXIA European project. However, terrific advances have been also made with the high harmonic generation (HHG) tabletop ultrafast sources operating in the extreme ultraviolet and soon in the soft X-ray range. X-ray sources can improve also through novel exotic schemes devised to compress the X-ray emission of synchrotrons down to the picosecond scale. Adaptive X-ray optics have been developed to extract picosecond pulses from longer synchrotron X-ray pulses. The combination of ultrafast electron and X-ray sources have been successfully attempted, permitting time resolved electron diffraction experiments on isochorically heated metals with 100 fs time resolution.

Notably, many of these advances involves Italian research teams and X-ray facilities, including Elettra-Sincrotrone Trieste. This keynote is intended to explore the potential of emerging ultrafast X-ray sources analyzing several examples of time resolved experiments and techniques accessible to scientists today and in the near future in Italy.

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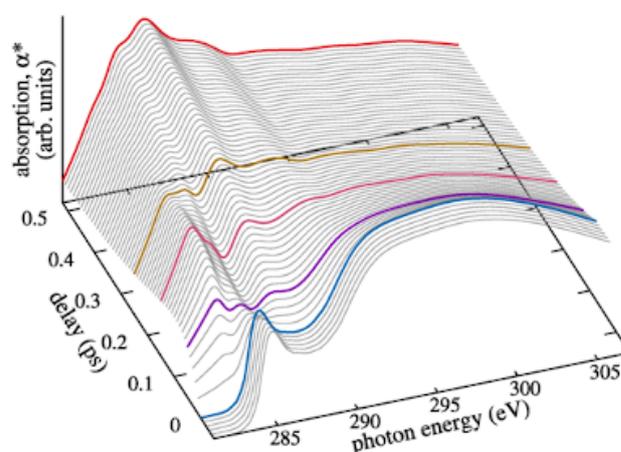


Fig. 1 Time resolved XAS at the C K-edge showing the ultrafast melting of an amorphous carbon sample.¹

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The EuPRAXIA FEL project: ultra-bright light pulses for imaging and spectroscopy.

Zeinab Ebrahimpour,^{a,b}

EuPRAXIA is a leading European project aimed at the development of a dedicated, ground-breaking, ultra-compact accelerator research infrastructure based on novel plasma acceleration concepts. The INFN Laboratori Nazionali di Frascati will be equipped with an X-band LINAC followed by a plasma wakefield acceleration stage driving the first fifth-generation free electron laser (FEL) source driven by a plasma-based accelerator, the EuPRAXIA@SPARC_LAB facility¹ The FEL will be characterized by a small footprint and will deliver ultra-bright photon pulses for experiments in the water window (3-5 nm) to the user community.² In addition, the possibility of building a second photon beamline with seeded FEL pulses in the range between 50 and 180 nm³ and of exploiting the X-ray betatron radiation emitted by the electrons accelerated in plasma⁴ are being explored.

We present an overview of the foreseen applications of these photon sources, which include imaging and spectroscopic studies on a variety of biological and inorganic materials, giving information on their structure and dynamical behavior.

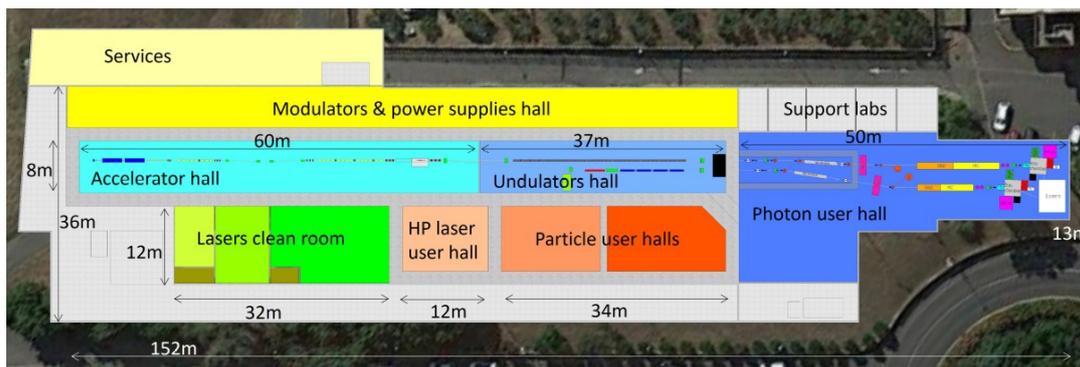


Fig. 1 Layout of the EuPRAXIA@SPARC_LAB facility.

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A machine learning-based web platform for crystal system classification: CrystalMELA.

Nicola Corriero,^{a,*} Domenico Diacono,^b Nicoletta Del Buono,^c Rosanna Rizzi,^a Gaetano Settembre.^c

A new machine learning (ML) based web platform, named CrystalMELA (Crystallographic MachinE LeArning), for crystal system classification, has been developed.

In the current version, the tool is able to run three different and complementary ML models: a Convolutional Neural Network (CNN), a Random Forest (RF) and an Extremely randomized trees (ExRT). The models have been trained on theoretical powder diffraction patterns of more than 280,000 crystal structures of inorganic, organic, organo-metallic compounds and minerals as collected in the POW_COD database¹. A 70% of classification accuracy was achieved, improved to 90% if the top-2 accuracy is considered.

CrystalMela is free availability at <http://www.ba.ic.cnr.it/softwareic/crystalmela/>, its home web page is shown in Figure 1.

The classification options in CrystalMELA platform are designed to be powerful and easy to use, supported by a user friendly graphic interface. Their main aspects and some examples of applications to real cases, will be presented.

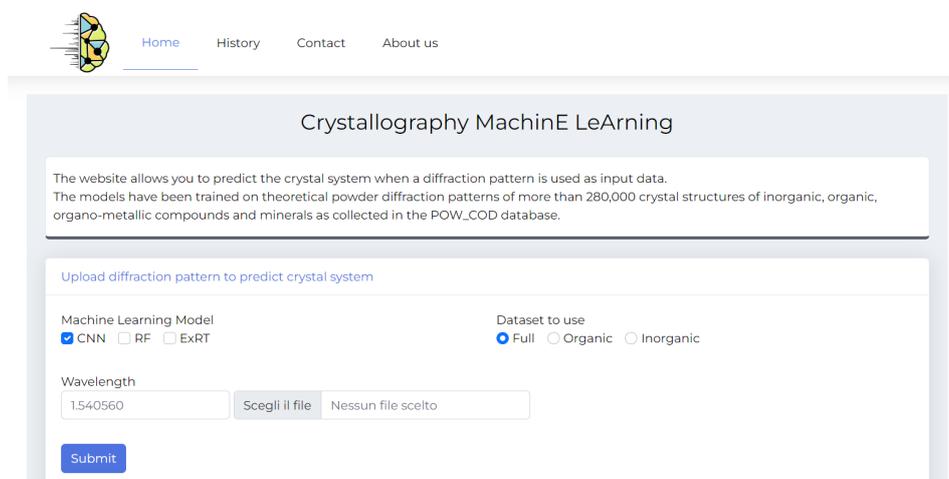


Fig. 1 Home page

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Unattended MX data collection and beamline monitoring at Diamond.

Marco Mazzorana,^{a,*} David Aragao^a Neil Paterson^a Mark Williams,^a Graeme Winter,^a Elliot Nelson,^a, Ralf Flaig,^a Katherine McAuley,^{a,b} Dave Hall.^a

Diamond Light Source, the UK national synchrotron, currently operates 7 macromolecular crystallography beamlines.¹ The core suite, comprising 4 highly automated beamlines for conventional cryo-crystallography, is complemented by dedicated ones for in-situ room temperature, long wavelength and sub-micron focusing data collection.

Low-level control of equipment is operated by EPICS, while at the user level, each beamline is driven by our data collection software GDA.^{2,3} Full integration between User Administration System, the ISPyB⁴ database (via the SynchWeb^{5,6} interface), and GDA, grants consistency across various aspects of the experiment, including logistics and data analysis/processing.

In the recent past, Diamond introduced fully unattended data collection.⁷ Users simply need to define for each sample a suitable data collection strategy (chosen from a set of optimized recipes), while on arrival of crystals at Diamond, they are loaded in the most suitable beamline and data collection occurs without any need of interaction from the User. The heart of this is a combination of software tools which oversee the status of the beamline and coordinate the queuing and data collection for unattended experiments.

The first task is carried out by daemons interacting with EPICS to report the status of vital PVs through HTTP restful interfaces, database connections and on-disk file analysis. Beamline health reporting occurs through systems such as Slack, Email, Signal/WhatsApp and can be configured through a Slack bot. This avoids overload of information and optimizes troubleshooting, especially during out-of-hours assistance.

On the other hand, a virtual user daemon ensures that unattended data collection is carried out every time the beamline is in a healthy state but idle. Since different instruments offer different beam properties, recipes are harmonized to capture these features. For example, at the variable focus beamline I04 dose is calculated using a built-in Raddose3D⁸ calculator to ensure optimal exposure times.

This concept maximizes the performance of beamlines, reducing idle times by interleaving interactive and automated experiments and supervising the efficiency of the instruments by constantly monitoring and reporting their performance.

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XRD2 to μ XRD: Italian Beamlines Dedicated to Macromolecular Crystallography.

Annie Héroux,^{a,*} Nicola Demitri,^a Raghurama P Hegde,^b Maurizio Polentarutti,^a Giorgio Bais,^a Iztok Gregori,^a Roberto Borghes.^a

Even though Elettra Sincrotrone has been around for three decades, XRD2 beamline is one of the newest additions with its operation starting in 2018. During this short life time, changes touching multiple aspects either at the beamline or from the facility were required to be more competitive with other facilities and pave the way for Elettra 2.0.

The beamline is still implementing new hardware such as a dual gripper for the automounter as well as new functionalities in the data collection software. Even though most users are choosing to collect remotely, the synergy of user friendly interfaces, access to more and faster live data analyses results and easy tracking of all experiments offer a convenient, customized and productive environment for all our users.

While still committed at improving the user experience, we are now dedicating efforts to the upcoming Elettra 2.0. New plans are seeing light and the MX User community will have the benefit of a brighter and smaller beam at a new location on the Elettra floor. We will describe the vision and the ongoing work which will hopefully start a dialogue with our user community.

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Structural Biology for Vaccine Development Against Emerging Pathogens.

Eliza Kramarska,^a Flavia Squeglia,^a Alessia Ruggiero,^a Rita Berisio.^{a,*}

Structural vaccinology is a rational-based approach to design immunogenic antigens aimed at generating an effective vaccine. It combines experimental methods like X-ray crystallography, molecular biology, electron microscopy and mass spectrometry, with computational methods like molecular modelling and epitope prediction¹⁻⁴

The first step of this approach is the three-dimensional structure determination of the antigen using structural biology tools such as X-ray crystallography, cryo-electron microscopy, nuclear magnetic resonance or computational approaches. Key to vaccine development is the knowledge of the exact regions of an antigen that are recognized and bound by antibodies. This knowledge may be acquired using a combination of experimental and computational methods. These methods provide the whole set of information needed to engineer new constructs with better properties in terms of elicitation of the immune response, stability in solution and ease of production.⁵ Using this approach, we have currently identified and developed several vaccine antigens against difficult emerging pathogens. These studies are being implemented through an integrative effort of Partners of the Marie Skłodowska-Curie Action BactiVax - Anti-Bacterial Innovative Vaccines.

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3D Electron Diffraction of Beam Sensitive Samples of Biological Interest: Proteins and Pharmaceuticals.

Mauro Gemmi.^a

The availability of a single crystal diffraction technique for crystals smaller than few microns is a breakthrough both in structural biology and in pharmaceutical sciences. In those disciplines it is quite common to have difficulties in crystallizing large single crystals, therefore the structural studies can be extremely challenging or even impossible. 3D electron diffraction (3D ED) has provided a valuable alternative.¹ Although proteins and pharmaceutical are usually quite beam sensitive, both hardware and methodological development allow to collect 3D ED data in low dose mode on crystals that can stand total doses of $1 \text{ e}/\text{\AA}^{-2}$ or less before their diffraction deteriorates below 2 \AA in resolution. This has been possible because new direct electron detectors became available and 3D ED data collection procedures have been improved allowing the total data collection time to be less than 1 minute.² During this presentation the different 3D ED methods will be discussed along with some significative examples. In particular the structure solution of important pharmaceutical compounds that remained unknown for decades will be presented: orthocetamol³ and δ -indometacine.⁴ Their structure determination have been possible by combining low dose 3D ED techniques with nanobeam diffraction, avoiding to have contribution from different crystalline domains.

The application of 3D ED to protein crystallography will be also discussed by highlighting the most recent development in the field.

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Towards the Cryo-EM structure of the ERAD glycoprotein folding checkpoint, the EDEM:PDI heterodimer.

Charlie J. Hitchman,^{a,*} Christos Savva,^a Timothy J. Ragan,^a Andrea Lia,^{a,b} Gábor Tax,^a Yusupha Bayo,^c Maria De Benedictis,^b Angelo Santino,^b Pietro Roversi,^{a,c,d}

The 130 kDa ER Degradation Enhancing Mannosidase (EDEM) selectively de-mannosylates an N-linked glycan on terminally misfolded glycoproteins, thereby dispatching it to retrotranslocation, cytosolic ubiquitination, and proteasome degradation. EDEM activity depends on association with a 60 kDa Protein Disulphide Isomerase (PDI) to form the EDEM:PDI heterodimer.¹⁻³ No EDEM selective inhibitors are known, and yet EDEM modulators would have therapeutic potential in virology, rare genetic disease and cancer, as well as constituting important reagents for biotechnology and agricultural science. No EDEM structures have been published yet. Furthermore, the molecular determinants of misfold recognition and selective de-mannosylation of the C-branch of the substrate N-linked glycan by EDEM:PDI remain elusive to date. We selected the *Chaetomium thermophilum* EDEM and PDI (*Ct*EDEM and *Ct*PDI, respectively) and confirmed that *Ct*EDEM is an EDEM in a plant model. *Ct*EDEM and *Ct*PDI (the latter without its ER retrieval signal) were cloned in the pHLsec vector for secreted expression in mammalian cells. Four days after co-transfection of HEK293F cells, the *Ct*EDEM:*Ct*PDI is purified from the cells supernatant by IMAC followed by SEC. The purified complex was vitrified on a transmission cryo-electron microscopy (Cryo-EM) grid. Data collection yielded a total of 11208 micrographs from which a total of 1,850,000 particles were picked and selected by rounds of 2D classification. A subset of 180,000 particles gave a 3.5 Å reconstruction of the complex, with approximate dimensions 120x90x70 Å. Phased molecular replacement has been used to dock domains from models of structurally similar proteins from the AlphaFold 2.0 database. The EDEM catalytic domain nestles inside the curved arc formed by the four thioredoxin domains of the PDI. The two topologically intertwined C-terminal EDEM domains⁴ stick out of the main body of the complex. Each of two EDEM free Cys residues are within disulphide bonding distance from one of the two redox-active SS bonds of the PDI, suggesting that redox chemistry is important for the function of the enzyme. Structure-based hypotheses about the function of EDEM:PDI ERAD and experiments to test them will be discussed.

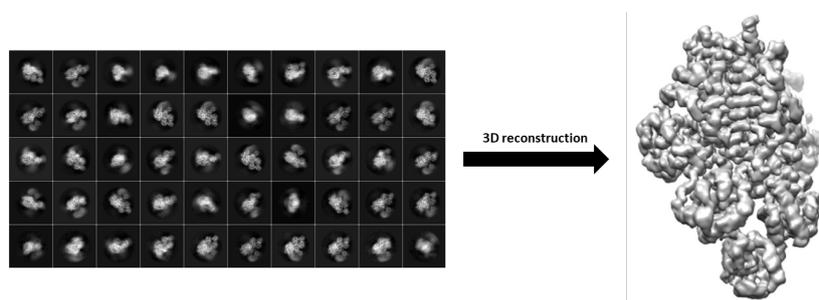


Fig. 1 180,000 particles of the *Ct*EDEM:*Ct*PDI complex were picked from cryo-electron microscopy micrographs, sorted into 2D classes (left), and used to produce a 3D electrostatic potential map (right).

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RNA-viruses inhibitors: unintended consequences of the target driven approach.

Francesco Boni,^{a,b} Rafaela Bonotto,^c Alessandro Marcello,^c Giuseppe Manfroni,^d Antonio Chaves-Sanjuan,^b Mario Milani,^{a,b} Eloise Mastrangelo,^{a,b,*}

Targeting, *in silico*, the RNA dependent RNA polymerase (RdRp) of Dengue virus, we selected a class of pyridobenzothiazolones (PBTZs, from a proprietary library), which showed broad-spectrum antflaviviral activity. In contrast to the enzyme kinetic measurements that showed a non-competitive inhibition, the X-Ray crystal structure of the targeted RdRp in complex with one PBTZ, suggested a competitive inhibition mechanism.¹ Furthermore, cell-based experiments with one of the most potent compounds of the class (HeE1-17Y) indicated that the antiviral activity was unrelated to the polymerase inhibition.² Indeed, we observed that viral infectivity was drastically reduced by incubating the compound with the virus before infection, suggesting its direct interaction with the viral particles.

The mode of action of HeE1-17Y has been studied for West Nile virus taking advantage of non-infective reporter replication particles (RRPs), that were analysed by a preliminary cryo-EM experiment, showing their identity to the native virions.

Electron microscopy analysis (negative staining) of RRP_s incubated with the inhibitor revealed a reduced number of virions, that were severely compromised showing a “gruyere” aspect (Figure 1).

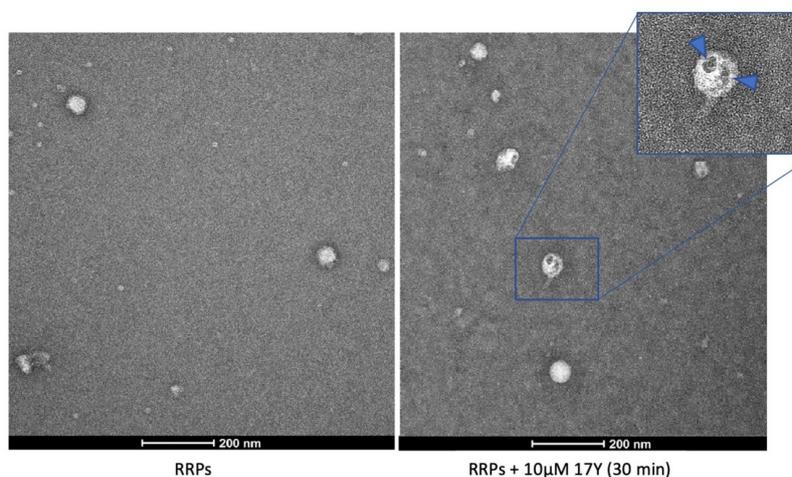


Fig. 1 Negative staining of WNV RRP_s (left) or treated with 10 μ M 17Y for 30 min (right). Close-up view of a particle with holes indicated by blue arrows.

We demonstrated that HeE1-17Y is an antiviral compound whose mechanism of action is based on the destruction of viral particles (virucidal activity), selective against several enveloped viruses (ineffective against different non-enveloped viruses). Given the low toxicity for cells, the potential use of PBTZs also in disinfectants, repellents, skin creams, aerosol, sanitizing product and nasal spray could be of particular interest to prevent viral infections, including flavivirus and coronavirus-³

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This work shows how, starting from a classical target driven approach, by means of a combination of different experimental strategies, it is sometime possible to unravel an unpredictable path to disclose the true nature of a novel class of active compounds.

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Fully autonomous end-to-end protein to structure pipelines at MASSIF-1 using the CrystalDirect harvester.

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Recent advances in automation and method development at synchrotron facilities has allowed the development of different data collection pipelines and plate-to-beam applications to respond to modern structural biology projects and to improve the efficiency for high throughput applications.^{1,2} This dynamic change in scientific needs, as well as the increased interest in structural data at physiological temperatures,^{2,3} has driven us to expand the beamline experimental capabilities.

The main goal of this upgrade is to develop different approaches for data collection that are both automated and target-based, with the initial focus on defining pipelines for challenging experiments, such as room temperature data collection and dehydration. To date, these require a large number of manual steps and the experimental set-up is time-consuming.²⁻⁴ Through the automation of this process, made possible by combining the already available resources on-site, we intend to render those experiments more reliable, reproducible, and accessible to non-expert users. The CrystalDirect harvester gives access to a fully automated protein crystallography workflow, integrating protein crystallization, sample harvesting and cryocooling into an automated process,^{5,5} while the automation of MASSIF-1 allows large amounts of high-quality data to be efficiently collected.¹ Combining the CrystalDirect harvester and MASSIF-1, we are aiming to help to respond to multiple technical and experimental challenges.^{2,3}

The commissioning phase is currently ongoing. The integration of the CrystalDirect harvester in the beamline environment enables multiple and sequential crystal harvesting, sample mounting, and data collection to be executed in automated mode, with no user intervention. The operation of each pipeline has been validated, showing the potential to develop different data collection pipelines at both cryogenic and room temperatures. Preliminary results indicate the possibility to collect complete datasets from single crystals at room temperature and the optimization of this pipeline, using different protein targets is ongoing. The upgrade will allow full automation of the entire spectrum of crystallography experiments, including the most complex room temperature experiments from gene to structure.

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Characterization of Ca-depositions evolution by cryo-XANES and cryo-STX in SaOS-2 osteosarcoma cells.

Francesca Rossi,^{a,*} Giovanna Picone,^a Andrea Sorrentino,^b Giovanna Farruggia,^a Concettina Cappadone,^a Iotti Stefano,^a Emil Malucelli.^a

OBJECTIVE: This study aims at characterizing mineral depositions in the early phase of bone biomineralization in SaOS-2 osteosarcoma cell line. Cryo-soft X-ray tomography (Cryo-STX) and cryo-XANES at the CaL2,3 edges imaging were combined to investigate the evolution of the Ca-depositions during differentiation. A deeper knowledge of the early phase of bone formation and its mineral nanostructure could elucidate the relationship between osteoblastic differentiation and osteosarcoma, opening new perspectives in the treatment of this disease.

MATERIALS and METHODS: We characterized minerals produced by SaOS-2, osteoblast-like cells with high mineralizing activity.¹ SaOS-2 cells were subject to osteogenic medium according to Pasini et al.² The combination of cryo-STX with cryo-XANES at the CaL2,3 edges allowed to identify respectively the spatial distribution and the chemical state of mineral depositions in frozen-hydrated cells at 4 and 10 days after osteoblastic induction.^{3,4}

RESULTS: Thanks to this emerging technique, we appreciated the evolution of Ca depositions from calcium phosphate ($Ca_3(PO_4)_2$) to hydroxyapatite (HA) from 4 days to 10 days after osteoblastic differentiation. The acquired spectra and tomography showed the presence of few calcite ($CaCO_3$) deposits on the ground plane in 4 days control samples. SaOS-2 after 4 days of differentiation revealed an increase in depositions number and the evolution of their chemical composition to calcium phosphate. While deposits mainly laid on the ground plane of the samples, the increasing presence of intracellular vesicles containing calcium carbonate compounds was depicted (see Figure 1). Intriguingly, at 10 days after differentiation, vesicles increased in number as well as depositions whose chemical state evolved to hydroxyapatite.

CONCLUSIONS: The presence of Ca-phosphate and HA crystals after osteogenic induction could suggest a restoration of the biomineralization process due to the induction of SaOS-2 cells towards a less aggressive phenotype even at 4 days. Furthermore, vesicles could play a central role in the genesis within the cell and the propagation of minerals in the extracellular matrix: at the moment their potential remains unveiled, especially in humans.

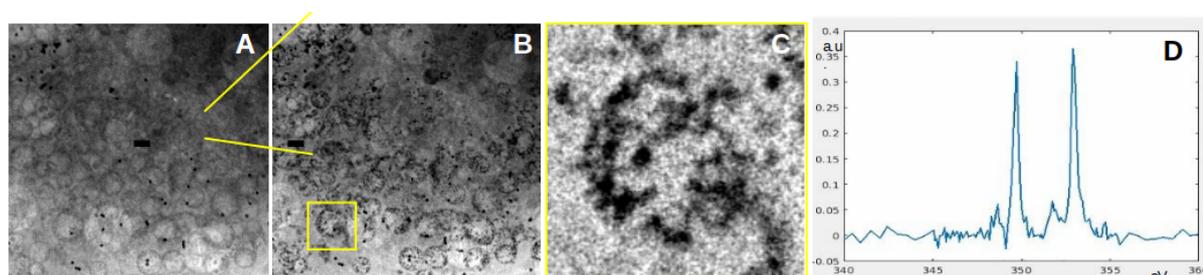


Fig. 1 Average absorbance of a cytoplasm cell region at pre-Ca-edge energy region (≈ 342 eV) and at the Ca L3 peak maxima (≈ 349 eV), for 4 days treated sample (A, B). C) Absorbance map of vesicles in C): square corresponds to the Ca-depositions. D) Average of XANES spectra of intra-vesicular Ca-depositions. Scale bar is 250 nm.

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Glycation in collagen macromolecule of diabetic biotissues.

Alberta Terzi,^{a,*} Luca Fusaro,^{b,c} Liberato De Caro,^a Teresa Sibillano,^a Davide Altamura,^a Ana Diaz,^d Oliver Bunk,^d Francesca Boccafoschi,^{b,c} Cinzia Giannini,^a

Glycation is the most important long-term reaction that leads to the structural and functional alterations of collagen macromolecules in diabetic tissues. It is due to a hyperglycemic condition, more than 110mg/dL of sugar in blood, over a long period and consists of the non-enzymatic formation of sugar bridges between sugars and biological macromolecules, leading to loss of physiological and mechanical functions in tissues and organs. As collagen is the main fibrous protein of the extracellular matrix it is widely glycated both in diabetes and when aging. Although the impact of glycation on nano-scale collagen fibrils is well established, less is known about the effects at the molecular level. Furthermore, there is a lack of ex vivo model systems. Ex vivo X-ray scattering (SAXS/WAXS) imaging techniques are here adopted for the characterization of intra- and inter-molecular structural parameters of collagen in decellularized bovine pericardial biotissues soaked with different sugars (D-glucose, D-galactose, D-ribose) at increasing concentrations (0, 2.5, 5, 10, 20 and 40 mg/ml), and incubated at 37°C for 3, 14, 30 and 90 days. Collagen was found to behave in a similar way when incubated with glucose and galactose, namely glycation processes occur near the arginine and lysine amino acids of the collagen structure, as proved by the Fourier difference synthesis, computed from the SAXS patterns. Regarding ribose, glycation occurred at the same amino acids but a factor 38 faster and abundant than with the other sugars.

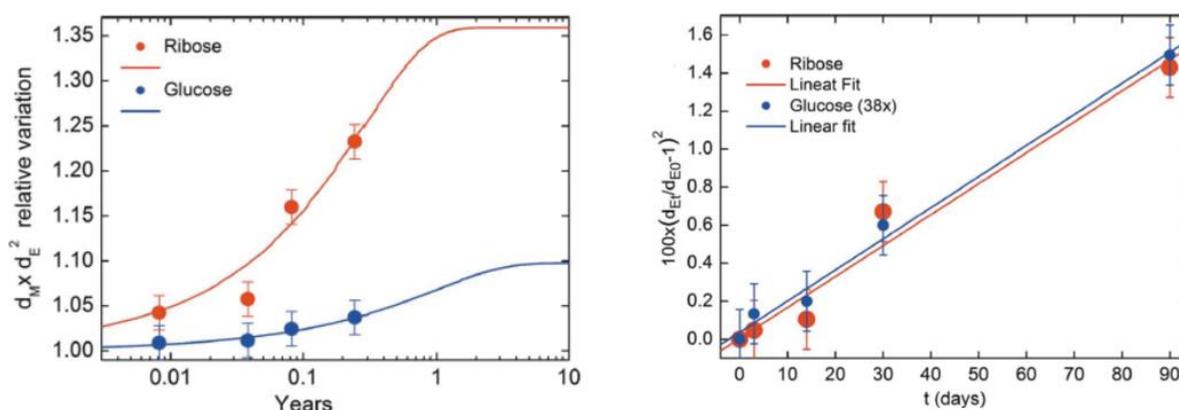


Fig. 1 Comparison between ribose and glucose in collagen glycation

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Refining Structures of Molecular Crystals through Modern Methods of Quantum Crystallography.

Alessandro Genoni.^a

Quantum crystallography is an emerging field of science having the goal of investigating properties and phenomena of the crystalline state that can be explained only if one uses the laws of quantum mechanics.¹ To accomplish this task, several methods have been developed over the years.² They range from the traditional multipole model techniques for the determination of experimental electron densities through X-ray diffraction data to the more recent X-ray restrained wavefunction (XRW) approach and Hirshfeld atom refinement (HAR) strategy, which are characterized by a stricter relationship with the methods of quantum chemistry.³

In this presentation, the focus will be on the Hirshfeld atom refinement,⁴ a technique that requires a quantum chemical calculation at each step of the procedure and that, using only X-ray diffraction data, allows the determination of hydrogen atom positions with the same precision and accuracy usually attained by means of neutron diffraction measurements. After a general introduction on the main features and capabilities of HAR, recent methodological advancements in this research field will be presented and discussed.

First of all, we will consider the extension of HAR to large molecules (e.g., macromolecules of biological interest) through its coupling with libraries of extremely localized molecular orbitals (ELMOs),⁵ namely with databanks of molecular orbitals that are strictly localized on small molecular fragments (i.e., atoms, bonds and functional groups) and that allow instantaneous reconstructions of wavefunctions and electron densities of biosystems. The validation tests of the recently proposed HAR-ELMO method on small polypeptides and proteins will be shown and analyzed in detail.⁶

In the second part of the talk, we will consider the coupling of HAR with the new multiscale embedding technique QM/ELMO,⁷ a quantum chemistry approach where only the chemically relevant region of the examined system is treated at fully quantum mechanical level, while the remaining part is described through transferred and frozen extremely localized molecular orbitals. In this context, we will present the development of the novel HAR-QM/ELMO strategy and we will show how the method has been already successfully exploited to accurately refine structures of molecular crystals characterized by strong intermolecular interactions.⁸

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From crystallography to physical properties: what the second harmonic generation property is due to?

Domenica Marabello,^{a,*} Paola Antoniotti,^a Paola Benzi,^a Carlo Canepa,^a Elena Cariati,^b Alma Cioci,^a Leonardo Lo Presti.^b

For many years, our research has been focused on saccharide derived Metal Organic Frameworks (MOFs) with SHG properties and their potential applications as biosensors, because of their high biocompatibility, their lack of inversion symmetry in the crystal structure that induces the SHG properties, and their attitude to complex metal cations and pull polarizable anions into the structure. Several $M(\text{sugar})_nX-2$ complexes ($M=\text{Ca}, \text{Sr}$; sugar=D-fructose, 2-deoxy-D-galactose, ribose; $X=\text{Cl}, \text{Br}, \text{I}$) were synthesized and their SHG behaviors were experimentally and theoretically studied, in order to elucidate the influence of different cations and/or anions and/or sugar and/or of their different spatial disposition in the crystals on the SHG behavior.¹⁻⁴

In order to better correlate the second harmonic emission with the nature and structure of the materials, theoretical calculations were carried out with two different computational approaches, that represent the two extremes in which the real crystalline powders lie. The calculated first-order static hyperpolarizability and second-order susceptibility were compared with the experimentally measured SHG intensities.

The same approach was applied to a second class of complexes, the metal porphyrinates of formula $M\text{-TPP}$ ($M=\text{Co}, \text{Cu}, \text{Ni}, \text{Zn}$, TPP=5,10,15,20-tetraphenylporphyrine). These compounds show a peculiar SHG behavior: the initial efficiency was very low, but surprisingly, under laser irradiation, it gradually increased reaching after few minutes a plateau at a value about fifty times with respect to the initial one. Preliminary results on the efforts to understand this phenomenon will be reported.

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Porous and luminescent coordination complexes and networks assembled from a new ligand of nanometric length.

Delia Blasi,^a Silvio Quici,^b Simonetta Orlandi,^b Pierluigi Mercandelli,^a Eugeny V. Alexandrov,^c Lucia Carlucci.^{a,*}

In our continued interest and search for new functional Coordination Networks (CNs)^{1,2} we have designed and synthesized a new ligand containing the β -diketone fragment in the center and peripheral nitrile groups at nanometric distance (HL) (Fig. 1a). In the solid state HL adopt a helical arrangement and crystallize in the acentric space group Cc . The coordination ability of HL towards different metals is exploited through both the diketone and nitrile groups.

In particular, the reaction with Ag(I), which has great affinity to nitrile donors, allowed to isolate and characterize the two highly interpenetrated 2D CNs, $[Ag(HL)_2](CF_3SO_3)$ (**1**) and $[Ag(HL)_2](NO_3) \cdot 3H_2O$ (**2**). Structural analyses show the presence, in both compounds, of similar layers of **sql** topology (Fig. 1b) whose large rhombic windows enable the realization of high degree of interpenetration (Z) of 7 and 8 for **1** and **2**, respectively (Fig. 1c). These are the highest value of Z reported so far for **sql** networks. The different Z is correlated to the conformational steric hindrance of the ligand, rather than to the size of the rhombic windows or to the nature of the counterions. To unveil the effect of interpenetration on the properties of the two compounds, we are investigating their photoluminescence and gas adsorption behaviour.

Reactivity of HL with different M(II) and M(III) metal ions is also under investigation and the results, comprising 3D networks and metal complexes, will be also presented.

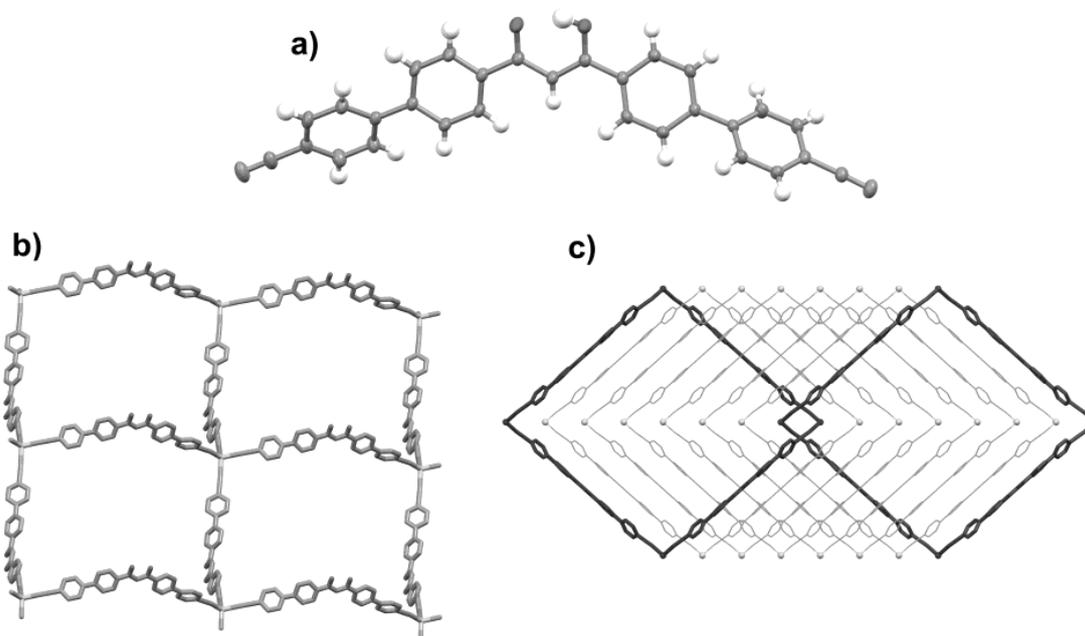


Fig. 1 a) Ortep view of the ligand HL; b) a single sql layer of **1**; the 7-fold interpenetration in **1**.

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Cocrystallization as effective tool for driving the release of natural active compounds.

Michele Prencipe,^{a,*} Paolo P. Mazzeo,^{a,b} Bruno Famiani,^a Matteo Masino,^a Alessia Bacchi.^{a,b}

The use of pesticides for chemical treatment of plants and soil is still an alarming issue since contributes to the accumulation of harmful by-products in the environment.¹ Some of most sustainable and effective alternatives have been found in essential oil (EOs), which are natural compounds based on terpenoids and directly produced by plants. EOs have been shown antibacterial, antifungal and insecticide effects, but their physical properties, such as low melting point and high volatility, have limited their application in agrochemical industry.

Cocrystallization has proved to be a practical solution for tuning the physical properties of EOs,² giving new crystalline materials with an enhanced thermal stability and able to deliver the active compounds in a more prolonged way. Cocrystals are indeed multi-component crystalline compounds obtained by the interaction of two or more different molecules, called coformers, in a defined stoichiometric ratio. However, the coformers often have just played a role of “co-builders” of a new crystalline scaffold, remaining their molecular properties untapped for further applications.³

The purpose of this work is thus to exploit cocrystallization to drive the release of EOs and control their availability. We here report an example of cocrystal, prepared through a mechanochemical reaction, where the release of the active component is triggered by an external stimulus and monitored along the time. To this end, X-ray powder diffraction (XRPD) and UV-vis measurements were performed before and after the triggering and were compared between the individual conformer and its cocrystal. Raman spectra were also collected using micro-focused laser on single crystals samples. At last, physical properties of the cocrystal and coformer were opportunely described by calorimetric measurements (DSC) and further characterized with single crystal X-ray diffraction (SCXRD).

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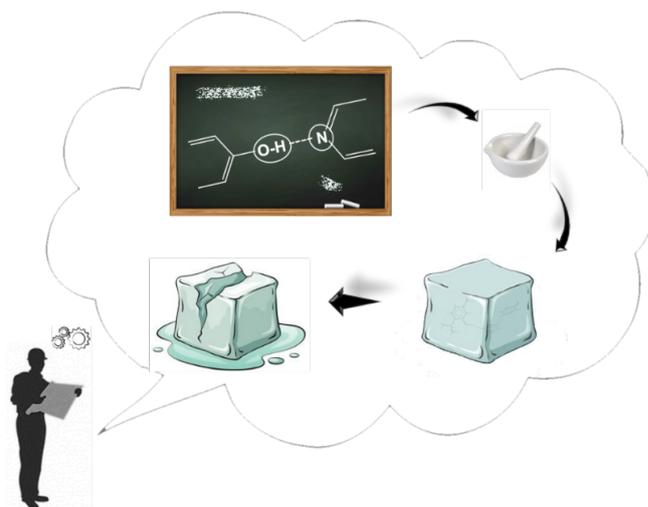


Fig. 1 Design of cocrystals for driving the release of active molecules.



Crystal Engineering as a tool for rational design of novel sustainable food, agrochemical and pharmaceutical formulations.

Elena Simone,^{a,*} Lorenzo Metilli,^b Panayiotis Klitou.^c

Recent progress in pharmacology, plant biology and biotechnology has led to a dramatic increase in potency and specificity of new generation drugs, active agrochemical ingredients and food nutraceuticals. Unfortunately, this has been accompanied by poor bioavailability and water solubility: it is estimated that around 40% of the active pharmaceutical ingredients currently on the market and 60% of the ones still in development are poorly soluble due to their high molecular weight and structural complexity. These issues have pushed scientific research towards the design of complex formulations, with enhanced dissolution rate and bioavailability, which allow more efficient and targeted delivery of active ingredients (AIs). Multiphase systems (e.g., emulsions, foams, creams) are a convenient and effective encapsulation and delivery strategy, particularly for oral and topical formulations. Currently, synthetic excipients, surfactants and specialty polymers are used to create formulations with enhanced properties. However, these compounds are derived from non-renewable resources through some of the most greenhouse gas-intensive manufacturing processes. For this reason it is now necessary to replace the common synthetic stabilizers used for these products with natural, biocompatible and biodegradable materials. These include natural micro and nanoparticles (Pickering stabilizers) such as proteins, polysaccharides and various crystalline materials including cellulose, chitin, fat crystals and polyphenol crystals.

Pickering systems are particularly promising since particles adsorb at interfaces more strongly than surfactants, providing significantly more stable formulations. The stability of Pickering systems is strongly affected by particle size and shape, but surface wettability is the most important property of Pickering particles. For faceted, anisotropic crystals surface wettability is not easy to determine. In fact, crystals present multiple crystallographic facets, whose surface properties (e.g., polarity, wettability) depend on the type and directionality of the intermolecular interactions that characterize each facet.

The purpose of the presented work is to understand how crystal properties (size, shape and polymorphism) of Pickering particles affect their surface properties, hence their orientation and adsorption behaviour at interfaces.¹⁻⁵ Molecular modelling (synthons analysis from crystallographic data) and experimental work (e.g., characterization using benchtop and synchrotron X-ray techniques, thermal studies, stability studies) were conducted on two model systems: quercetin and cocoa butter.

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MOVPE of III-V materials: the (neglected) role of surface dynamics and its potentials for next generation devices and integration.

Emanuele Pelucchi,^{a,*} Ayse Ozcan-Atar,^a Agnieszka Gocalinska,^a

Over the last ~50 years, semiconductor epitaxy has shaped our high-tech society. While several epitaxial growth technologies have been successfully used for decades, few have been utilised industrially and are implemented for large-scale, high-volume applications. Metalorganic Vapor Phase Epitaxy (MOVPE) is one of these well-established technologies, underpinning the majority of III-V semiconductor device fabrication (especially in photonics), and underlying key developments not only for III-Vs, but also III-Ns for lighting and power solutions.

Despite the broad technological use of MOVPE, there still persist a large number of fundamental unresolved issues. These are tightly tied to a lack of understanding of the complexity of the epitaxial process and dynamics, and, as a result, are effectively limiting a broad range of further device developments. Here we will discuss ~20 years of research and related results which importantly contributed to establish the current understanding, starting from highlighting the relevance of metalorganic precursors for growth on planar and patterned substrates.^{1,2} We will highlight the surprising “zoology” of the reported surface organization and underline the need for proper theoretical modelling, including describing unexpected surface organization paths, such as Volmer-Weber dot formation at the lattice matched InP/AlInAs interface.³

We will also present novel results on surfactant physics, including presenting clear evidence that one of the main device design limiting factors in today’s MOVPE processes (i.e. Zn diffusion complicating P-I-N device stacking) actually is not often linked to “*crystallographic*” diffusion but indeed induced by surfactant effects.⁴

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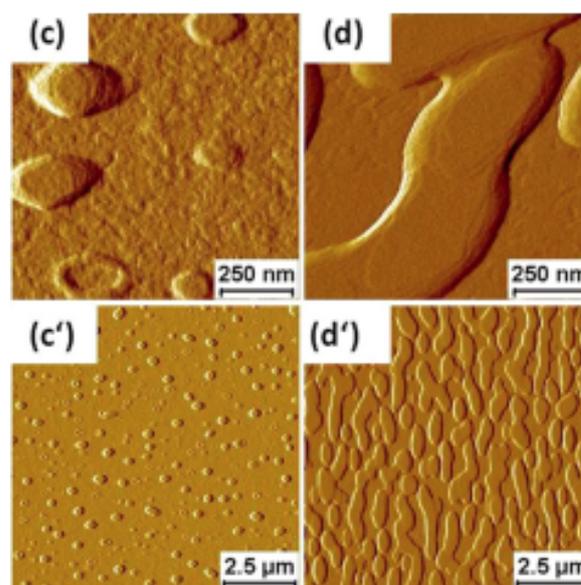


Fig. 1 Representative examples from ³ (AFM) of Volmer-Weber physics in the lattice matched InP/AlInAs system. Panels c,d are obtained with different InP coverage. In lower panels a larger area was scanned

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Monitoring Chemical Processes in (Photo)Catalysts and Energy Storage Materials by Operando X-Ray Absorption Spectroscopy.

Arčon Iztok.^{a,b}

X-ray absorption spectroscopy (XAS) is a powerful tool for characterisation of local structure and chemical state of selected elements in different new functional materials and biological or environmental samples. The XAS spectroscopy is based on extremely bright synchrotron radiation X-rays sources, which allow precise characterisation of bulk, nanostructured or highly diluted samples. The rapid development of extremely bright synchrotron sources of X-ray and ultraviolet light in recent years has opened new possibilities for research of matter at the atomic or molecular level, indispensable in the development of new functional nanostructured materials with desired properties. The talk will present the possibilities offered by X-ray absorption spectroscopy with synchrotron light for ex-situ or operando characterization of various functional porous and other nanomaterials, before, after and during their operation.¹⁻⁴. New generation of synchrotron light sources also opened the possibility of combining X-ray absorption with high-resolution emission⁵ and inelastic scattering spectroscopy,⁶ and microscopy with sub-micron resolution.⁷ Examples of operando XANES and EXAFS analysis to track changes in the valence states and local structures of selected elements in different energy storage materials and in various (photo)catalysts, during chemical reactions under controlled reaction conditions, will be presented, which provided insight into the dynamic functional properties and reaction mechanisms of these materials. Access to SR facilities of Petra III (beamlines P65, P64 and P01), ESRF (beamlines BM23, ID21, ID26) and Elettra (beamlines XAFS, XRF), for the presented research is kindly acknowledged.

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Kinetic-control of morphology and composition during the 3D growth of semiconductor nanostructures.

Roberto Bergamaschini.^a

Growing three-dimensional epitaxial nanostructures opens a new world of opportunities, unique properties and novel designs for next-generation semiconductor devices. However, the increased complexity and wide variability of parameters to be controlled in order to achieve the desired structures demand for an in-depth understanding of the growth mechanism. In particular, the morphology of the growing crystal stems from the interplay of either thermodynamic and kinetic driving forces, whose relative strength depends on the actual growth conditions and is strongly influenced, if not directly templated, by the substrate geometry and patterning. Moreover, in the case of alloys, the local composition tightly binds to such a dynamics, frequently resulting in different faceting and/or segregation effects. The development of reliable growth models and simulations comprising all of these physical contributions is then of great value for the characterization of growth experiments and to restrict the parameter space for targeting a desired outcome. Here we present a growth model based on a phase-field approach,¹ including both deposition and surface diffusion dynamics, and allowing for the modeling of morphological and compositional evolution in single-component and alloyed materials on different substrate geometries. First, the faceted growth of ring-like structures,¹ as obtained experimentally by selected-area epitaxy, will be analysed. The different role of anisotropic surface energy density, orientation-dependent incorporation rates and nonuniform deposition fluxes in determining the crystal shape will be investigated. In particular, it will be discussed how the behavior of convex and concave regions reveals the dominance of thermodynamic or kinetic contributions. Then, the case of alloyed core-shell nanowires will be inspected as a peculiar example of kinetically-coupled morphology-composition dynamics. In particular, the occurrence of segregation in Ge-GeSn² and GaP-Si-SiGe(hex.)³ core-shell nanowires will be discussed and related to the deposition-vs-diffusion ratio.

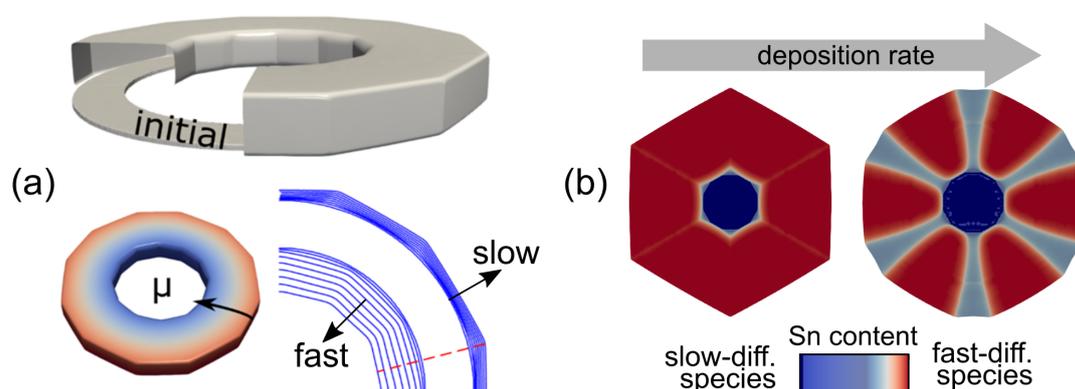


Fig. 1 (a) Growth simulation of an InP faceted ring-like crystal. (b) Shape and composition cross-sectional profiles of a Ge-GeSn core-shell nanowire for different deposition rate.

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Defects characterization of GaN heteroepitaxial growth wafer using nSPEC images vs ECCI.

Domenico Mello,^{a,*} Andrea Severino,^a Nicolò Piluso,^a Giuseppe Sciuto,^a Giuseppe Anastasi,^a Roberta Ricciari,^a Antonio Burtone.^b

The new challenges of the green economy are related at high efficiency power converters for energy efficiency, electrical mobility and connectivity high speed (5G). These applications required new technological approach and new and more efficient materials on which to develop these devices. Wide band gap materials are becoming increasingly important for their characteristics and the excellent performance that can be achieved in power devices. In particular, SiC and GaN are attractive materials for power devices owing to superior physical properties, such as its high breakdown electric field strength, high electron mobility, and low anisotropy.¹

The GaN technology is quite mature, but the new challenges are large-diameter bulk growing, in that case, both SiC and GaN power devices will be widely employed for the high performance and low cost. However, cost-effective heteroepitaxial growth of GaN goes along with high defect densities as compared to a pure GaN based approach. Clarifying the role of defects in terms of their impact on device performance and reliability needs to fulfill several requirements when aiming for an overall technology improvement. The development of an understanding of how they form, what consequences they have on local material properties as well as the relation of this knowledge to the behavior of devices and the ability to detect defects it appears fundamental. Especially the last point is very difficult to accomplish from an experimental point of view when high densities of defects are involved and many of them are superficial without any consequence for the device.²

Many inspection tools have been developed to be able to try to identify and classify this type of defects (eg. KLA Candela,³ nSpec,⁴ Altair,⁵ etc.) but all based on optical or surface scattering inspections. It is not easy to characterize the defects detected by these tools by electron microscopy due to the difference in the nature of the image Electron Channeling Contrast Imaging (ECCI) is a Scanning Electron Microscopy (SEM) technique that allowing to observe a variation in the periodicity of the sample lattice using electron backscattering (EBS) detector. Normally in typical BSE image, three kinds of contribution at the contrast can be observed. The main contribution is given by Z-contrast, the second is given by surface topography the smallest contribution is given by Channeling contrast. When well-collimated electron beam is aligned with crystal zone axis increase the likelihood of electron channeling and the third contribution became prevalent.⁶

In this paper we start from some unknown with spots not yet classified coming from optical inspection in dark field mode on a GaN Epy-Layer to reach a defect characterization by Transmission Electron Microscopy (TEM) using ECCI technique to identify the points. In particular, the methodology to identify the area of analysis, the ECCI results and the TEM photo are detailed described.

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Direct-ARPES and STM Investigation of FeSe Thin Film Growth by Nd:YAG Laser.

Sandeep Kumar Chaluvadi,^{a,*} Shyni Punathum Chalil,^a Federico Mazzola,^a Debashis Mondal,^a Chiara Bigi,^a Jun Fujii,^a Giancarlo Panaccione,^a Giorgio Rossi,^{a,b} Ivana Vobornik,^a Pasquale Orgiani.^a

Research on ultrathin quantum materials requires full control of the growth and surface quality of the specimens in order to perform experiments on their atomic structure and electron states leading to ultimate analysis of their intrinsic properties.^{1,2} We report results on epitaxial FeSe thin films grown by pulsed laser deposition (PLD) on CaF₂ (001) substrates as obtained by exploiting the advantages of an all-in-situ ultra-high vacuum (UHV) laboratory allowing for direct high-resolution surface analysis by scanning tunneling microscopy (STM), synchrotron radiation X-ray photoelectron spectroscopy (XPS) and angle-resolved photoemission spectroscopy (ARPES) on fresh surfaces. FeSe films are optimized via PLD growth protocols and were fine-tuned by optimizing target-to-substrate distance d and ablation frequency, atomically flat terraces with unit-cell step heights are obtained, overcoming the spiral morphology often observed by others. In-situ ARPES with linearly polarized horizontal and vertical radiation shows hole-like and electron-like pockets at the Gamma and M points of the Fermi surface, consistent with previous observations on cleaved single crystal surfaces. The control achieved in growing quantum materials with volatile elements such as Se by in-situ PLD makes it possible to address the fine analysis of the surfaces by in-situ ARPES and XPS. The study opens wide avenues for the PLD based heterostructures as work-bench for the understanding of proximity-driven effects and for the development of prospective devices based on combinations of quantum materials.

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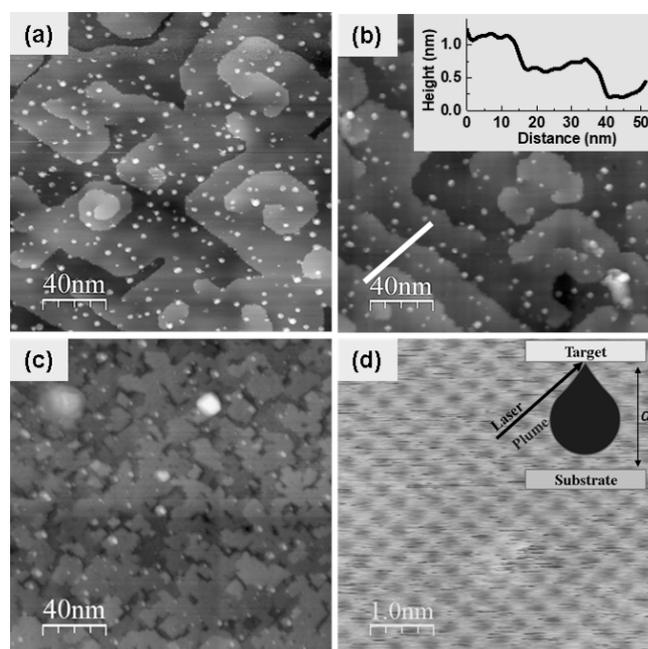


Fig. 1 Substrate to target distance d dependent in-situ morphological studies of FeSe films by STM³

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Observing Nanomaterials in Action Using Synchrotron Radiation.

Jasper Rikkert Plaisier,^{a,*} Lara Gigli,^a Mattia Gaboardi.^a

Exactly 15 years ago, in September 2007, the beamline MCX (Material Characterisation by X-ray diffraction) was officially inaugurated at the Italian synchrotron facility, Elettra – Sincrotrone Trieste. The powder diffraction beamline was designed to study nanostructured materials, investigating details of crystalline domain size and shape, lattice defects, and local atomic displacement of static and dynamic nature using Line Profile Analysis (LPA).¹ However, the flexible set-up of the experimental station² allows for a wide variety of diffraction experiments in different fields ranging from phase identification in cultural heritage to operando battery studies in energy research, and from residual stress analysis in engineering to structure determination of new pharmaceuticals. Furthermore, the beamline is equipped with a specially designed furnace that allows to perform temperature dependent studies under controlled conditions.³

Thanks to this flexible experimental set-up, MCX has not only hosted experiments to fully characterize nanostructured materials, but has also been the place to study these type of materials in action. Here, some recent results obtained at the beamline from these *in situ* and *operando* studies will be presented. These include the structural evolution of nanostructured materials, chemical reactions inside nanoparticles and the effect of nanostructures on catalytic reactions and battery performance.

Currently, within the scheme of the upgrade of Elettra, MCX is preparing for a major upgrade of the beamline. This will already start in 2023 with the installation of a brand new 3-circle diffractometer with a Mythen-II detector covering $120^\circ 2\Theta$. This upgrade will have a major impact on the type of experiments addressed here. Therefore, also the future prospects for studying nanostructured materials in action will be discussed.

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It is just a matter of surfaces: how multidimensional (nano)modifications can modulate neuronal network activity.

Denis Scaini,^{a,b,c,*} Laura Ballerini.^a

In the past decade, (nano)technology applications to the central nervous system have often involved studying and using novel materials to modulate neuronal activity. The ability to govern neuronal excitability could have a significant impact not only on fundamental neurophysiology but in developing therapeutic approaches to treat neurological diseases. Surface (nano)modification via carbon-based nanomaterials (CBNs) was demonstrated to have a pivotal role in neuromodulation. In particular, we have shown that 2D and 3D materials functionalized with graphene¹ or carbon nanotubes^{2,3} are fully biocompatible and, remarkably, able to induce in cultured neurons an increased network synaptic activity via the combined effect of their physicochemical and morphological properties.

In this regard, we discovered that neuronal network activity is modulated by the synergic contribution of the nanomorphology, chemical activity, and local mechanical compliance possessed by the surface interfacing the neuronal cells. This multimodal surface modification could be used to recapitulate the different cues provided by the extracellular matrix (ECM) to neurons within the central nervous system. By growing neuronal cells on/within 2D/3D supports and measuring the electrical activity by patch-clamp recordings, we demonstrated how neuronal activity could be modulated by different surface modifications opening the possibility of orchestrating the firing activity of the entire neuronal network.

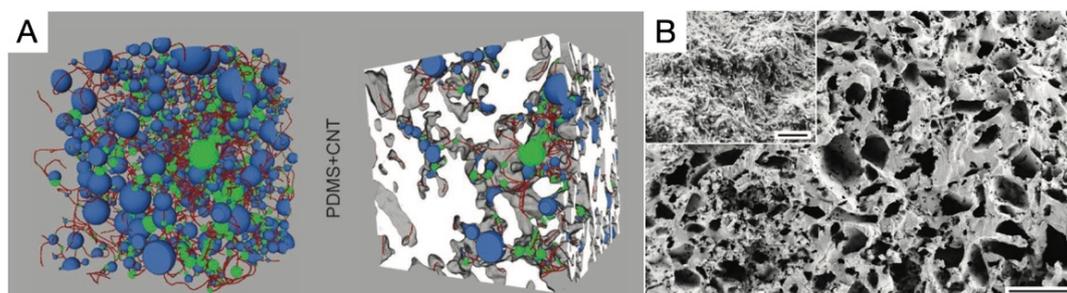


Fig. 1 (A) μ CT volumetric reconstructions of a nanomodified porous scaffold. In blue and green, the maximal filling sphere for pores and throats, in red the interconnection path, and in white the scaffold's matrix. (B) SEM image of a PDMS+CNT scaffold slice showing macroscopic porous morphology. In the top-left inset, the carpet of MWCNTs decorating pores' walls. Scale bars: 100 μ m and 1 μ m, respectively.

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A Multidisciplinary Approach to Unveil the Structural Arrangement of Deep Eutectic Solvents: from Local Order to Nano-scale Organization.

Matteo Busato,^a Valerio Di Lisio,^a Alessandra Del Giudice,^a Alessandro Tofoni,^a Giorgia Mannucci,^a Francesco Tavani,^a Valentina Migliorati,^a Andrea Martinelli,^a Mauro Giustini,^a Alessandra Gentili,^a Paola D'Angelo.^a

Deep eutectic solvents (DESs) deal with mixtures of two or more compounds which, for a well-defined molar ratio, display a unique and minimum melting point that is lower than the ideally predicted one, allowing the achievement of a liquid phase even from solid starting materials. This behavior relies on the extensive interplay among the components, so that it has become evident that DESs are high-entropic systems with tens of punctual interactions ruling the overall chemical-physical properties. This complexity makes the achievement of a clear picture about the structural arrangement of these materials a fundamental knowledge to understand their macroscopic behavior and ultimately promote their applications.

In this work, we demonstrate how a multidisciplinary approach combining X-ray absorption spectroscopy (XAS), small- and wide-angle X-ray scattering (SWAXS), UV-Vis, attenuated total reflection Fourier transform infrared (FTIR), and near-infra-red (NIR) spectroscopies with molecular dynamics (MD) and *ab initio* simulations is a powerful strategy to unveil the structural arrangement of DESs and their mixtures with co-solvents (i.e., water, methanol) ranging from short- to intermediate-scale levels. More specifically, we focus on the eutectic formed by choline chloride (ChCl) and sesamol in 1:3 molar ratio and on the metal-based deep eutectic solvent (MDES) formed by $NiCl_2 \cdot 6H_2O$ and urea in 1:3.5 molar ratio. In the former system, the employed techniques were able to detect a nano-phase segregation between water pools confining most of the ChCl and sesamol-rich domains (Fig. 1a), which is formed for high water contents,¹ differently from methanol addition.² In the $NiCl_2 \cdot 6H_2O$:urea 1:3.5 MDES, we observed a close packing of Ni^{2+} ion clusters forming oligomeric agglomerates thanks to the mediation of bridging chloride anions and water molecules [3]. Conversely, urea acts as a sort of “inner solvent” owing to the formation of nanostructures intercalating the Ni-rich regions (Fig. 1b). This arrangement is disrupted upon the introduction of additional water, diluting the system up to an aqueous solution of the MDES constituents. In this way, our digression from shorter to larger lengths allowed the achievement of an all-round picture able to clarify the structural arrangement of these inherently complex systems.

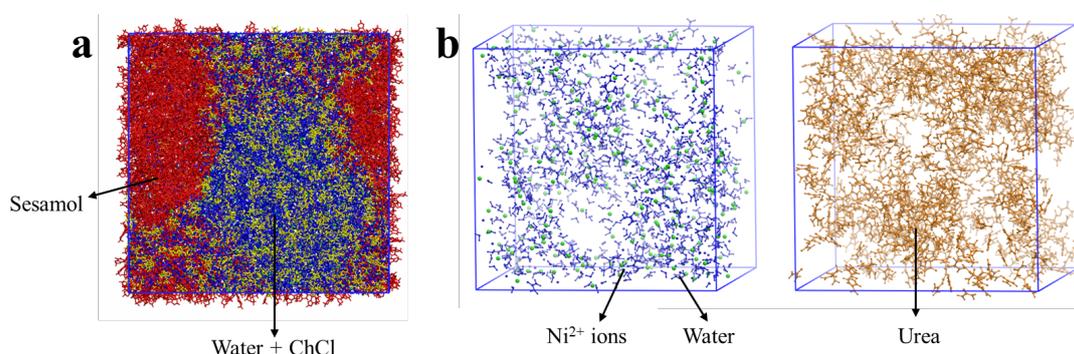


Fig. 1 Nano-scale structures formed in the ChCl:sesamol 1:3 (a) and $NiCl_2 \cdot 6H_2O$:urea 1:3.5 (b) DESs.

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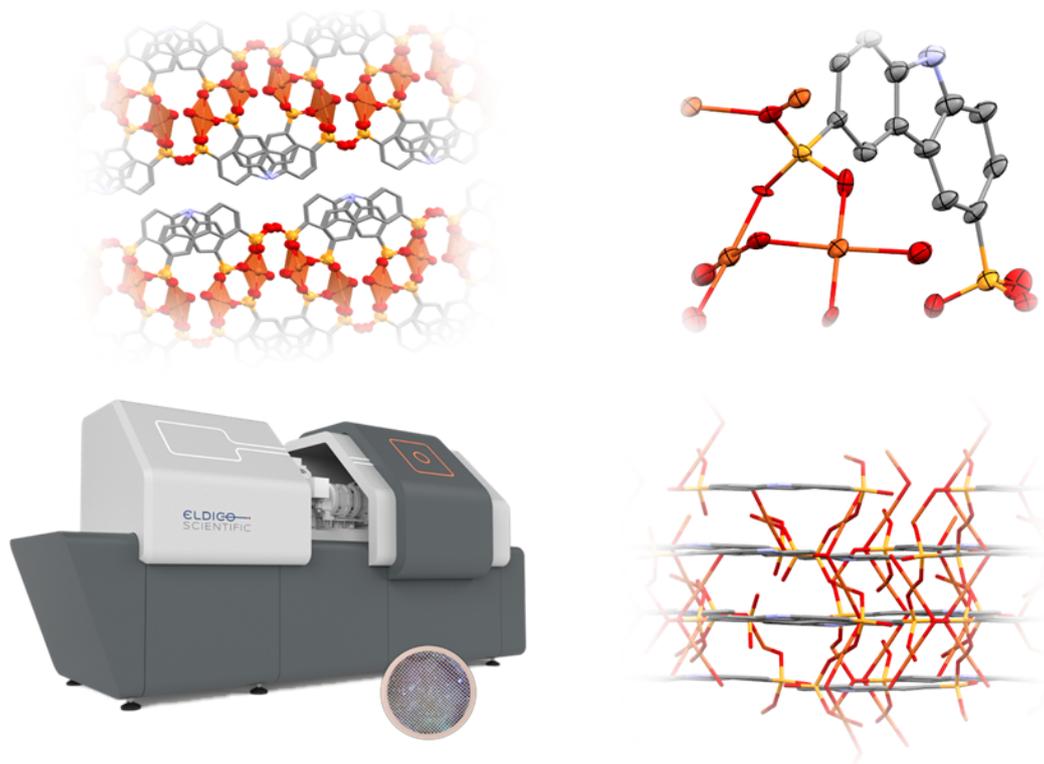
Structure Determination of Nanocrystalline MOFs Using Electron Diffraction.

Christian Jandl,^a Johannes Merkelbach,^a Danny Stam,^a Gunther Steinfeld,^a Eric Hoverstreydt,^{a,*} Gustavo Santiso-Quinones.^{a,*}

Electron diffraction (3D-ED, MicroED) is gaining more and more momentum as a technique for the structural elucidation of challenging compounds as it bypasses the main limitation of growing crystals of suitable size for single-crystal X-ray diffraction. As such it has already found applications in all fields of research from organic and inorganic compounds, over polymorphism, pharmacology, natural products, geological sciences, biomolecules, materials science to energy-storage materials and others.

As porous materials commonly obtained from solvothermal synthesis MOFs often pose a challenge for traditional X-ray crystallography as their inherent properties do not allow for a recrystallisation, which makes structural analysis dependent on obtaining suitable single crystals straight from the synthesis. Being able to use nanocrystalline as synthesized material makes electron diffraction the perfect tool to tackle this problem and determine structures from crystals that are too small even for synchrotron facilities.

We show a range of examples from recent literature measured on our ED-1 electron diffractometer demonstrating the reliability and potential of 3D-ED for applications in the field of porous coordination compounds and benefits of a dedicated electron diffractometer.



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Insights into dissipative and oscillatory chemical reactions by combining X-ray absorption and NMR/UV-Vis spectroscopies.

Francesco Tavani,^{a,*} Federico Fratello, ^a Marika Di Berto Mancini,^a Daniele Del Giudice,^a Matteo Busato,^a Giorgio Capocasa,^a Osvaldo Lanzalunga,^a Stefano Di Stefano,^a Paola D'Angelo.^a

Chemical reactions mainly occur in solution and the use of different techniques to monitor the advancement of a chemical process in the liquid phase is often a powerful tool to gain a satisfactory understanding of the underlying reaction mechanism. Among the spectroscopic techniques that have been applied to follow chemical reactions occurring in solution, X-ray absorption spectroscopy (XAS) is a unique method that allows one to follow the variations in both the local electronic and structural configuration of a selected photoabsorbing atom. An advancement of this experimental approach is to combine XAS with ¹H-NMR and/or UV-Vis spectroscopies. Indeed, XAS and the conventional spectroscopic methods can be considered complementary. On the one hand, XAS allows one to quantitatively monitor the evolution of species often silent to conventional detections with an unrivaled degree of accuracy. On the other hand, the fate of the organic components of the reaction, namely ligands and reagents, can be tracked by ¹H-NMR/UV-Vis measurements. Notably, a multivariate and theoretical analysis of the XAS data may further complement the information acquired on the chemistry of the given reactive system.

In this presentation, we apply our method to gain a comprehensive view on: (i) a prototypical reaction involving the dissipative translocation of the Zn(II) cation from two different organic ligands (see Figure 1)¹, and (ii) the evolution of the main Bromine-related species during the classic cerium ion catalyzed Belousov-Zhabotinskii reaction.²

Through our combined experimental and theoretical approach we gain insights into the nature, concentration time evolution and structures of the key metal and non-metal reaction species. Our method may prove to be useful in the toolbox necessary to reach a full mechanistic picture of reactive processes in solution.

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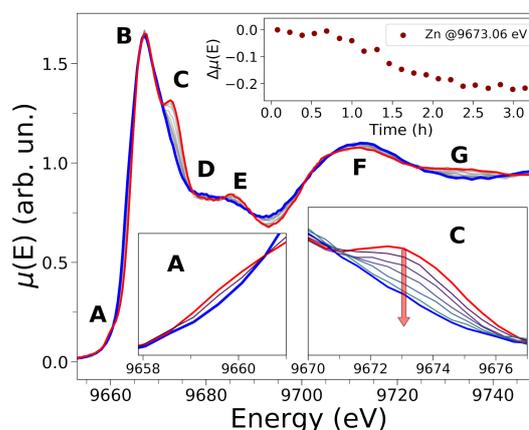


Fig. 1 Time evolution of the Zn K-edge XANES spectra measured during the dissipative translocation of the Zn(II) cation between the hexaaza-16-crown-8 and terpyridine ligands.

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Exploring anisotropic growth conditions of hydrophilic gold nanorods.

Simone Amatoria,^a Alberto Lopez,^a Chiara Battocchio,^a Iole Venditti,^a Giovanna Iucci,^a Cassandre Boixeda,^b Carlo Meneghini.^a

In the past 20 years gold nanorods (AuNRs) gained popularity within the nanomaterials field also thanks, among the several valuable properties, to the tunability they provide with a two-component surface plasmon resonance (SPR), associated respectively to the Transversal and Longitudinal components of the plasmon which, in turn, are related to the specific dimensions and aspect ratio obtained. These systems are suitable for several applications ranging from optoelectronic and sensing to drug delivery.^{1,2} The AuNRs seed-mediated synthesis relies on a complex and delicate equilibrium of reactants to achieve anisotropic growth conditions: silver ions and a surfactant agent show preferential adsorption onto specific facets of gold and hinder reduction in these directions in presence of a weak enough reducing agent.³ In this framework we synthesized AuNRs using silver nitrate and cetyl-trimethyl-ammonium-bromide (CTAB) with either Ascorbic Acid or Hydroquinone as a reducing agent, and carefully characterized with complementary laboratory techniques (Uv-Vis-NIR, FTIR, DLS, XPS, TEM/SEM). The AuNRs were further investigated by XAFS, being a chemical selective and local atomic structure probe, to specifically describe the local coordination chemistry of Au, Ag and Br ions.⁷ Emphasis has been placed to understand the Ag and Br (from CTAB) local atomic structure to clarify the interfacial structure of these AuNRs, as being composed by both metallic gold and silver, alongside bromide atoms that stabilize the overlying multilayer of surfactant molecules.

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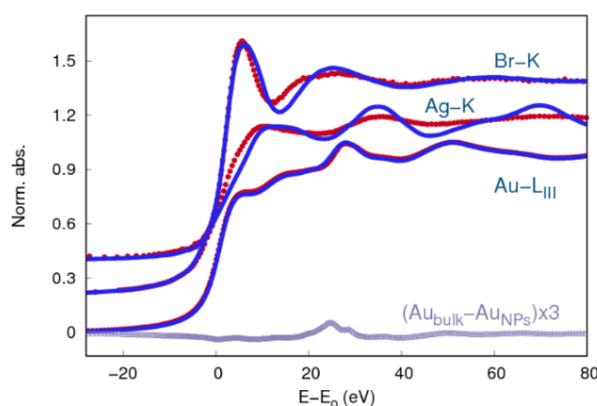


Fig. 1 Au-L_{III}, Ag-K and Br-K XANES spectra measured on AuNRs (red points) compared with those measured on reference compounds (blue lines). Ag and Br, being located at the NP surfaces depict the largest differences respect to the bulk reference compounds.

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Crystal Structure Study of Manganese Hexacyanoferrate Cathode Material in Organic Na-ion Battery by using XAS and XRD.

Min Li,^{a,*} Mattia Gaboardi,^b Angelo Mullaliu,^{c,d} Mariam Maisuradze,^a Giuliana Aquilanti,^b Jasper Rikkert Plaisier,^b Stefano Passerini,^{c,d} Marco Giorgetti.^a

Manganese Hexacyanoferrate (MnHCF) as promising electrode material has been widely used as cathode in organic Na-ion batteries, and displaying large specific capacity (>130 mAhg⁻¹) and high discharge potential.¹ However, the phase and structure changes of MnHCF associated with the electrochemical reaction, especially the Jahn-Teller (JT) distortion of Mn-sites during the charge process, result in the lower cycling stability. As we reported previously, the X-ray diffraction (XRD) and X-ray absorption spectroscopy (XAS) results demonstrate that a non-cooperative JT distortion of Mn sites was observed in Li-ion and Na-ion batteries of MnHCF.^{2,3}

In order to highlight the influence of framework of MnHCF on the stability of Na-ion battery, we synthesized two MnHCF samples with different vacancy content. The electrochemical result shown that the sample with lower vacancy content (4%) exhibits higher capacity retention (71.1%) after 100 cycles at C/5. Ex-situ XAS and ex-situ XRPD characterization provide insight into the different oxidation states of Metal-sites and the crystal structure change during cycling. We found that the sample with higher vacancy content (11%) exhibits a cooperative JT distortion during cycling, while which is confirmed that not favor to the cycling stability. Instead, the sample with lower vacancy content displayed an irreversible structure changes, and which result in higher cyclability.

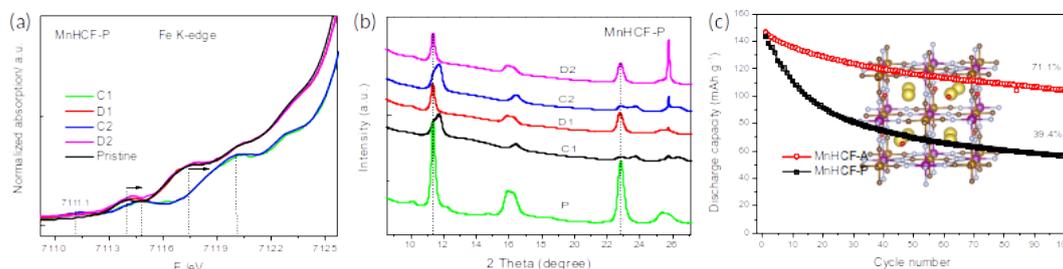


Fig. 1 (a) pre-edge peaks of the Fe k-edge of MnHCF-P; (b) ex-situ XRD patterns of MnHCF-P; (c) cycling stability of MnHCF-P/A at C/5 for 100 cycles.

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The Coronavirus Structural Taskforce.

Gianluca Santoni.^a

Keywords: coronavirus, structural biology, biocrystallography, cryo-em, validation

During the COVID-19 pandemic, structural biologists rushed to solve the structures of the 28 proteins encoded by the SARS-CoV-2 genome in order to understand the viral life cycle and to enable structure-based drug design. In addition to the 204 previously solved structures from SARS-CoV-1, over 2000 structures covering SARS-CoV-2 viral proteins have been released in a span of a 2 years. As structural models are available, researchers from different backgrounds use them as a basis for further analysis. Molecular dynamics simulations, docking studies and bioinformatics modelling are just an example of the possible use of those data. However, all modelling is prone to error and structural biology is not immune to that. I will present here the efforts of the Coronavirus Structural Task Force¹ a spontaneous gathering of scientists who tried to target the issue by fixing errors when possible, sharing our findings with the broader community and communicating about the culture of errors in structural biology. A few key findings, as well as a wider discussion about the role of open science in the current days will be the core of my presentation.

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Science with and for society: a crystallographic perspective.

Annalisa Guerri,^a Chiara Massera.^b

Promoting and divulging science at all levels of education is a fundamental part of scientific activity, not the least in the field of crystallography. For this purpose, during the ECM in Basel in September 2016 GIG3 – The General Interest Group on Education in Crystallography was launched. The main objectives of GIG3 are the creation of a network for the efficient coordination of common activities and of new projects, and ultimately increasing the awareness of the general public about the existence, utility and versatility of crystallography as a field of study and application. Moreover, one aspect of the mission of a scientific association also includes the promotion of a positive culture among the next generations of scientists in order to overcome inequality issues, being them of gender, racial, religious or any other.

This presentation will outline some of the past and ongoing activities of the Group, and, more in general, the challenges that science and education (considered in its widest sense) are currently facing in terms of trust and in promoting a shared culture of equality.

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The Power of Museums: the case of Crystallography in Parma.

Alessia Bacchi.^a

The International Council of Museums (ICOM) has declared its 2022 theme as ‘The Power of Museums’. This is declined in three lines:

- **The power of achieving sustainability:** Museums are strategic partners in the implementation of the Sustainable Development Goals of the United Nations. As key actors in their local communities, they contribute to a wide variety of Goals, which include fostering short-circuit and social economy and disseminating scientific information on environmental challenges.
- **The power of innovating on digitalisation and accessibility:** Museums have become innovative playing-grounds where new technologies can be developed and applied to everyday life. Digital innovation can make museums more accessible and engaging, helping audiences understand complex and nuanced concepts.
- **The power of community building through education:** Through its collections and programmes, museums thread a social fabric that is essential in community building. By upholding democratic values and providing life-long learning opportunities to all, they contribute to shaping an informed and engaged civil society.details.

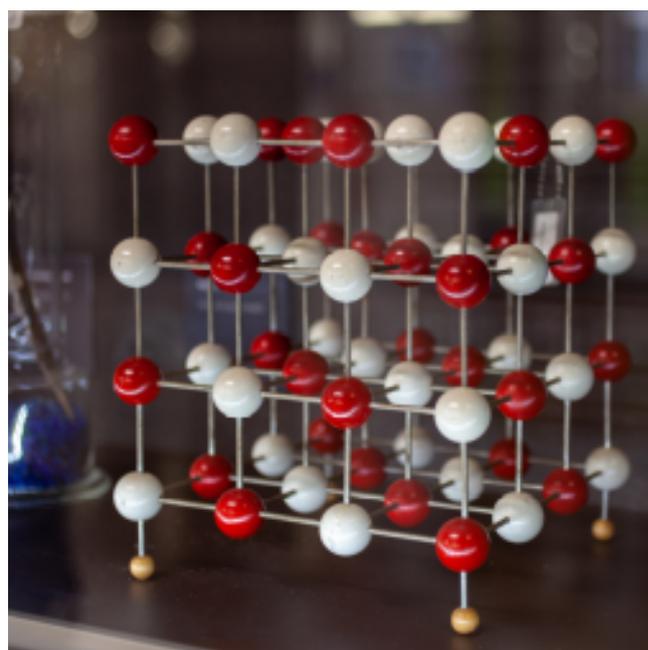


Fig. 1 Structural model of NaCl at the Museo di Cristallografica in Parma

These themes will be commented in the light of how crystallographic communication to the public can express these super-powers towards the society. Crystallography has in fact changed the way in which scientist see the material world, and this has migrated to the vision that people have of structures (Figure 1). The case of the Museum of Cristallografica at the University of Parma¹ will be taken as an example.

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STEM Learning Paths for High School Students.

Andrea Ienco,^{a,*} Renata Lapiska-Viola,^b Alberto Zanelli,^b Armida Torreggiani.^b

In the last few years, a series of learning paths for high school students from 16 to 19 years old has been tested thanks to a national network of researchers of the Italian National Research Council collaboratively working in the framework of national and European Projects targeted to youngsters.[1] The main goal is to increase the interest in STEM (science, technology, engineering and mathematics) disciplines, as well as the sustainable use of raw materials in view of the transition of a low carbon society. A combination of approaches such as open discussion, learning-by-doing, and peer-to-peer education have been used. The students are involved in an experiential learning process to develop communication competencies and increase their awareness about the role of science in sustainability development.¹

A “5E” protocol is followed. The activity starts with one or more lessons (ENGAGE), followed by the visit in a research laboratory (EXPLORE). The students will strengthen the topic knowledge by themselves through web searches or selected scientific papers (EXPLAIN) and produce a communication product (i.e. poster, video, etc.) (ELABORATE). At the end of the learning path, they are asked to present their work at school or during science fairs (EVALUATE).²

At the same time, a series of educational tools, created by experts, have been implemented and tested such as “RAWsiko – Materials Around Us”, a videogame on the distribution of critical raw materials in the world,³ “BetterGeo” a Minecraft mod that adds realistic geology to Minecraft, adding new rocks, minerals and metals, as well as realistic ways to find these⁴ and ecoCEO, a board game about circular economy strategies and circular business models.⁵



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The CrystalloGame.

Francesco Boni,^{a,*} Gabriele Princiotta,^b Elisa Fagnani,^c Emanuele Scalone,^c Monica Zoppé,^a Marco Tarini^b Mario Milani.^a

X-ray crystallography has been developed as the main experimental technique to investigate the 3D structure of proteins, giving knowledge at atomic resolution of the molecular details of macromolecules. Nevertheless, still many people even among the scientific community ignore the basic principles of X-ray crystallography that allow to use a diffraction pattern to build the electron density map used to derive a 3D model of a molecule.

Here we present *The CrystalloGame*, a prototype of puzzle-game based on the phenomenon of X-ray diffraction which proposes the main aspect of crystallography in a playful way.

This videogame is structured as a sequence of levels of increasing difficulty, each consisting of a puzzle to be solved. Actually, the videogame is equipped with an interface that allows the player to modify the 3D configuration of a crescent number of atoms in search of the correct spatial disposition that produces a given diffraction pattern. For this purpose, we developed an algorithm able to reproduce the interference pattern generated by a configuration of the atoms, simulating the real phenomenon with a certain approximation. The simulation is operated by a GPU software in order to guarantee the computational efficiency necessary for the execution in real time during the game. Many important aspects that characterize a real diffraction experiment are introduced in the videogame in form of *power-ups* available at different levels, for instance the possibility to modulate the X-ray wavelength, the ability to rotate a fixed atomic configuration and the introduction of atomic repetitions simulating a crystalline structure. The aim of this videogame is to guarantee a gradual understanding of the aspects underlying X-ray diffraction experiments and to stimulate the player to verify through direct experience how a diffraction experiment works.

Hopefully, *The CrystalloGame* will contribute to the dissemination and popularization of crystallographic sciences by fascinating a new generation of desirable future crystallographers.

We are grateful to the Associazione Italiana di Cristallografia for funding the creation of our prototype through “Fondo Mazzi 2020 per la divulgazione delle scienze cristallografiche”.

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New strategies and tools to fight antimicrobial resistance: A structural point of view.

Flavia Squeglia,^{a,*} Eliza Kramarska,^a Alessia Ruggiero,^a Zuzanna Drulis-Kawa,^b Rita Berisio.^a

Antimicrobial resistance (AMR) is a serious public health crisis worldwide. The excess and improper use of antibiotics is increasing the number of reported resistant microbial strains, compromising the conventional clinical treatments. The World Health Organization (WHO) has declared AMR a health emergency and has announced that the deaths attributable to AMR every year will be of 10 million in 2050, exceeding all the other major causes of death. To respond to AMR threat, an immediate action is required. Structural insights of key molecular players of AMR are fundamental for a deeper understanding of antimicrobial resistance and for the exploration of alternative therapeutic strategies. A group of six scary nosocomial pathogens is named with the acronym 'ESKAPE' because capable of 'escaping' the biocidal action of antibiotics classified as highly important for human medicine. ESKAPE increase frequency of treatment failures and severity of human infections by adapting to altered environmental conditions and by acquiring resistance determinants.^{1,2} Among ESKAPE bacteria, three are most problematic, the highly resistant Gram-negative (Gram -) *K. pneumoniae*, *P. aeruginosa* and *A. baumannii*, typically associated with infections in severely ill hospitalized patients.³ As in other bacteria, their cell envelope shield is the first line of defence against stress conditions and is crucial to resistance to antibiotics. This complex structure exposes two important barriers: capsule polysaccharides (CPS) and lipopolysaccharides (LPS). We have identified several CPS depolymerases synthesized by *K. pneumoniae* bacteriophages⁴⁻⁶ and we have shown that they are effective against native capsule of specific clinical *K. pneumoniae* strains and significantly inhibit Klebsiella-induced mortality in a time-dependent manner. We also proposed the first structural characterization of a CPS depolymerase, named KP32gp38, encoded by a bacteriophage against *K. pneumoniae* (K-type 21 CPS).⁷ Recently, other phage depolymerases directed against hypervirulent strains (K-type 1 and K-type 2 CPS) of *K. pneumoniae* have been structurally characterized.^{8,9} Structural and functional data on these cell envelope depolymerases will be presented as a tool for novel therapeutic development against AMR.

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The structural approach to vaccine development against ESKAPE pathogens .

Eliza Kramarska,^{a,*} Flavia Squeglia,^a Alessia Ruggiero,^a Rita Berisio.^a

ESKAPE group includes pathogens with extreme capacities to develop antibiotic resistance, which makes them insusceptible to conventional treatments. *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter sp.* are members of this unglorious group. These bacteria are leading etiological agents of dangerous hospital-related nosocomial infections and pose a serious risk to immunocompromised patients.¹ In 2017, the World Health Organisation highlighted five out of six ESKAPE bacteria as the highest threat to human health.² Under the framework of the Marie Skłodowska-Curie Action BactiVax - Anti-Bacterial Innovative Vaccines, we are investigating new strategies to combat these pathogens through the development of novel, effective vaccines. These strategies allow to produce long-lasting immunity in a pre-infected patients and prevent the life-threatening conditions. Importantly, introduction of a successful way to protect from diseases will help to stop antibiotics administration, thus limiting the resistance problem.³ AdcA is a surface exposed, metal-binding lipoprotein from the ABC-transporter family of *E. faecium*. The protein is a key component in a zinc homeostasis and is an essential molecule for bacterial survival. Also, it is able to induce an immune response in mice.⁴ We adopt a structural vaccinology approach to develop enhanced AdcA based vaccine antigens against *E. faecium*. Moreover, we detected possible cross-reactivity due to conservancy of zinc-binding protein in *S. aureus* and confirmed activity of our antigen in staphylococci.

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Structural studies on ornithine decarboxylase from *Leishmania infantum*, a key enzyme in the polyamine and trypanothione metabolisms.

Annarita Fiorillo,^{a,b} Lorenzo Antonelli,^{a,b} Giancarlo Tria,^c Gianni Colotti,^b Andrea Ilari.^{b,*}

Ornithine decarboxylase (ODC) is a homodimeric, PLP-dependent enzyme that plays a key role in the polyamine biosynthesis, catalysing the rate-limiting decarboxylation of ornithine to putrescine. Polyamines are essential promoters of the proliferation of cells and are fundamental in cellular processes such as replication of DNA and apoptosis. Moreover, in trypanosomatids the synthesis of polyamines is strongly connected to the redox metabolism. Indeed, the polyamine spermidine is needed for the synthesis of trypanothione, a dithiol used by trypanosomatids to neutralize the reactive oxygen species produced by macrophages to fight the infection. For this reason, ODC is an appealing target to develop drugs against the diseases caused by trypanosomatids (leishmaniases and trypanosomiases). As a matter of fact, eflornitine also known as DFMO (DiFluoro Methyl Ornithine) is the first line drug for the treatment of the neurological stage of sleeping sickness caused by *Trypanosoma brucei gambiense*. Sequence analysis shows that, besides the canonical domain, ODC from *Leishmania* spp. is characterized by an additional N-terminal extension of around 250 aminoacids with unknown structure and function. We crystallized ODC from *Leishmania infantum* (Li-ODC) and collected a diffraction dataset at 3.6 Å resolution, allowing us to build a model that comprises about the 60% of the protein sequence; in addition to the canonical C-terminal domain, a portion of the N-terminal domain is visible in the structure (segments: 122-180 and 211-224) resulting to be folded into three alpha helices. The first 120 N-terminal residues as well as four long insertions in the C-terminal domain are not visible in the structure. SAXS and preliminary Cryo-EM experiments reveal the presence of multiple conformations for the LiODC dimers supporting a strong flexibility of the first 120 residues and of the C-terminal domain loops.

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Molecular architecture of the PTG/PP1 holoenzyme.

Marta Stefania Semrau,^{a,b,*} Gabriele Giachin,^c Sonia Covacheuszach,^d Alberto Cassetta,^d Paola Storici,^a Graziano Lolli.^b

Lafora disease (LD) is a rare, genetic, neurodegenerative disorder manifested by severe teenage onset of progressive myoclonus epilepsy. The patients usually die within 10 years of first symptoms occurrence. There is no cure available. LD is caused by mutations in laforin-malin complex which leads to appearance of neurotoxic inclusion bodies formed by insoluble polyglucosans called Lafora Bodies (LB).^{1,2} One of the key regulatory enzymes in glycogen metabolism is PP1 (type 1 protein phosphatase) which “switches” on or off glycogen synthase and phosphorylase responsible for glycogen synthesis and degradation. PP1 is involved in many cellular processes and acquires its specificity by forming holoenzymes with scaffolding proteins. In neurons PTG (protein targeting to glycogen) binds to PP1 and brings it to its substrates. In healthy neurons PTG is downregulated by laforin-malin complex, mutations in any of these proteins causes accumulation of PTG, which promotes glycogen synthesis by directing PP1 to glycogen synthase and glycogen phosphorylase. In LD mice models knocking out PTG resulted in a nearly complete disappearance of LB and resolution of neurodegeneration and myoclonic epilepsy, indicating that small molecules interfering with the PTG/PP1 interaction emerges as a promising therapeutic strategy for LD.³⁻⁵ Up to date, there was no structural data of PTG and PTG/PP1 complex allowing for identification of potential druggable pockets. We present our efforts to obtain structural information of PTG-CBM21 and PTG/PP1 complex. Herein we report the first structures of human PTG: PTG-CBM21 in complex with β -cyclodextrin, PP1 in complex with PTG N-terminal peptide containing the conserved binding motif RVXF and finally PTG/PP1 holoenzyme.

Our findings contribute to elucidating the interplay mechanism between PTG and PP1 and provide the basis for further structural analysis in order to identify druggable pocket.

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A drug repurposing approach targeting SARS-CoV-2 PLpro in the fight against Covid-19.

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Papain-like protease (PLpro) coded by SARS-CoV-2 genome is a key enzyme in viral replication. This enzyme is a subdomain of the viral non-structural protein 3 (nsp3).¹ PLpro is a cysteine protease which recognizes and cleaves the LXGG consensus sequence of both viral and host proteins showing deubiquitinating and deISGylating activity on key proteins in cytokines response pathways, which relates this enzyme to a major inflammatory response and immune system evasion.^{2,3} PLpro has been drawing interest as a pharmacological target to fight the pandemic emergency.⁴

The aim of the project is to identify novel inhibitors of PLpro providing biochemical and structural information to support rational drug discovery and repurposing campaigns. Thanks to a collaboration started within the Exscalate4Cov consortium (www.exscalate4cov.eu), an HT-*in vitro* repurposing screening was conducted by ITMP in Hamburg. Activity assays were performed on recombinant proteins expressed in *E. coli* and successfully purified at the Elettra Protein Facility. Different WT and mutated constructs were produced of the PLpro catalytic domain and of a longer sequence (PLpro_L) containing the nucleic acids binding domain (NAB) at the C-terminal. The PLpro_L construct was probed in the repurposing screening while the catalytic domain was used in the reconfirmation assay. A list of active compounds was selected and further characterized in our lab by TSA and by setting up numerous crystallization trials. So far, crystals obtained resulted to be of the apo form, indicating that the protein is difficult to crystallize in complexed with a ligand. The PLpro_L low resolution structure has been recently determined by SAXS, considering both wild type and two frequent mutants of the SARS-CoV2 Delta variant.⁵ The overall shape is much elongated and interestingly the mutations induce higher flexibility of the molecule in solution. Crystallization of PLpro_L in *apo* and *holo* forms are still on development with the aim to characterize the binding, together with biophysical binding properties in a drug development optics.

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Experimental design for X-Ray phase-contrast microtomography of breast samples for virtual histology.

Lucia Mariel Arana Peña,^{a,b,c,*} Sandro Donato,^d Deborah Bonazza,^e Luca Brombal,^b, Fulvia Arfelli,^{a,b,c}, Giuliana Tromba,^c Renata Longo.^{a,b}

The small difference in X-ray attenuation properties of tumor and normal breast tissue demands for X-ray breast imaging techniques that deliver high contrast, high spatial resolution images acquired at a low dose. Previous studies¹⁻³ have shown the potential usefulness of 3D phase-contrast micro-tomography (micro-CT) imaging as an adjunct tool to conventional histological techniques. We present a methodology to deliver micro-CT images of breast tissue specimens to accompany current histological examinations.

Tomographic acquisitions of three paraffin-embedded breast tissue samples with a polychromatic synchrotron beam (average energy-24 keV) were carried out at the SYRMEP beamline of Elettra, the Italian Synchrotron facility in Trieste. Phase-contrast tomography can deliver a considerable gain in signal-to-noise ratio (SNR) at small pixel sizes when it is combined with the free-space propagation technique and a suitable phase retrieval filter.⁴ In this study, the pixel size was adjusted to 1, 2.5 and 4 micrometers (μm) and the sample-to-detector distances of 150, 250 and 500 mm were used.

We performed micro-CT scans of the areas with histological features of interest of the breast specimens by acquiring 1800 evenly spaced projections over a 180-degree angle at a fixed source-to-sample distance of 22.3 meters for each pixel size. Micro-CT reconstructions were then compared with their respective histological images. We found a very good match between the techniques. The combination of the free-space propagation phase-contrast technique and the phase-retrieval algorithm resulted in better quality images than in conventional x-ray imaging, showing an excellent visibility of the samples' structural features. These structures can undergo alterations in pathological processes of benign and malignant origin. Recognition of these components could provide additional information and important feedback to the pathologist in the evaluation of tumor architecture.

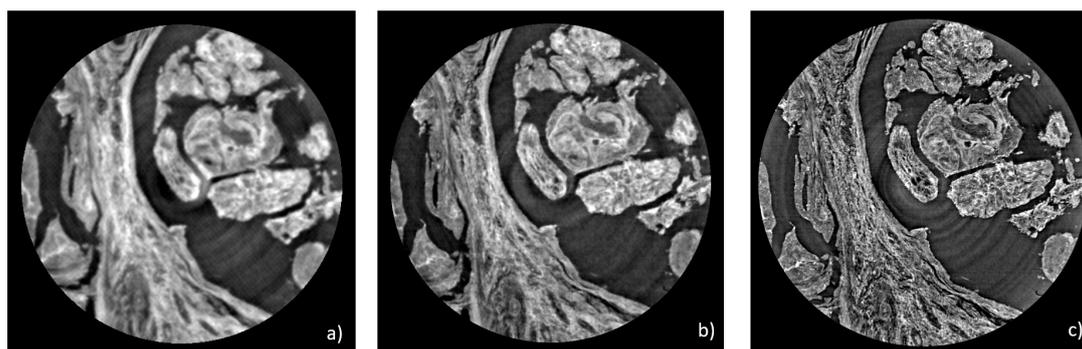


Fig. 1 Comparison of the micro-CT images of a detail of the breast sample acquired at different pixel sizes: a) 4 μm , b) 2.5 μm and c) 1 μm , respectively.

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Towards a multimodal pipeline to characterize lung fibrosis: Phase-Contrast imaging and Porosity analysis.

Lorenzo D'Amico,^{a,b,*} Christian Dullin,^{a,c,d} Giuliana Tromba.^a

The gold standard for pathological tissue analysis is histology. Histology is a destructive technique and can provide only 2D information. To overcome these drawbacks a 3D imaging method such as computed micro tomography (microCT) can be used, providing a non destructive 3D view of the entire specimen.

Conventional microCT systems, based on benchtop microfocus X-ray generators, generally require the application of heavy metal based staining protocols to improve the image contrast. The use of a phase contrast approach can overcome this limit, providing a high quality volume rendering of unstained fixed samples.

In this work, we used phase contrast μ CT to study unstained mouse lungs embedded in paraffin as a first step of a multimodal imaging pipeline including also IR spectroscopy, Atomic Force Microscopy and SAXS, and aiming to comprehensively characterize lung fibrosis.

To induce the pathology, an injection of bleomycin through the trachea of the mice was performed. This is the most common way to trigger fibrosis development.

Porosity analysis was performed in the reconstructed μ CT slices in order to characterize the degree of fibrosis and to correlate it with pathological evaluation of consolidation, surface area and body volume. From these parameters we were able to distinguish between healthy and fibrotic model, and subsequently also recognize different degrees of fibrosis. Moreover, the μ CT data allowed the identification of fibrotic regions and thereby to plan sectioning of the specimen for subsequent analysis.

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Investigating the solid form of Naproxen-Aminoindanol diastereomeric salts.

Patrizia Rossi,^{a,*} Martina Lippi,^a Paola Paoli,^a Jacopo Ceccarelli,^b Juliana Morais Missina.^c

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) are a group of widely used medicines that includes different classes of compounds, the most important of which is that of the arylpropionic acids (ibuprofen, ketoprofen, naproxen etc). Due to the presence of one stereogenic center these acids exist as a pair of enantiomers and, although only the S one is the Active Pharmaceutical Ingredient (API), they are usually given as racemic mixture. Over the last years the interest in the single-enantiomer drug has increased due to some advantages, for example: easier pharmacokinetic and pharmacodynamic profiles, lower prescribed amount, higher therapeutic index.

A cheap and easy method to obtain enantiopure APIs involves the formation of diastereomeric salts using enantiopure bases.

As a matter of fact, the selection of the best performing resolving agent as well as the best experimental conditions are usually time-consuming and largely empirical. Studies on structurally related diastereomeric salts can help to overcome this trial-and-error approach providing useful hints for the resolving agent choice.¹

As part of a work aimed to study, in a systematic way, the resolving abilities of different molecules toward NSAID arylpropionic acids, we decided to investigate the diastereomeric salt formation of S-naproxen² with (1S,2R)-cis-1-aminoindan-2-ol (SR_AIO), and (1R,2S)-cis-1-aminoindan-2-ol (RS_AIO). In fact, aminoindanols represent an important family of indane-containing compounds, and their use in racemic resolution arises from their high resolving efficiency for a variety of racemic acids. We present here the result of an experimental and in-silico investigation of the solid forms of the following three diastereomeric salts: the anhydrous S_NAP-SR_AIO and S_NAP-RS_AIO and the hydrate S_NAP-RS_AIO.

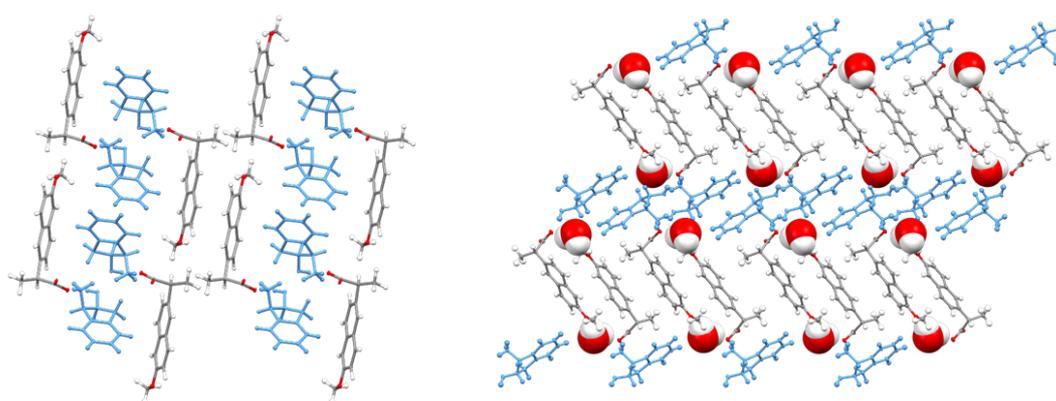


Fig. 1 Crystal packing, view along the b-axis, of the hydrate and anhydrous S_NAP-RS_AIO.

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Specific Recognition of Methylated Lysines by Fluorescent Calixarenes in Protein Crystal Structures.

Barbara Medagli,^a Neal Hickey,^a Rita De Zorzi,^a Silvano Geremia.^{a,*}

Arginines (Arg) and Lysines (Lys) on protein surfaces undergo several post-translational events, such as acetylation, ubiquitination, and methylation. Lysine or arginine residues can undergo different extents of methylation (mono-, di- and, for lysine, also trimethylation). These modifications affect protein-protein or protein-substrate interactions and can act as the trigger of different cellular pathways. The involvement of protein methylation in disease is driving the development of new molecules both for detection of these post-translational modifications and/or for specific delivery of therapeutic drugs.¹ Calixarenes are aromatic macrocycles with well-defined cavities that can easily host Arg or Lys residues.² Functionalization with different ionic groups at the upper and/or lower rims is an important step to confer metal coordination abilities and water solubility, which make them potential candidates for protein labeling.³ Water soluble sulfonate calixarenes have a strong affinity towards methylated side chains. It has been demonstrated that a sulfonated calix[4]arene binds a specific dimethylated Lys residue of lysozyme⁴ and recent studies have shown that it can be used to isolate methylated peptides from complex biological samples.⁵ We will describe the synthesis and characterization by X-ray diffraction of the complexes formed by the octanionic-sulfonate calix[4]arene (sclx4mc) and lanthanide (terbium or gadolinium) ions and their interactions with a methylated lysozyme protein. The effects of pH and stoichiometry on the protein-calixarene-Ln complex formation will also be analysed.

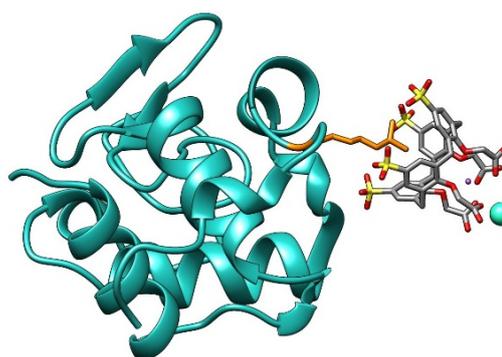


Fig. 1 Structure of the Lys2Met-sclx4mc-Ln complex

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ULK1 inhibition for autophagy deregulation recovery.

Theo Battista,^{a,b,*} Marta S. Semrau,^b Viktoryia Sidarovich,^c Valentina Adami,^c Graziano Lolli,^c Paola Storici.^b

Autophagy is responsible for degradation and recycling of damaged cellular contents, as misfolded proteins, aggregates and organelles.¹ Its deregulation is linked to different health disorders and in recent years is under evaluation as a target for cancer treatment. In human cells, autophagy is initiated through ULK1 complex, which triggers the activation of the autophagy cascade upon nutrient starvation or energy stress signals.^{2,3}

ULK1 complex is composed of the serine/threonine protein kinase ULK1 (unc-51-like kinase 1), FIP200 (focal adhesion kinase family interacting protein of 200 kDa), ATG (autophagy-related protein) 13 (ATG13), and ATG101. In addition to stress stimuli, ULK1 activation passes through an autophosphorylation mechanism encompassing Thr180, whose mutation determines a dramatic drop in the activity.⁴

Particularly ULK1 represents an intriguing target for autophagy modulation and related disorders restoration; in this perspective a structure-based drug discovery campaign has been initiated.

We succeeded in producing the ULK1 kinase domain and setting up a small molecule autophosphorylation-based screening, which has been implemented, in collaboration with the HTS Core Facility of University of Trento, for the identification of active molecules from two libraries (TimTec and KCGS). Different chemotypes have been identified, endowed with low nanomolar to micromolar activities. Efforts are being attained for the structural basis characterization: an X-ray crystal structure of ULK1-inhibitor complex has been obtained so far, paving the way for a future SAR study.

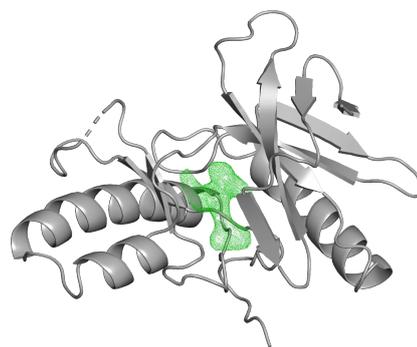


Fig. 1 Omit map of an identified inhibitor in complex with ULK1.

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Production, characterization, and optimization of engineered enzymes for application in artificial photosynthetic systems.

Beatrice De Bonis,^{a,*} Giusy Tassone,^a Marco Mazzorana,^b Cecilia Pozzi.^a

The increasing exploitation of fossil fuels for the production of energy is closely related to increased CO₂ release into the atmosphere, with climate change as main consequence.¹ Photosynthesis has been the subject of inspiration for the development of systems able to convert solar energy into chemical energy. Artificial photosynthesis (AP) might allow the production of not-polluting gases (O₂ and H₂) through light-driven water splitting.²

The main focus of this project is the development and optimization of biological catalysts for their application in AP. Specific enzymes, such as Ir-substituted carbonic anhydrase,³ Ni-Fe and Fe-Fe hydrogenase,⁴ and Ni-Fe carbon monoxide dehydrogenase,⁵ have been selected, and will be investigated and modified to improve their chemical and physical properties for integration in AP systems.

To develop this project, the synthetic genes encoding for selected proteins of interest, including human carbonic anhydrase, were cloned in expression plasmids. The enzymes, produced in *E. coli*, are purified by combining different chromatographic techniques, including affinity and size exclusion. The structure and function of these enzymes will be characterized and investigated by combining various techniques, including structural studies by means of X-ray crystallography.

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Integration of biomolecular simulations and crystallographic approaches to develop enzymes for plastic hydrolysis and recycling.

Demi Vattovaz,^{a,*} Anamaria Todea,^a Fioretta Asaro,^a Danilo Di Stefano,^b Lucia Gardossi,^a Rita De Zorzi.^a

Since the last century, plastics became indispensable for our everyday life. Nowadays, less than 20% of the global plastic waste is recycled and plastic pollution causes a huge impact on the global ecosystem: prompt action is needed to face one of the most pressing environmental issues.¹

Plastics represent a major challenge for the recycling industry and enzymatic degradation is an innovative and greener alternative to mechanical plastic recycling, allowing to recover valuable monomers that can be re-used for the synthesis of new polymers.² Biocatalysts inspired by the great variety of natural hydrolases can be optimized by protein engineering to improve their performance (e.g. thermostability) or tune their activity. Among the most investigated hydrolases, cutinases, which hydrolyze a natural polyester (cutin), have been proposed for the biodegradation and the synthesis of polyesters.³

Wild type cutinases can be engineered and their activity can be altered through computationally designed mutagenesis.⁴ In fact, computational protein design is a powerful tool for tailoring enzymes for specific biotechnological applications. The development of a computational and experimental integrated workflow will allow to design and produce enzymes able to hydrolyze different polymers.

In our approach, a number of hot-spot residues are selected using bioinformatic analysis.⁵ Mutants are generated *in silico* and automatically scored through molecular dynamic simulations and molecular docking, in order to identify proteins with the desired features. The second step is the production and purification of selected mutants to assess the activity and stability and to determine the 3D structure by X-ray crystallography. Experimental results are used to optimize the workflow. After the completion of the iterative process, the “best” virtual mutants are produced in large scale, reducing both the computational cost and the number of experiments, with a clear economic advantage.

The integration of experimental and computational results paves the way to a greener solution to the plastic environmental issue. The innovative and sustainable strategy to design enzymes will represent a convenient alternative, with the potential to revolutionize industrial applications.

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In silico-designed nanobodies: from the computer to the bench.

Federico Nolasco,^{a,*} Barbara Medagli,^a Miguel Soler,^b Sara La Manna,^c Daniela Marasco,^c Rita De Zorzi,^a Sara Fortuna,^d

VHH antibodies, also known as nanobodies, are the engineered version of antigen-binding domains from heavy-chain-only antibodies found in camelid serum.¹ As the smallest antibody fragments preserving the binding capacity of a whole antibody, they are largely employed for diagnostic and therapeutic applications.^{2,3} The small size (≈ 15 kDa) and stability of nanobodies allow their recombinant production in bacterial systems. Lately, a computational-based protocol was developed for the design of VHH sequences against specific epitopes.⁴

Here the same algorithm was used to produce nanobodies active against a model protein, the Hen Egg White Lysozyme (HEWL), by starting from a nanobody sequence against an unrelated target. With the aim of improving the *in silico* design algorithm, complexes between the artificial nanobodies and their target HEWL were studied through structural and biophysical techniques. The VHH protein sequences selected by the algorithm were expressed in *Escherichia coli* using different protein tags. Their stability was evaluated using a Thermal Shift Assay protocol and results were used to select a suitable buffer for purification and crystallization experiments. An enzymatic inhibition assay was carried out using *E. coli* cells as substrate of the lysozyme. Despite some predicted overlap between the artificial VHH binding site and the active site of HEWL, no significant inhibition was reported. Nevertheless, for two artificial VHH KD in the nanomolar range were experimentally determined through microscale thermophoresis. The structural characterization of the VHH-HEWL complexes is underway.

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Structural and functional characterization of the *Aspergillus fumigatus* transacylase SidF..

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Iron acquisition via chelation by siderophores plays a crucial role in the virulence of numerous bacterial and fungal pathogens. Therefore, the biosynthetic pathway for siderophores has great potential for improving the diagnosis and treatment of fungal infections. In this study, we characterized SidF, an essential enzyme of extracellular siderophore biosynthesis from *Aspergillus fumigatus*, the causative agent of deathly aspergillosis in immunocompromised patients, employing X-ray crystallography, SAXS, and enzymatic assays. We discovered that the structure of the N-terminal domain largely resembles that of the C-terminal domain of SidF. However, the GCN5-related N-acetyltransferase (GNAT) domain is found only in the C-terminal domain. SidF is a tetramer in crystal structure and in solution, as confirmed by SAXS analysis. Previous studies indicated that the transacylase function of SidF uses anhydromevalonyl-CoA as a donor and N5-hydroxy-L-ornithine as an acceptor to produce N5-anhydromevalonyl-N5-hydroxy-L-ornithine. We found that SidF can also accept acetyl-CoA as a donor and that the specificity for N5-hydroxy-L-ornithine may involve its hydroxylamine group. Our results provide insights into the SidF structure and suggest another potential SidF function in the siderophore biosynthesis pathway.

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The peculiar SHG behavior of solid Co-, Ni- and Cu-porphyrinates.

Domenica Marabello,^{a,b} Paola Antoniotti,^{a,b} Carlo Canepa,^a Elena Cariati,^c Alma Cioci,^{a,*} Giorgio Volpi,^a Paola Benzi,^{a,b} Leonardo Lo Presti.^c

Porphyrins are the most studied heterocyclic macrocycle organic compounds for numerous applications, due to their optical properties and chemical stability. Among the optical properties, porphyrins show in solution interesting Non Linear Optical (NLO) Properties, i.e. Second (SHG) and Third (THG) Harmonic Generation.^{1,2} At our knowledge, up to now in solid state the SHG properties of porphyrins or their derivatives were not investigated. Thus, we decided to investigate the SHG behaviour of three metal porphyrinates of formula M-TPP (M = Co, Cu and Ni, TPP = 5,10,15,20-tetraphenylporphyrine) in the solid state, that crystallize in the same acentric I-42d space group and are isomorphous.

We synthesized and characterized them and we measured the Second Harmonic Generation (SHG) response of powdered samples with a 1.907 μm pulsed laser radiation. For all the complexes, after few minutes of laser irradiation, a sudden enhancement of the intensity of the SH was observed. We attempted to understand the origin of this peculiar SHG behavior both through experimental analysis and theoretical calculations. In order to better correlate the second harmonic emission with the nature and structure of the materials, theoretical calculations were carried out with two different computational approaches: a model in which the crystalline fragment is represented as a nanoparticle (nanoparticle calculations) and a model in which the crystal is infinite and perfect (bulk calculations). In both cases the geometrical parameters were optimized and compared with the experimental XRD data; the first-order static hyperpolarizability and second-order susceptibility were also calculated and compared with the values obtained for the sucrose used as a reference. These results were compared with the experimentally SHG intensity ratios measured on the powders of the material with the method of Kurtz and Perry.³

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Recovery of Rare Earth Elements from Multi-Metal Mixtures using 8-Hydroxyquinolines.

Matteo Melegari,^{a,*} Martina Neri,^a Alex Falco,^a Matteo Tegoni,^a Luciano Marchiò.^a

Rare Earth Elements (REEs) (Y, Sc, La-Lu) are widely used for their outstanding magnetic and luminescent properties. Their applications range from fluorescent light tubes to electric car batteries to permanent magnets. However, the supply of REEs is presently struggling to meet the demand. REEs deposits are located only in some regions leading to delicate geopolitical considerations and the current recycling rates reach the 5% mark.¹ REEs are currently considered among the highest Critical Raw Materials by both European Commission and the U.S. Department of Energy. The need for a large scale, green, cheap, and selective process for the separation and recycling of REEs is therefore important. The widespread use of in everyday objects, makes Waste Electrical and Electronic (WEE) and End-of-Life (EOL) products valuable sources of those elements. In particular, permanent neodymium magnets (NdFeB) are among the richest and most readily available sources of lanthanide containing scraps.

We investigated the separation and recovery of the REEs contents in NdFeB magnets (usually composed by 65% Fe, 30% Nd and 2% Dy). The use of 8-Hydroxyquinolines (8-HQs) enables the fine tuning of the complexes topologies upon changing the steric hindrance of the substituents, the metal ion and the base used for the deprotonation of the ligand.² The different complexes formed were separated via simple selective precipitation of one of the metal complexes. We systematically tested differently substituted 8-HQs and various reaction conditions for the complexation of Fe(III), Nd(III) and Dy(III). Two separation processes were successfully developed: 1) The separation of Fe(III) from the REEs using 5-chloro-7-iodo-8-hydroxyquinoline (5Cl,7I-8HQ); 2) The intra-series separation of Nd(III) and Dy(III) using 5-chloro-8-hydroxyquinoline (5Cl-8HQ). The simplicity and cost effectiveness of the process developed could help increasing the current recycling rate of REEs and in reducing the supply risk associated to those resources.

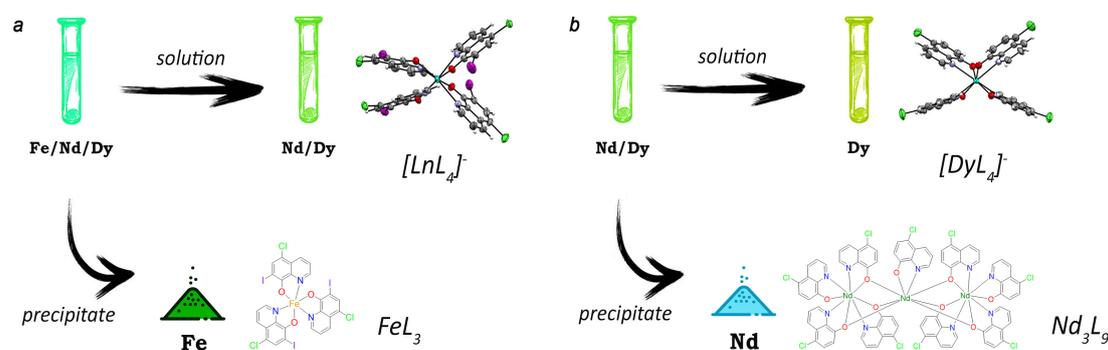


Fig. 1 a) Schematic representation of the process of separation of REEs from Iron using 5Cl,7I-8HQ; b) Schematic representation of the process of intra-series separation of REEs using 5Cl-8HQ.

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X-ray Structure Investigation of Confused-Prism[5]arene: a Conformationally Adaptive Host with Stereoselective Opening of its 1,4-bridged Naphthalene Flap.

Neal Hickey,^{a,*} Paolo Della Sala,^b Rocco Del Regno,^b Placido Neri^b Carmine Gaeta,^b Silvano Geremia.^a

We have recently reported a new class of macrocycle, denoted prism[n]arenes, composed of n ($n=5,6$) methylene-bridged naphthalene units, each with two identical alkoxy substituents ($R = \text{Me, Et, Pr}$) at the 2, 6 positions.^{1,2} The new molecules possess chiral planes and show high structural flexibility as well as a strong tendency to encapsulate ammonium cations. Symmetric prism[n]arenes are characterised by all the methylene bridges at the 1, 5 positions of the naphthalene units. However, a variation of this bridging pattern was obtained for a 1,4-confused-prism[5]arene (**c-PrS[5]^{Me}**), for which 1/5 of the naphthalene rings is bridged at the 1,4-positions. In this case, the asymmetric macrocycle is self-filled by the confused naphthalene moiety and its two C-C bridging single bonds are aligned so that the naphthalene can rotate more freely than its PrS[5]^{Me} analogue.

Here we show that **c-PrS[5]^{Me}** shows adaptive conformational behaviour. The X-ray structures of host-guest complexes of **c-PrS[5]^{Me}** with 1,4-dihexyl-DABCO and with *n*-butylammonium were obtained using synchrotron radiation. A stereoselective opening of the 1,4-bridged naphthalene flap toward the homochiral conformation of the host, inverting its planar chirality, occurs during the complexation. X-ray studies, supported by NMR spectra and DFT calculations, show that the homochiral complexes are stabilized by $C-H \cdots \pi$ interactions. Furthermore, the *n*-butylammonium directional axle produces up/down directional isomers. Therefore, symmetry breaking introduced by the 1,4 link in **c-PrS[5]^{Me}** creates a new scenario in terms of the stereochemistry of these systems, characterized by an adaptive macrocycle which can open the 1,4-bridged naphthalene flap in a stereoselective and directional manner.

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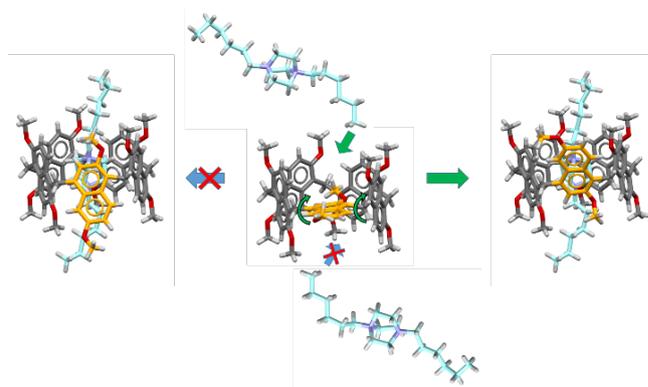


Fig. 1 Stereoselective insertion of ammonium guests in **c-PrS[5]^{Me}**

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Engineering Phase Change Behaviours of Organic Ionic Plastic Crystals for Development of Solid State Electrolytes.

Samet Ocak,^{a,*} Michele R. Chierotti,^b Dario Braga,^a Tommaso Salzillo,^c Simone d'Agostino.^a

Plastic Crystals are materials in which the molecules or ions occupy the same center of mass as in regular crystal lattice but have freedom of rotation. They show typical disorder-order transitions that lead to realize various sort of functional materials. Especially, organic ionic plastic crystals (OIPCS) have gained much attention over the past years thanks to their potential usage as solid-state electrolytes^{1,2}

The aim of this work is basically twofold. Firstly, we are interested in investigating the counter-anion dependence of the plastic phase transitions in a series of R-(+)-(3)-hydroxyquinuclidinium salts [QH]X. By varying size, shape, and charge of the anion, we expect to obtain different behaviors in terms of plastic phase transition and type. Second, we want to explore the possibility of preparing crystalline solid solutions, studying how the composition of the resulting materials further affects the phase transition compared to the pure parent systems.

To that end, we synthesize a series of [QH]X salts with various counter-anions, including the tetrahedral anions sulfate (SO_4^{2-}), tetraphenylborate (BPh_4^-), tetrafluoroborate (BF_4^-), and the octahedral hexafluorophosphate (PF_6^-) by the metathesis of [QH]Cl using metal salts of the corresponding anions. A combination of solid-state techniques, including variable temperature XRD, thermal analyses, multinuclear (^{11}B , ^{13}C , ^{15}N , ^{19}F and ^{31}P) solid-state NMR spectroscopy, variable temperature wide-line ^{19}F T₁ relaxation measurements and micro-Raman spectroscopy are used to elucidate crystal structures and phase transition behavior of the so-obtained materials. The figure below shows the structural outcomes of one of the compound we are working on quinuclidinol hexafluorophosphate [QH]PF₆⁻³

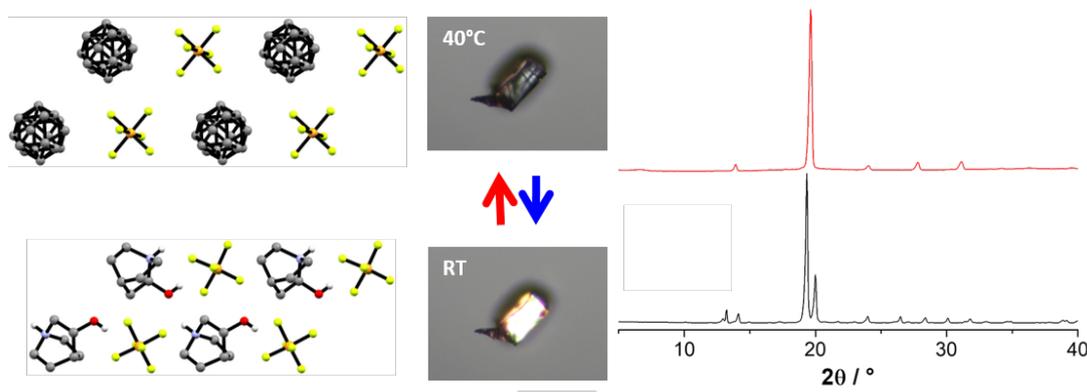


Fig. 1 Representation of the disorder-order transition of [QH]PF₆.³

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MOVPE of GaAsP/GaAs heterostructures for fabrication of 1.7 eV cell junctions in 4-terminal tandem III-V/Si solar cells.

Daniele Calabriso,^a Fabio Marzo,^a Emiliano Burrese,^b Leander Tapfer,^b Paola Prete,^{c,*} Nico Lovergine.^a

Multi-junction (tandem) solar cells in the form of monolithically stacked III-V cells, each absorbing a different interval of the solar spectrum allow to reach external quantum efficiencies well beyond the Shockley-Queisser limit for single-junction solar cells.¹ Tandem solar cells based on a Silicon bottom junction are very attractive due to the relative low cost of Silicon substrates; a dual-junction cell with a 1.7 eV top junction based on III-V semiconductors (e.g. GaAsP) and a Silicon (1.12 eV) bottom cell has a theoretical efficiency of $\approx 38\%$. However, serious structural constraints limit the monolithic growth of III-V compounds onto Si and performances of as-fabricated tandem solar cells remains far from theoretical figures. Four-terminal tandem solar cells composed of a thin GaAs film mechanically stacked onto interdigitated back contact Silicon solar cell with a glass interlayer have shown efficiency up to 32.6%.² The main advantage of such approach is that high quality III-V top cells could be monolithically grown on a GaAs substrate. Despite using costly GaAs wafers in the epitaxy of the III-V top cells increases the production costs, detach (by chemical lift-off) of the cells from the underlying substrates and multiple re-utilization of the latter have been demonstrated in the literature,³ as viable strategies to keep production costs low.

We present a study on the metalorganic vapor phase epitaxy (MOVPE) growth and structural-optical properties of GaAsP-based heterostructures on (100)GaAs, with the aim to fabricate a high efficiency 1.7 eV top cell for utilization in a stacked 4-terminal tandem III-V/Si solar cells. Despite GaAsP epilayers grown by MOVPE are commonly used in the fabrication of (In)GaAs-based heterostructures for applications to solar cells and laser diodes, not so much as been reported to date on growth details and related structural (strain, plastic relaxation) and radiative (luminescence) properties of tensile-strained GaAsP epilayers on GaAs. In this work P incorporation into GaAsP alloys has been determined along with the solid-vapor distribution curve as function of growth temperature by employing tertiary-buthylarsine and tertiarybuthyl-phosphine as As and P precursors respectively, in combination with trimethylgallium. Analysis of as-grown samples by high-resolution X-ray diffraction evidenced the elastic deformation state of the material and the onset of plastic deformation, which turned out to agree well with what expected from People-Bean relaxation model (values of critical thickness turned out to range up to few-hundreds nanometer).⁴ Low temperature photoluminescence spectra further showed a near band-gap emission for most GaAsP samples. Examples of high quality (pseudomorphic) step-graded GaAsP buffer layers on (100)GaAs will be finally reported.

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Graphene nucleation on Si(100): a DFT study on toluene decomposition steps and condensation reactions.

Onofrio Tau,^{a,b} Paola Prete,^{b,c,*} Nico Lovergine.^{a,b}

The direct chemical vapor deposition (CVD) of graphene on industrially preferred semiconductor (like Si wafers) or dielectric substrates has been considered a valid alternative to directly incorporate graphene into electronic devices, thus preventing the common transfer process of the as-grown film which inevitably induce residual contamination and mechanical defects.¹ Usually, the thermal CVD synthesis of graphene on Si substrates is realized with methane at high temperature (>900°C), although the low diffusivity of carbon species and the strong carbon solubility on Si which induce unavoidable formation of SiC buffer layers severely hamper an efficient growth.² Though several strategies have been adopted to overcome such limitations, few studies are focused on aromatic hydrocarbons as possible carbon precursors.³

In this work, we investigate at the molecular-level the first decomposition steps of toluene and possible recombination pathways of as-formed active species onto the reconstructed Si(100)-c(4x2) surface through density functional theory (DFT) calculations with van der Waals corrections (DFT-D3). First, toluene molecules can chemisorb with several configurations onto the Si surface by addition reactions.⁴ We found the most stable configuration (the aromatic ring forming four sigma bonds with two adjacent Si dimers) with adsorption energy of -1.39 eV which is higher than the value reported in,⁴ mainly due to the inclusion of the DFT-D3 corrections in this work. Then, the minimum energy pathway (MEP) and transition state (TS) of chemical reactions (decomposition and recombination steps) were investigated through the climbing-image nudged elastic band (CI-NEB) method. The dehydrogenation of the methyl group of toluene were found the most likely early decomposition path with an energy barrier of 1.4 eV. However, the formation of CH_3 radicals is strongly hampered by the much higher energy required for demethylation. Finally, we investigated the formation of anthracene (three connected phenyl rings) as one of the possible stable graphene nuclei for which we found a strong adsorption energy of -2.43 eV. Such carbon structure was achieved by a recombination of two C_7H_5 radicals and described by a two-step reaction, as shown in Fig.1. However, the cost to produce anthracene through this pathway is rather high with an energy barrier of at least 2.6 eV which is not beneficial for the low-temperature CVD synthesis of graphene on Si(100).

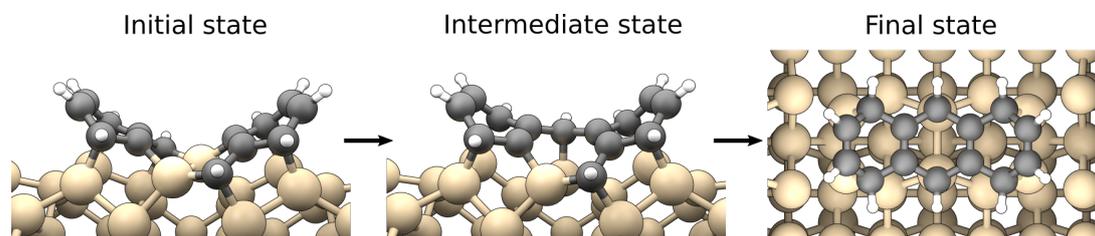


Fig. 1 Condensation reaction of two C_7H_5 producing anthracene, described as a two-step process.

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High Efficiency Lead-Free Perovskite Solar cells for indoor-outdoor Applications.

Paola De Padova,^a Carlo Ottaviani,^a Sofia Caretto,^b Angelo De Paolis,^b Paola Prete.^{c,*}

In 2009 Kojima et al.,¹ reported the first hybrid organometal halide perovskites as visible-light sensitizers for photovoltaic cells. They studied the photovoltaic function of the organic-inorganic lead halide perovskite compounds methylammonium (CH_3NH_3^+ , MA) PbBr_3 and MAPbI_3 as visible-light sensitizers in photoelectrochemical cells, opening a fruitful worldwide field of research. Halide perovskites, generally are represented as AMX_3 , where A is an alkyl ammonium cation, such as MA, dimethyl-ammonium ($(\text{CH}_3)_2\text{NH}^+$, DMA), formamidinium ($\text{CH}_3(\text{NH}_2)_2^+$, FA), or Cs; M is Pb^{2+} , and X is a halide ion (I^- , Br^- , Cl^-).

Although the efficiency of hybrid perovskite solar cells is today competitive with Si, achieving power conversion efficiencies exceeding 23%,² some drawbacks regarding these systems are the environmental toxicity of water-soluble Pb, and their air/humidity stability. In order to solve these disadvantages a fervent research is currently going on, and in 2016, materials with complete replacement of lead in the perovskite structure, by other cations such as nontoxic Ag^+ and Bi^{3+} , leading to the double perovskite $\text{Cs}_2\text{AgBiBr}_6(\text{Cl}_6)$ structure,^{3,4} were synthesized. Amazingly, very soon, in 2019, these new perovskites exhibited increasing power conversion efficiencies up to 2.5%.⁵⁻⁷

This work aims to present the HELFO (High Efficiency Lead-Free Perovskite Solar cells for indoor-outdoor Applications) project and the preliminary results on fully-inorganic lead-free $\text{Cs}_2\text{AgBiBr}_6(\text{Cl}_6)$ double-cations perovskites. HELFO is a challenging interdisciplinary project, which involves three Institutions of CNR from both fundamental condensed matter (CNR-ISM-Roma) and applied physics (CNR-IMM-Lecce) fields up to plant biology (CNR-ISPA-Lecce) field, aiming to combine different competences intrinsically belonging to CNR. Semitransparent lead-free $\text{Cs}_2\text{AgBiBr}_6$ and $\text{Cs}_2\text{AgBiCl}_6$ perovskites are synthesized by using both in-situ ultra-high vacuum molecular beam epitaxy deposition and ex-situ solution-processing, and investigated by XRD, SEM/AES/PL and UV-Visible optical techniques. Furthermore, these materials will be applied in green-houses for investigating, indoor-and-outdoor, the influence of solar light radiation shielding, through the $\text{Cs}_2\text{AgBiBr}_6(\text{Cl}_6)$ perovskites, on seed germination and plant metabolic profiles at a molecular level of *Artemisia annua* and *Solanum lycopersicum* plant species. Photovoltaic devices will be assembled by matching the $\text{Cs}_2\text{AgBiBr}_6(\text{Cl}_6)$ perovskites-based band alignment, with both electron- and hole-transporting layers.

Acknowledgements. This work has been funded through the Research Project @CNR “High Efficiency Lead-Free Perovskite Solar cells for indoor-outdoor Applications (HELFO)”.

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Study on Pulsed Electron Deposition as a new method for thin films growth of room temperature multiferroic BaFe₂O₄.

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According to the formal definition, materials can be described as multiferroics if they exhibit the coexistence of two or more primary ferroic orderings, such as ferroelectricity and ferri/ferro/antiferro-magnetism. Most of the increasing interest around this class of materials arises from the possibility of mutual control of both electric and magnetic domains, as this feature could allow to achieve significant advances in various innovative fields (from improving the capacity of data storage and reducing energy consumption in logic-memory devices to exploiting different ferroic orders in heterostructures in order to obtain spin valves).¹ However, to date very few single-phase materials are known being characterised by stable electric and magnetic states at room temperature.² γ -BaFe₂O₄, a non-centrosymmetric stuffed tridymite-type compound (space group *Cmc2*₁), is an interesting example of a previously unrecognized single-phase multiferroic material with high ordering temperatures ($T_{FE} > 1038\text{K}$ and $T_N = 890\text{K}$). By comparing single-crystal X-ray and neutron diffraction data with magnetic and ferroelectric macroscopic measurements, we found out that this barium ferrite is an antiferromagnetic improper ferroelectric (G-type spin ordering and *Pcca2*₁ magnetic space group; coercive electric field $E_c = 12 \text{ kV cm}^{-1}$ and remnant polarization $P_r = 0.18 \mu\text{C cm}^{-2}$). Since all the mentioned results are related to the bulk form of barium ferrite, the next critical step is to transfer all the structural features into a thin film form, in order to have suitable conditions for devices fabrication. Therefore, a thin film growth method was performed by using Pulsed Electron Deposition (PED), a technique based on the formation of a plasma plume from the interaction between a high energy pulsed electron beam and a target material with proper composition. The γ -BaFe₂O₄ films were grown on various substrates in the temperature range 700-850° C. Powder X-ray diffraction (XRD) patterns, combined with Raman spectroscopy and energy dispersive X-ray analysis, allowed to identify the formation of the target phase over all the tested substrates, without significant amounts of impurities. Moreover, partial control of crystalline orientation was achieved through the proper choice of the substrate, growth temperature and deposition parameters, as confirmed by texture coefficients determined from XRD data and pole figures measurements. The relevance of this step is related to the strong anisotropy of the polar *mm2* point group, so that the device applicability strongly depends on the orientation of crystals with respect to the substrate surface. In conclusion, despite more in-depth studies are needed to fully unveil the rich features of γ -BaFe₂O₄, the present results suggest that the PED technique is optimal for producing good quality barium ferrite films compatible with key materials in the electronic device industry.

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Analysis of TiO₂ nanocomposite using x-ray spectrometry.

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Nanostructures of Titanium oxide are being studied for many promising applications due to their excellent photocatalytic properties.¹ We have synthesized low-dimensional TiO₂ nanoparticles by laser pyrolysis technique. The synthesis process has been optimized for the deposition of highly pure and nearly mono-dispersed TiO₂ nanoparticles on silicon substrates.² The surface morphology of the TiO₂ nanostructure has been investigated using combined x-ray reflectivity and grazing incidence x-ray fluorescence measurements.³ Transmission electron microscopy and grazing incidence x-ray diffraction measurements were also carried out for the deposited TiO₂ nanostructures to evaluate surface coverage and crystalline structure of the particles. The average particle size of TiO₂ nanostructure estimated using transmission electron microscopy was found to closely agree with the x-ray standing wave analysis. The combined x-ray spectrometry and Transmission electron microscopy profiles are shown in Fig. 1(a) and Fig. 1(b) respectively.

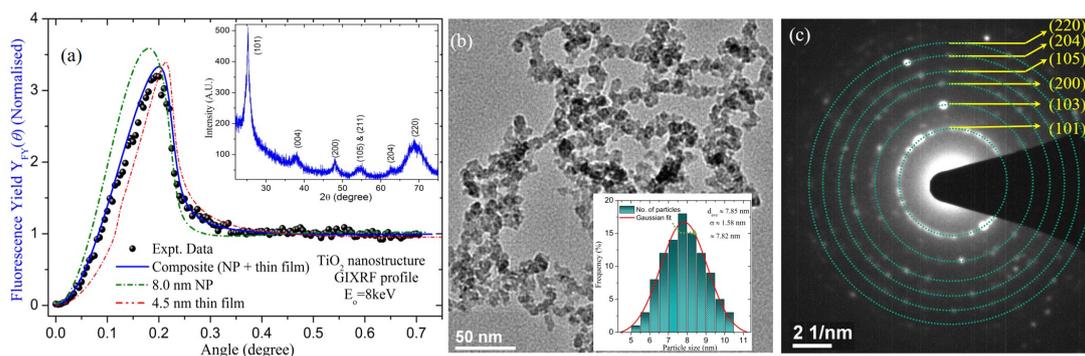


Fig. 1 Measured and simulated XSW induced GIXRF profiles of TiO₂ nanostructures at 8 keV x-ray energy. In the inset of (a) GIXRD profile of the nanostructure measured using a BRUKER system at Cu-K α radiation. (b) TEM micrograph, and (c) Electron diffraction profile of TiO₂ nanoparticle deposited on Cu grid.

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A deep-learning approach to fast classification of quantum dots size and size dispersion from total scattering data in reciprocal space.

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Colloidal synthesis has emerged as a powerful bottom-up approach for the preparation of semiconductor nanocrystals with narrow size dispersion, exhibiting optoelectronic properties that can be tuned by controlling their size and morphology.

Binary Quantum Dots (QDs) of the II-VI, III-V classes and ternary nanocrystals of the metal halide perovskite family, are of major interest in the field due to their cost-effective production processes and their competitive performances in various electronic and optoelectronic applications.¹

Reciprocal-space X-ray total scattering methods based on the Debye Scattering Equation (DSE) demonstrated themselves to be a powerful approach for the atomic-to-nanometre scale characterisation of these nanocrystals and their size/surface-induced defects²⁻⁶ A drawback of these techniques is that they rely on onerous procedures for the development of custom-made material-oriented atomistic models.

We try to address these limitations by implementing machine learning principles into the reciprocal-space total scattering topic, specifically developed for application to colloidal nanocrystals. At this aim we propose, here, a deep-learning-based approach to predict the average size and size distribution of colloidal PbS QDs.

Taking advantage of routines implemented into the Debussy Suite program package,⁷ we simulated by the DSE the total scattering patterns of PbS QDs characterized by different sizes, size distribution and lattice strain. We then applied a physic-informed data augmentation to the simulated patterns, in order to take into account real sample features, such as different signal-to-noise ratios and the presence of different solvents redispersing the QDs in colloids.

Using these synthetic data, we trained an all-convolutional neural network⁸ with a supervised-learning approach and obtained a testing accuracy of $\sim 95\%$.

Application of this method to experimental data of colloidal QDs is foreseen in order to provide the chemist and material scientist communities with an intuitive tool for the fast screening of QDs size and size dispersion, based on statistically robust data providing distribution properties of the ensemble sample as a whole.

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Self-standing nanoporous zeolite/cellulose deposits prepared with ultrafiltration for energy storage applications.

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Metal-organic frameworks (MOFs) are a class of crystalline solids containing metal ions and organic ligands. Owing to their high porosity and tuneable selectivity, they have been intensively researched for their application in gas separation, filtration, catalysis, sensing and energy storage.¹ However, MOFs are typically produced in forms of powders, which require further processing before being applied on a larger, industrial scale. In the field of liquid separation, synthesis or deposition of MOFs on polymeric membranes has been regarded as a viable solution, however further research is needed to evaluate the microstructure-function relationship of these hybrid materials. The use of biopolymers-based membranes for supporting MOFs constitutes an attractive fabrication route, owing to their intrinsic physiochemical properties, sustainability and biocompatibility.² The present work focuses on the use of a hydrophobic MOF (ZIF-8), which exhibits energy storage capability through cycles of liquid intrusion/extrusion.³ The ZIF-8 powder was mixed with crystalline nanocellulose (CNC) and used to fabricate a hybrid deposit by means of ultrafiltration. The flow behaviour of the ZIF-8/CNC suspensions was probed using oscillatory rheology. The effect of the composition of the feed solution on the deposit formation has been also investigated, and the deposit was characterized with optical and electron microscopy, and ultra-small angle X-ray scattering. Results show that low amounts of CNC enable formation of a homogeneous and resistant ZIF-8/CNC composite material which maintains its performance as an energy storage system, with intruding pressures up to 250 bar.

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