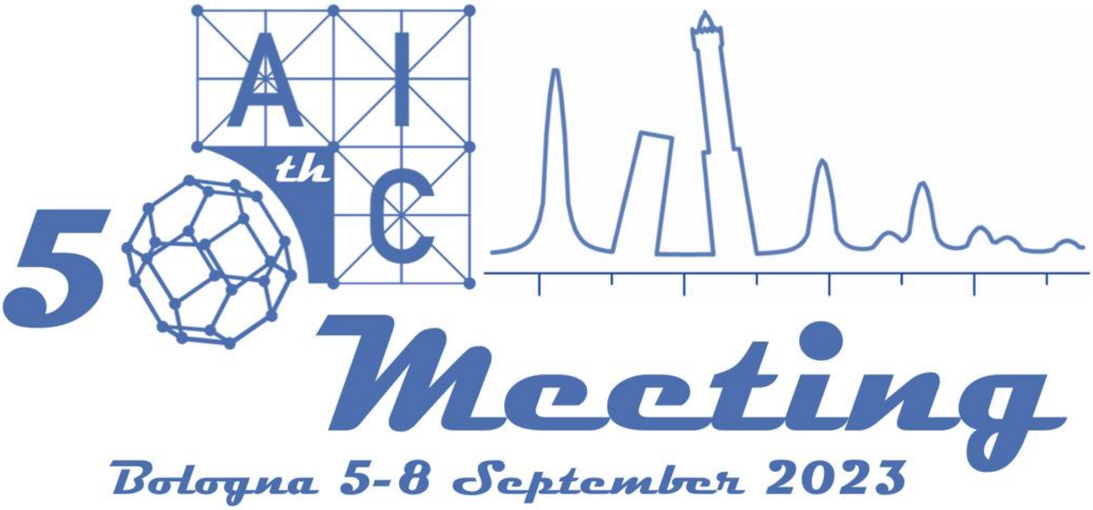

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Scientific Programme

Micro Symposia

MS1 - Tailoring noncovalent interactions to design organic crystals

Chairs: P. Metrangolo (Polytechnic University of Milan); P. Paoli (University of Florence)

Understanding and controlling noncovalent interactions, which guide the supramolecular arrangement in crystals, is a crucial step for the bottom-up design and synthesis of materials featuring the desired properties/functions. This micro symposium welcomes contributions to using hydrogen, halogen, and chalcogen bonds, van der Waals, pi-stacking, and other supramolecular interactions in crystal engineering. The aim is to provide a forum for researchers working across different molecular-based crystalline solids such as pharmaceuticals, organic semiconductors, agrochemicals, organic pigments, organic frameworks, etc. Contributions are welcome that cover fundamental to applied research, experimental and *in-silico* approaches, and structure-property/function rationale.

Keynote lectures:

Prof. Alessia Bacchi (University of Parma) - "Tweaking interactions to achieve release performances in co-crystals"

Prof. C. Malla Reddy (IISER Kolkata, India) - "Crystal engineering of adaptive smart materials"

MS2 - Combined structural methodologies to address complex biological systems

Chairs: M. Milani (IBF-CNR, Milan); L. Cendron (University of Padua)

In the last ten years, Structural biology has extended its tools to extremely powerful methodologies that allow integrated approaches to address important questions about cellular complexes involved in key processes and their aberrations linked to transcription, translation, transport, modification, catalysis, protein synthesis, and degradation. This micro symposium is focused on recent examples that highlight important achievements obtained by applying structural, biophysical, and computational techniques.

Keynote lectures:

Dr. Matteo De Rosa (Institute of Biophysics-CNR) - "Structural bases of gelsolin-related diseases"

Dr. Alessandra Magistrato (CNR-IOM) - "Unraveling the molecular mechanism of pre-mRNA splicing via all-atom simulations"

MS3 - Growth of crystalline functional materials and thin films

Chairs: A. Sassella (University of Milano-Bicocca); S. Rubini (CNR-IOM)

State-of-the-art technology relies on functional materials designed, grown and studied for different applications, and often integrated in devices as thin solid films. In this respect, studying and controlling the growth process, the role of interfaces and epitaxy in thin films and heterostructures, and the relationship between the growth and the properties is the goal of many research efforts. This Micro Symposium intends to collect contributions from scientists working on the growth of functional bulk crystalline materials, thin films and nanostructures, on their characterization, and on the modelization of their properties. Materials of interest span from inorganics to organics to 2D materials in thin films or integrated into more complex structures.

Keynote lectures:

Dr. Pasquale Orgiani (CNR IOM) - "Crafting the structure of materials for tailoring their quantum properties: the case of anatase TiO2 thin films"

Dr. Cristiano Albonetti (CNR-ISMN) - "Identification of ultra-thin molecular layers atop monolayer terraces in sub-monolayer organic films with scanning probe microscopy"

MS4 - Structural approaches to disclosing molecular recognition and targeting

Chairs: A. Ilari (Institute of molecular biology and pathology-CNR); F. Sica (University of Naples Federico II)

Progress in modern-day biology requires an understanding the mode of interaction between partners of different natures. Elucidating fundamental mechanisms of molecular recognition sheds light on the basic principles responsible for cellular function and opens new opportunities to use this knowledge for various biotechnological and biomedical applications. Traditionally, X-ray crystallography, with its ability to give detailed structural information, has proven to be an invaluable tool for investigating this phenomenon. Complementary methodologies have enabled a deeper understanding of the binding between different interactors and the analysis of the dynamic aspects. The micro symposium aims to provide a collection of interesting recent results using single/multiple structural approache/s.

Keynote lectures:

Dr. Giuseppina De Simone (CNR-IBB) - "Carbonic Anhydrase IX as target for the design of novel anticancer drugs: an integrated biochemical, structural, and computational approach"

Prof. Francesco Angelucci (Università degli Studi dell'Aquila) - "Circumventing nucleophilic active sites of thioredoxin reductases for selective inhibition”

MS5 - Challenging 3D structure: equipment, methodologies, and computing

Chairs: D. Siliqi (institute of Crystallography-CNR); A. Rosato (University of Florence)

The Micro Symposium aims to demonstrate how to cope with difficult 3D structures, from molecules to novel materials, by developing creative experimental and computational methodologies. We welcome contributions focusing on structural methods such as cryo-EM, NMR, and crystallography (x-ray, neutron, and electron diffraction). In modern practice, statistical tools are essential for all of these techniques. Applications ranging from the 3D structure of molecules (from small molecules to biopolymers) to the validation of structural results have been impacted by the availability of huge data- and knowledge bases. Machine learning and artificial intelligence tools are one field that has made significant progress recently.

Keynote lectures:

Prof. Enrico Ravera (University of Florence) - "Integration in Structural Biology”

Dr. Corrado Cuocci (IC-CNR) - "Challenging structure solution of microcrystalline materials by the direct space approach in action using the EXPO software”

MS6 - Understanding materials properties through in situ non-ambient and in operando studies

Chairs: P. Lotti (University of Milan); M. Milanesio (University of Eastern Piedmont)

The instrumentation and computing improvements of the last decade significantly fostered our capabilities to perform crystallographic analyses at non-ambient and operando conditions. In situ experiments at non-ambient conditions allow to track the structural changes that control the physical properties of crystalline compounds, and in operando experiments allow us to follow reactions and transformations from a structural viewpoint at real-world conditions. For both, computational modelling provides a complementary approach. The goal of this microsymposium is to highlight how non-ambient crystallography can shed light and open new avenues in a wide range of disciplines, spanning from Earth sciences to chemistry and to biopharmaceutical fields

Keynote lectures:

Dr. Georgia Cametti (University of Bern) - "Tracking in situ the structural transformations occurring in zeolite as a function of temperature"

Prof. Heinz Amenitsch (Graz University of Technology) – “Operando Small Angle X-ray Scattering as a tool in energy research”

MS7 - Giovani Cristallografi Italiani

Chairs: R. Vismara (University of Granada); G. Pierri (University of Salerno)

We are happy to announce the first symposium dedicated to young crystallographers! The spirit of the GCI symposium is to provide a welcoming environment for young scientists to present and discuss their research and establish future collaborations and networks. All main topics of crystallography will be covered. The symposium will include oral communications and flash presentations to promote your poster!

MS8 - Mineralogy: recent developments and applications

Chairs: P. Ballirano (Sapienza University of Rome); P. Comodi (University of Perugia)

This micro-symposium aims to show the current state-of-the-art investigation of several aspects of crystal structure, chemistry, and reactivity of minerals, glasses, melts, and fluids of interest in the Earth Sciences and their synthetic counterparts. Moreover, the link of such aspects with physical-chemical properties and, in turn, the geological and technological applications should be stressed. We encourage the submission of contributions reporting experimental and/or theoretical investigations covering different aspects of mineralogy, particularly emphasizing the green revolution-ecological transition and the interaction between minerals and biosphere.

Keynote lectures:

Dott. F. Bardelli (CNR-Nanotec) - "Combining X-ray diffraction and X-ray absorption spectroscopy to study Asbestos Bodies in human lung tissues"

Prof.ssa R. Arletti (University of Modena and Reggio Emilia) - "Secondary and alternative raw materials for ceramic tile production: a mineralogical point of view"

MS9 - Structural aspects of metal-based systems for the sustainable development

Chairs: V. Colombo (University of Milan); L. Marchiò (University of Parma)

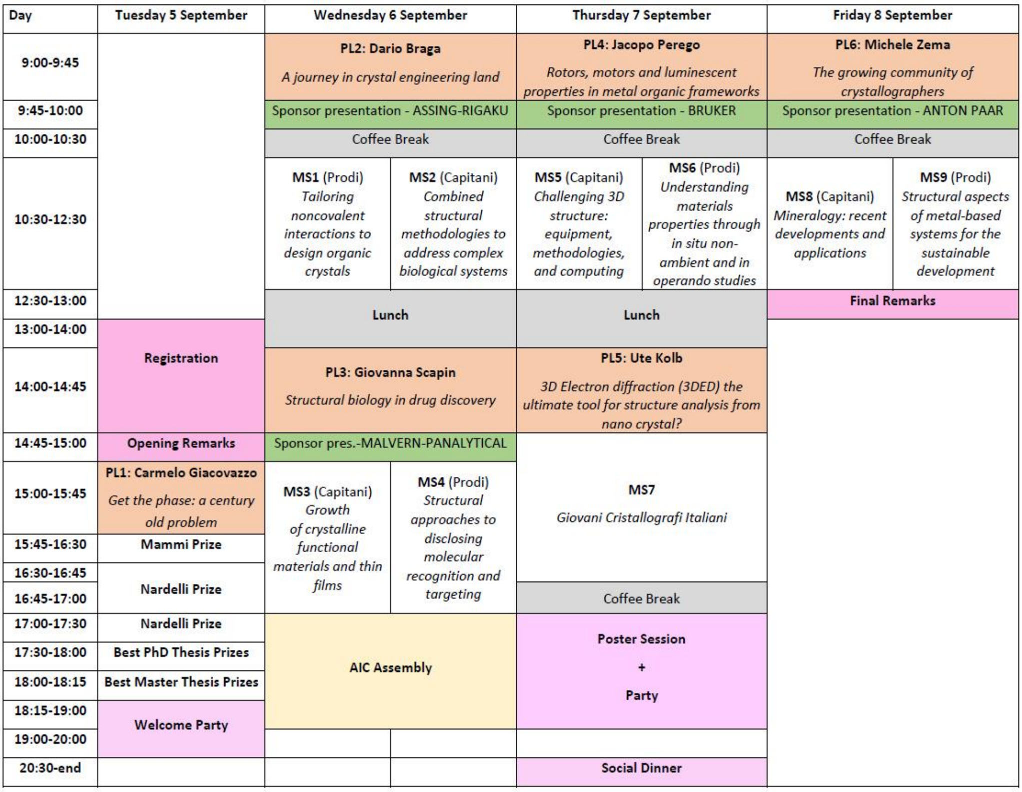
This micro symposium will focus on structural aspects of metal based-systems relevant to improving the efficient use of resources. The systems of interest will comprise mono-, poly-nuclear entities and extended frameworks. Discussion topics will be related to materials and compounds for energy storage and conversion, catalysis, recycling of materials, and any other issue relevant to sustainable development.

Keynote lectures:

Prof. E. Borfecchia (University of Turin) - "Understanding local structure and reactivity of copper-based catalysts for the valorization of light alkanes: from Cu-zeolites to Cu-MOFs"

Prof. L. Malavasi (University of Pavia) - "Structure-property correlations in metal halide perovskites: a route to design optimized and novel materials for energy applications"

Schedule



Day	Tuesday 5 September	Wednesday 6 September		Thursday 7 September		Friday 8 September	
9:00-9:45		**PL2: Dario Braga** *A journey in crystal engineering land*		**PL4: Jacopo Perego** *Rotors, motors and luminescent properties in metal organic frameworks*		**PL6: Michele Zema** *The growing community of crystallographers*	
9:45-10:00		Sponsor presentation - ASSING-RIGAKU		Sponsor presentation - BRUKER		Sponsor presentation - ANTON PAAR	
10:00-10:30		Coffee Break		Coffee Break		Coffee Break	
10:30-12:30		**MS1** (Prodi) *Tailoring noncovalent interactions to design organic crystals*	**MS2** (Capitani) *Combined structural methodologies to address complex biological systems*	**MS5** (Capitani) *Challenging 3D structure: equipment, methodologies, and computing*	**MS6** (Prodi) *Understanding materials properties through in situ non-ambient and in operando studies*	**MS8** (Capitani) *Mineralogy: recent developments and applications*	**MS9** (Prodi) *Structural aspects of metal-based systems for the sustainable development*
12:30-13:00		**Lunch**		**Lunch**		**Final Remarks**	
13:00-14:00	**Registration**						
14:00-14:45		**PL3: Giovanna Scapin** *Structural biology in drug discovery*		**PL5: Ute Kolb** *3D Electron diffraction (3DED) the ultimate tool for structure analysis from nano crystal?*			
14:45-15:00	**Opening Remarks**	Sponsor pres.-MALVERN-PANALYTICAL		**MS7** *Giovani Cristallografi Italiani*			
15:00-15:45	**PL1: Carmelo Giacovazzo** *Get the phase: a century old problem*	**MS3** (Capitani) *Growth of crystalline functional materials and thin films*	**MS4** (Prodi) *Structural approaches to disclosing molecular recognition and targeting*				
15:45-16:30	**Mammi Prize**						
16:30-16:45	**Nardelli Prize**						
16:45-17:00				Coffee Break			
17:00-17:30	**Nardelli Prize**	**AIC Assembly**		**Poster Session** **+** **Party**			
17:30-18:00	**Best PhD Thesis Prizes**						
18:00-18:15	**Best Master Thesis Prizes**						
18:15-19:00	**Welcome Party**						
19:00-20:00							
20:30-end				**Social Dinner**			

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Award winners

The aid of crystallography to address health and environmental issues caused by mineral fibres

Alessandro F. Gualtieri

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This acceptance speech of the 2023 Mario Mammi medal awarded by the Associazione Italiana di Cristallografia (AIC) will celebrate the mineralogical-crystallographic methods as powerful tools for the understanding of physical and crystal-chemical properties of carcinogenic mineral fibres like asbestos. Building on the experience gained in the areas of toxicology and bio-chemistry that require information on the structure–activity relationship to predict the toxicity and toxicity-related properties of molecules [1], it is clear now that only a deep knowledge of the crystal-structure of these complex minerals permits to disclose their very nature at a molecular level and to reveal the parameters prompting detrimental adverse effects *in vivo*. With a suite of powerful crystallographic tools, it is possible today to develop models to predict *a priori* the toxicity/pathogenicity potential of mineral fibres [2,3].

In this lecture, special attention will be devoted to asbestos and fibrous erionite. The latter is a unique "system" as it is the only known zeolite classified as Group 1 carcinogen by the International Agency for Research on Cancer (IARC) [4,5]. As a matter of fact, erionite is considered today one of the most insidious global environmental health hazards as it may cause malignant mesothelioma in humans by inhalation.

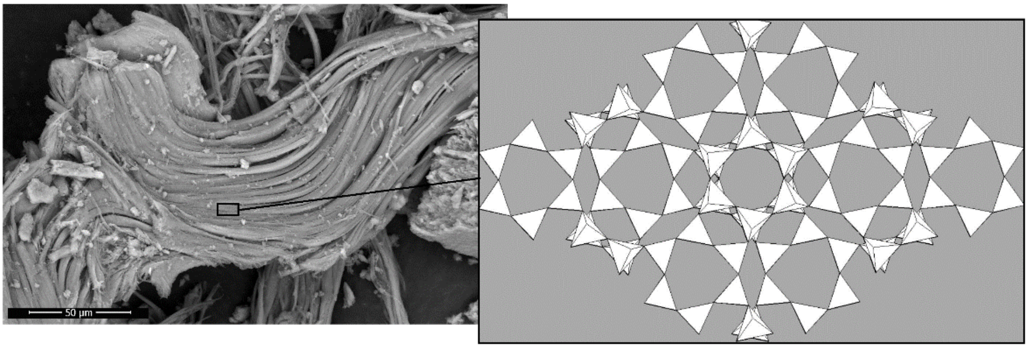

Figure 1. A bundle of carcinogenic asbestiform erionite (left) and its hexagonal 3D framework (right).

[1] G. Idakwo, J., Luttrell IV, M. Chen, H. Hong, P. Gong, C. Zhang. A review of feature reduction methods for QSAR-based toxicity prediction. Springer International Publishing, **2019**, 119-139.
[2] A.F. Gualtieri. *Toxicology and applied pharmacology*, **2018**, *361*, 89-98.
[3] B.T. Mossman, A.F. Gualtieri. Lung cancer: Mechanisms of carcinogenesis by asbestos. *Occupational cancers*, **2020**, 239-256.
[4] IARC. **1997**, *42*, 225–239.
[5] B.S. Van Gosen, T.A. Blitz, G.S. Plumlee, G.P. Meeker, M.P. Pierson. *Environmental Geochemistry and Health*. **2013**, *35(4)*, 419-4

Beyond the average: a journey to the multiscale diversity of framework materials

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If the structure of our universe was a poem, its language would be ‘local order’, and ‘randomness’ its blank page. While perfect order or complete lack thereof are human-made concepts, the way matter is structured can be described as ‘organized disorder’[1]. Porous framework materials are no exception, yet the gold standard of atomic structure determination remains the analysis of single-crystal Bragg intensities, which provide a space-averaged information known as ‘crystal structure’. This is how my academic journey started, as doctoral student focusing on the crystallography of metal–organic frameworks (MOFs), yet already striving to extract from crystal structures non-average details such as defects and disorder.

In this lecture I will cover a few selected stories from my past and present research aimed at elucidating the 3D real structure of MOFs and other framework materials. I will thereby introduce single-crystal total scattering as essential tool to determine non-periodicity in porous frameworks with 3D atomic resolution, and for ultimately re-shaping their chemistry by enabling the design of their real multiscale diversity [2].

[1] A. Simonov and A. L. Goodwin *Nature Reviews Chemistry*. **2020**, *4(12)*, 657–673.
[2] S. Canossa, Z. Ji, C. Gropp, Z. Rong, E. Ploetz, S. Wuttke and O. M. Yaghi *Nature Reviews Materials*. **2022**, *8*, 331–340.

Phase transition and crystal structure evolution of hydrated borates at high pressure

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Hydrated borates are a class of minerals composed of clusters or chains of $B\varphi_x$ groups (where φ represents an oxygen atom, a H_2O molecule, or an OH^- group) organized either in tetrahedra or planar triangular groups. Hydrated borates are considered a more cost-effective alternative to B_4C in radiation-shielding concretes [1], primarily due to the significant cross-section (~3840 barns) for thermal neutrons of the ^{10}B isotope, which represents approximately 20% of natural boron. It is advisable to comprehensively characterize the crystal chemistry, elastic properties, *P*-*T* phase stability fields, and structural behaviour of natural borates under varying temperature and pressure conditions to model and understand their role as aggregates in radiation-shielding concretes [2], where the components experience pressure (*via* static compression) and temperature (*via* irradiation). Since 2018, my research group has conducted an extensive study of economically valuable hydrated borates, as well as common complementary phases occurring in borates deposits. High-pressure investigations of all studied hydrated borates have revealed one or more phase transitions occurring at pressures below 11 GPa (Fig 1), and the occurrence of these transitions appears to be highly correlated with the H_2O content of the minerals (*e.g.*, [3-4]). In response to the phase transitions, the most significant structural change observed in our experiments is the increase in the coordination number of alkali/alkaline-earth cations as well as of part of the boron population, from ^{III}B to ^{IV}B, due to the interaction between ^{III}B and H_2O molecules. This, on the other hand, emphasizes the importance of the hydrogen bond network, usually with complex and pervasive configuration, in preserving the stability of the crystalline edifice of this class of materials.

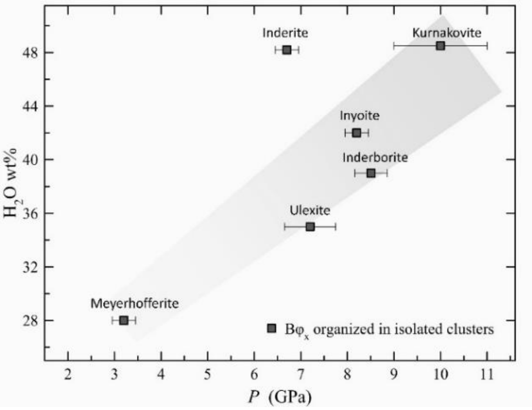

Figure 1. H_2O content *vs.* pressure at which the phase transition occurs in borate structures characterized by isolated polyions. A qualitative linear correlation is represented by the grey shade.

[1] Okuno K. *Radiat. Prot. Dosimetry*. **2005**, 115, 258–261.
[2] Torrenti J., Nahas G. *Int. Conf. Concr. under Sev. Cond*., Merida, Yucatan. **2010**, 3–18
[3] Comboni D., et al. Am. Ceram. Soc. **2020**, 103:5291–5301
[4] Comboni D., et al. Acta Crystallogr. **2021**, B 77:940–945.

Zeolites as a scaffold for UV filters: from sunscreens to crystallography

Riccardo Fantini,[a] Giorgia Confalonieri,[b] Giovanna Vezzalini,[a] Francesco Di Renzo,[c] Lorenzo Mino,[d] Michael Fischer,[e] Rossella Arletti[a]

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[b]European Synchrotron Radiation Facility, Grenoble, France.
[c]ICGM, University of Montpellier, CNRS, ENSCM, Montpellier, France.
[d]Department of Chemistry, NIS Centre of Excellence, University of Turin, Torino, Italy.
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Zeolites are particularly suitable for high-value technological applications based on ion exchange and selective adsorption of organic molecules. In the last decades the attention was focused also on the realization of novel functional materials based on the encapsulation of organics (e.g. dyes, polymers) inside zeolites.

UV filters (UVfs) are organic or inorganic compounds employed to block UV rays to protect goods and human health. Unfortunately, organic UVfs easily undergo photodegradation, and several UVfs and co-formulants are often combined to enhance their stability and efficacy. In the last decades, the encapsulation of UV filters in diverse inorganic or organic matrixes demonstrated to be an effective stabilization strategy.

We recently developed hybrid UVfs (here after ZEOfilters) obtained by the encapsulation of the two organic UVfs octinoxate (OMC) and avobenzone (AVO) into zeolites with different topologies (MOR, FAU, MFI, and LTL) and Si/Al ratios [1]. The use of ZEOfilters should: i) inhibit the UVf-skin and UVf-UVf interactions; ii) allow to reduce the content of UVf, stabilizers, and other co-formulants thanks to the enhanced filtering efficacy.

Potassium LTL and sodium 13X zeolites were found to be the most promising hosts for UVfs and were thus investigated more deeply. Recently [2], some selected ZEOfilters were also investigated from a structural perspective, by high-resolution synchrotron X-ray powder diffraction, Fourier-transformed IR spectroscopy, and DFT modelling. In the LTL/OMC ZEOfilter, FT-IR highlighted a perturbation of the ν(C=O) mode of the OMC carbonyl group which was demonstrated, by structural refinement, to bond the extraframework K cations of LTL zeolite. Meanwhile, DFT calculations are investigating the behaviour of ZEOfilters based on FAU-type zeolites, which showed strongly variable properties depending on Si/Al ratio and UVf. The observed properties are promising for the future development and exploitation of ZEOfilters, which can be a more effective, safer, and eco-friendly alternative to traditional UVfs.

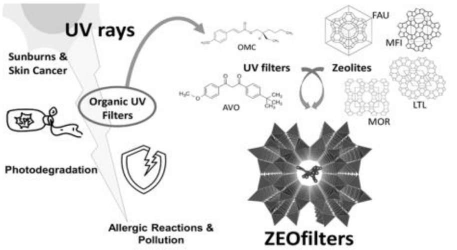

Figure 1. Overview of ZEOfilters project.

[1] R. Fantini, et al. *Micropor. Mesopor. Mat.* **2021**, 328,111478
[2] G. Confalonieri, et al. *Micropor. Mesopor. Mat.* **2022**, 344, 112212

Differential scanning diffraction for in situ investigations of choline-based deep eutectic solvents

Mattia Lopresti,[a] Luca Palin,[a] Marco Milanesio,[a] Matteo Bonomo,[b] Claudia Barolo[b]

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Over the past decades, laboratories have gained access to hot/cold stages, allowing in situ X-ray diffraction experiments under non-environmental conditions [1]. This advancement, coupled to improved detectors and data collection systems, reduces the need for large-scale synchrotron facilities, as now enable the collection of extensive data within a few hours of experimentation, even in lab settings. Using this new instrument setup, in situ experiments at non-ambient temperatures have been carried out, capturing imaging and diffraction data simultaneously to study both the structural and morphological features of materials in a single observation [2]. The key advantage of these experiments lies in the ability to observe the gradual transformations of the analyzed samples throughout the entire process. These transformations can include phase transitions, polymorph conversions, or chemical reactions. By leveraging in situ imaging and X-ray diffraction data, coupled with multivariate analysis techniques like principal component analysis (PCA) [3], two novel methods have been presented in a recent article: differential scanning diffraction (DSD) and differential scanning imaging (DSI) [2]. These techniques provide insights into the structural changes induced by temperature gradients, similar to those obtained through differential scanning calorimetry (DSC). These innovative techniques have proven effective in investigating diverse materials, providing valuable insights into their behavior and driving progress in materials science and engineering. DSD in particular has been successfully applied to the study of various materials, such as inorganic compounds as test cases and are currently exploited to study organic-based eutectic mixtures known as deep eutectic solvents (DES) [4]. DES are a class of solvents formed by mixing a hydrogen bond acceptor (HBA) and a hydrogen bond donor (HBD). DES have a lower melting point than the individual components and exhibit low volatility, low toxicity, and good thermal stability. Moreover, DES can dissolve a wide range of organic and inorganic compounds, making them versatile materials for application in green chemistry, electrochemistry, catalysis, and biomass processing. DSD/DSI techniques [2] are applied Choline-based DES to investigate the liquid/solid transition coupling the morphological and structural viewpoints.

[1] Conterosito, E.; Lopresti, M.; Palin, L. *Crystals* **2020**, *10,* 483. DOI:https://doi.org/10.3390/cryst10060483.

[2] Lopresti, M; Mangolini, B; Conterosito, E; Milanesio, M; Palin, L. *Crystal Growth & Design* **2023,** *23 (3),* 1389-1402. DOI: 10.1021/acs.cgd.2c00917.

[3] Guccione, P.; Lopresti, M.; Milanesio, M.; Caliandro, R. Multivariate Analysis Applications in X-ray Diffraction. Crystals **2021**, *11*, 12. https://doi.org/10.3390/cryst11010012.

[4] Hansen, B.B. et al. J.R. *Chemical Reviews* **2021** *121 (3),* 1232-1285. DOI: 10.1021/acs.chemrev.0c00385

Best master or bachelor thesis in crystallography,
in memory of Prof. Fiorenzo Mazzi

Thallium incorporation in hydropyrochlore crystals

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Hydropyrochlore is a cubic mineral (space group *Fd*-3*m*, *a* = 10.56-10.59 Å, Z = 8) belonging to the pyrochlore supergroup (general formula: $A_{2-m}B_2X_{6-w}Y_{1-n}$), with the ideal formula $(H_2O,\square)_2Nb_2(O,OH)_6(H_2O)$ [1].

In 1978, van Wambeke [2] described it for the first time while studying carbonatites from the Lueshe deposit (Kivu, D.R. Congo) and named the new mineral *kalipyrochlore* due to its K^+ enrichment. At Lueshe, K-rich hydropyrochlore is found as a secondary product of primary $(Ca,Na)_2Nb_2O_6F$ pyrochlores. The weathering processes undergone by magmatic pyrochlores lead to a major loss of Ca, Na and F, compensated by a minor uptake of Sr and K, the formation of a significant number of vacancies at the A site and hydration (up to 12 wt.% H_2O). Water molecules can enter the structure at both A and Y sites, namely the sites located within the large tunnels generated by the BO_6 framework, up to 1.75 apfu [3].

All these features give rise to the remarkable ion-exchange capacity of hydropyrochlore, which is very interesting from an environmental point of view: hydropyrochlore is, in fact, a promising candidate as a sink for heavy metals, especially thallium, dispersed in aqueous matrices.

This study aims to investigate structural and chemical variations induced by Tl^+ incorporation in the hydropyrochlore structure by means of imbibition experiments in a diluted Clerici solution, in order to assess its exploitability in the decontamination of polluted natural and/or industrial waters. The soakings were performed on single crystals extracted from a large octahedral fragment of hydropyrochlore. Tl^+ incorporation was then evaluated through single-crystal X-ray diffraction (SC-XRD) and electron microprobe analysis (EMPA).

After the imbibitions, SC-XRD data show a lengthening of the cell parameter of 7-9 ‰, together with a significant increase of electron density at the A site (from 6 to 57 e^- before and after the treatment, respectively) and a decrease at the Y site (from 10 to 3 e^-). Accordingly, chemical analyses revealed the presence of significant amounts of Tl^+ (up to 1.40 apfu). Taking into account all the crystal-chemical variations and the charge balance, these results suggest that Tl^+ enters the A site possibly at the expense of H_3O^+, which is thus hinted to be the dominant water species in K-rich hydropyrochlore from Lueshe.

[1] D. Atencio, M.B. Andrade, A.G. Christy, R. Gieré, P.M. Kartashov *Can. Mineral.* **2010**, *48*, 673.
[2] L. van Wambeke *Am. Min.* **1978**, *63*, 528.
[3] T.S. Ercit, F.C. Hawthorne, P. Černý *Can. Mineral.* **2004**, 32, 415.

Best master or bachelor thesis in crystallography,
in memory of Prof. Fiorenzo Mazzi

Stimuli Responsive Hybrid Coordination Polymers based on Copper Iodide as luminescent mechanochromic materials

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The quest for novel hybrid inorganic-organic compounds to be used in various applications points to the abundant, cheap, and environmentally friendly copper iodide. CuI hybrid coordination polymers (HCP) exhibit a high structural diversity and stimuli-responsive photophysical properties, making them interesting for potential applications as sensors, displays and memories [1]. In this work, interest has been devoted to the study of four CuI-based HCPs: $[(\mathrm{CuI})_2\mathrm{pyrazine}]_n$, $[(\mathrm{CuI})_2\text{3-picolylamine}]_n$, $[(\mathrm{CuI})\text{3-Bromopyridine}]_n$ and $[(\mathrm{CuI})\text{4-Aminopyridine}]_n$.

All HCPs are luminescent under UV light irradiation; additionally, for all compounds, the emitted colour changes by grinding the crystallites in an agata mortar. This property is called luminescent mechanochromism [2]. The emission properties of the HCPs before and after grinding have been measured with spectrofluorometric measurements while the introduction of defects in the crystalline structure has been assessed from PDXR data using WPPM approach [3]. The luminescent mechanochromism of these HCPs is interesting for the application perspective in the field of sensors, however, being fragile crystalline material, they do not possess the mechanical properties required for this kind of application. To overcome this intrinsic limitation, they can be used as fillers for the preparation of stimuli-responsive composite materials able to sense impact damage. To work for this purpose, the composite must have an adequate response threshold and display irreversible mechanochromism. Additionally, to preserve the aesthetic of the coated object, no change in the absorption properties should be detected under visible light. Preliminary tests using PVAc as matrix have been carried out.

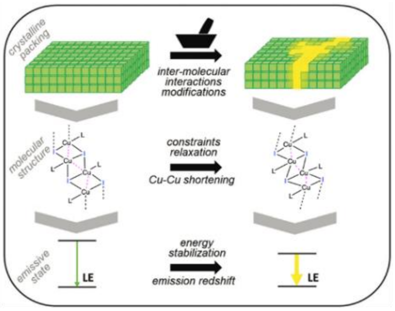

Figure 1: Schematic representation of the mechanism of the luminescence mechanochromism phenomenon of $[(\mathrm{CuI})_x\mathrm{L}]_n$

[1] Cariati, E.; et al. Cu(I) Hybrid Inorganic-Organic Materials with Intriguing Stimuli Responsive and Optoelectronic Properties. *Coord. Chem. Rev.* **2016**, *306*, 566–614. https://doi.org/10.1016/J.CCR.2015.03.004.

[2] Perruchas, S. Molecular Copper Iodide Clusters: A Distinguishing Family of Mechanochromic Luminescent Compounds. *Dalt. Trans.* **2021**, *50 (35)*, 12031–12044. https://doi.org/10.1039/d1dt01827b.

[3] Scardi, P.; at al. A. Whole Powder Pattern Modelling Macros for TOPAS. *J. Appl. Crystallogr.* **2018**, *51 (6)*, 1752–1765. https://doi.org/10.1107/S160057671801289X

Best master or bachelor thesis in crystallography,
in memory of Prof. Fiorenzo Mazzi

Structural investigation of *Pseudomonas aeruginosa* SOS machinery components by cryo-EM

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Recombinase A, RecA, is a ubiquitous protein, conserved among different bacterial species, and it is involved in a wide range of molecular mechanisms triggered upon DNA lesion, such as the SOS response induction. Indeed, in presence of single stranded DNA (ssDNA), several monomers of RecA assemble on it in an ATP-dependent manner to form a nucleoprotein filament (RecA*), which stimulates LexA auto-proteolytic activity. LexA self-cleavage leads to the de-repression of SOS genes, including those coding for error-prone translesion DNA polymerases, recombinases and integrases. This response determines a sudden increase in mutagenesis rate (hypermutation), leading to the rapid evolution of antibiotic-resistant bacteria [1].

In this context, the structural characterization of the *Pseudomonas aeruginosa* SOS response components proves to be crucial for the design of drugs able to inhibit the binding between RecA and LexA and thus, the onset of resistance.

For this reason, we decided to investigate the structure of both RecA* alone (RecA monomers assembled with 72-mer ssDNA, non-hydrolysable ATPγS and MgCl2+) and in complex with LexA, by using cryo-electron microscopy (cryo-EM). The images were acquired on the Titan Krios microscope of the CM01 facility of the European Synchrotron Radiation Facility (ESRF). We managed to solve RecA* filament, obtaining an overall resolution of 4.2 Å, reaching 3.8 Å in the core. The residues involved in the binding of ssDNA, ATPgS and Mg2+ are well defined and conserved compared to the ones that are involved in ligands binding in the RecA ortholog from *Escherichia coli*.

Probably due to the partial occupancy of LexA bound to RecA*, causing a general heterogeneity of the filaments, the data processing of RecA -LexA complex is more challenging than the one of RecA* filaments alone and thus, it's still ongoing. Since all the attempts to set the autopicker failed, 209610 filaments were manually picked, and particles extracted for several rounds of 2D classification. Particles were selected from the best 2D classes and used for generating an ab-initio model using RELION, then imported in CryoSPARC for the subsequent processing.

In this presentation I will give a brief overview of how RecA switches to its activated form, self-assembling around ssDNA, and anticipate some preliminary results on its binding to LexA [2].

[1] Maslowska *et al.*, The SOS System: A complex and tightly regulated response to DNA damage. *Environmental and Molecular Mutagenesis* (**2018**).

[2] Gao *et al.*, Structural basis for regulation of SOS response in bacteria. *Proc Natl Acad Sci U S A* (**2023**).

Plenary lectures

Get the phase: a century old problem

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The phase problem is one of the most fascinating problems in crystallography. The study of the organization of matter in the solid state often requires a diffraction experiment, which produces tens or even hundreds of thousands of experimental intensities. Each intensity can be related to the square modulus of the corresponding structure factor. Unfortunately, each structure factor is a complex number, whose modulus is provided by the experiment but whose phase is lost in the experiment.

Recovering the phases using the prior information of the moduli is essentially the phase problem in crystallography.

Various methodologies have been employed to solve the problem, which can be distinguished into two branches: one for small molecules and one for macromolecules. These two branches have developed independently: the first has led to the solution of the phase problem for small molecules through Direct Methods, while the second has significantly improved the procedures for macromolecules. The two branches have rarely interacted, except starting from the 1990s when the solution to the phase problem for small molecules had been achieved.

This talk aims to summarize the efforts made by two generations of crystallographers in solving the phase problem for small molecules. In addition, there will be a short time devoted to the automatic crystal structure solution of the macromoleules through Molecular Replacement.

A journey in crystal engineering land

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In the beginning there was no crystal engineering, only crystallization. The products of crystallization were crystals, and determining the "molecular and crystal structure" was the challenge, the beginning and the end of the work of a crystallographer. It is easy to understand why synthetic chemists and crystallographers were bound by a love-hatred relationship: the former depended on things that could not control: availability of the diffractometer, hence time, queue, priorities, diffraction quality of the crystals, etc., while the latter depended on the preparative chemist to be given good crystals to work with, exciting scientific problems, and challenges. At the end of the 80's things changed. On the one hand, diffraction and computational facilities became cheaper, faster, and more accessible, crystal data were stored in databases that could be interrogated. At the same time, the strong wind of supramolecular chemistry, the chemistry beyond covalent bond, begun to blow bringing many to realize that a crystal is, after all, an "organized entity of higher complexity held together by intermolecular forces". **A paradigm shift: crystals as solid supermolecules with collective properties** resulting from the convolution of molecular properties with crystal periodicity. Hence, crystals as materials with collective properties resulting from the complex, and often not unique, compromise between optimization of molecular and crystal structure. Crystal engineering was born, and **many crystallographers became crystal makers**. This evolutionary step had consequences: first, the need to minimize the chance of investing on thermodynamically unstable materials, by gaining some degree of control on crystal polymorphism; second, the need to explore viable alternatives to crystallization from solution, for example by mechanically mixing solid reactants; third, the need to strengthen methods for structure determination in the absence of suitable single crystals, hence structure solution from powder and computational simulations, and, fourth, the need to expand competence in solid state techniques beyond crystallography. Thanks to the success in all these directions, we are able today to build, compute and characterize crystalline materials for an incredible variety of applications. Crystal engineering has turned into the wholesome **"holistic" discipline** that we enjoy today beyond the boundaries of chemistry, across different areas of science, connecting physics, engineering, biology, pharmacy, environment and agriculture, still growing at exponential pace. **Crystal engineering is now at the "delivery" stage**. The literature shows the vastity of successful applications of the "making crystals by design" approach. In this talk, I will only be able to touch upon a limited number of examples coming mainly from the work of the Molecular Crystal Engineering group at the University of Bologna.

I acknowledge the long-standing collaboration with Fabrizia Grepioni, Lucia Maini and Simone d'Agostino, and that with many great friends and scientists in Italy and abroad I have had the fortune to work with. There is not enough space to list them all.

Structural Biology in Drug Discovery

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In recent years cryo-EM has revolutionized structural biology by enabling high-resolution structure determination of systems previously inaccessible. The Biopharma community quickly understood that cryo-EM could potentially transform our thinking about structures and biology, and as a result cryo-EM access has become an essential commodity for life science companies big and small. In order to integrate cryo-EM into a successful drug discovery campaign, several hurdles need to be addressed, from instrument availability and cost to speed of data collection and processing, to data storage and retention.

A successful SBDD project relies on a fast supply of structural data to inform subsequent cycles of design. This could correspond to the determination of several atomic-level structures a week. Though not yet routine in cryo-EM, this pace is now achievable with current hardware and software. The rate limiting step now becomes the reproducible generation of grids suitable for good data collections. Unfortunately, reproducibility with the current vitrification robots is difficult to achieve. Novel vitrification devices are poised to improve the reproducibility and the quality of the grids, but they still require more extensive testing, particularly in SBDD pipelines. Even further upstream from grid preparation, but critically important for the success of a project, is the quality of the sample itself. Even if cryo-EM offers multiple advantages over crystallography, especially in that there is more tolerance for discrete compositional and/or conformational heterogeneity, having a reliable source of good quality protein is as necessary in cryo-EM as it is in any other structural approach.

While the industry’s focus in the most recent years has been in the single particle application of cryo-EM, it should not be forgotten that TEM and cryo-EM can also provide comprehensive insights for characterization of nanoparticle therapeutics, from lipid nanoparticles to vaccines. Cryo-EM can unveil many aspects of a sample simultaneously, in a single image (for example size, drug encapsulation, shape, morphology, impurities, integrity, aggregation). This makes cryo-TEM a powerful orthogonal technique to complement many characterization toolkits. Use of TEM and Cryo-EM is particularly advantageous when a sample is heterogeneous, available in limited quantities and/or needs to be analyzed at a concentration similar to drug preparation for IV administration.

TEM and cryo-EM are increasingly becoming the technique of choice for drug discovery processes, but diverse skill sets and state-of-the art technology are necessary to really make cryo-EM accessible to companies of all sizes, and to teams across the drug discovery and development pipeline.

PL4

Rotors, motors and luminescent properties in metal organic frameworks

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Rotors, motors and switches in the solid state find a favorable playground in Metal Organic Frameworks (MOFs), thanks to their large free volume, which allows for fast dynamics. We have realized a fast molecular rotor in a Zn-MOF whose rotation speed approaches that of unhindered rotations in organic moieties even at very low temperatures (2 K) [1,2]. Geared molecular rotors with negligible energy-requirements in pillared MOFs enabled fast yet controllable and correlated rotary motion [3], showing an unprecedented cascade mechanism. Chemical stimuli such as the use of CO2 diffused through the open pores changed dramatically the global rotation mechanism and rotor speed.

Attractive functional properties, such as dielectric, optical and ferroelectric switchable properties, can be activated by incorporating fast-reorientable dipoles onto molecular rotors to produce materials responsive to static or oscillating electric fields. In fluorinated MOFs comprising a wheel-shaped ligand with geminal rotating fluorine atoms, we tailored benchmark dipole rotational dynamics in the presence of a concerted dance of dipoles with practically null activation energy of 17 cal mol-1[4]. Furthermore, motors were inserted into MOFs wherein two distinct linkers with complementary light absorption-emission properties were integrated into the same material. Unidirectional motion was achieved by exposure to sunlight of the solid material, which thus behaves as an autonomous nanodevice [5].

We demonstrated that fluorescent metal–organic framework (MOF) nanocrystals can work as fast scintillators [6]. The MOF comprised high-Z linking nodes that interact with the ionizing radiation and are arranged in an orderly fashion at a nanometric distance from ligand emitters. Their incorporation in the framework enabled fast sensitization of the ligand fluorescence, showing an ultrafast scintillation rise time of ~50 ps. Additionally, two ligands of equal molecular length and connectivity, yet complementary electronic properties, were co-assembled in a Zr-MOF, generating crystalline hetero-ligand MOF nanocrystals which resulted in high efficiency luminescence with significant Stokes shift and benchmark performances [7].

Moreover, scintillating MOFs were simultaneously capable of concentrating radioactive gases and efficiently producing visible light revealed with high sensitivity. We demonstrated the capability of a hafnium-based MOF incorporatingdicarboxy-9,10-diphenylanthracene as a scintillating conjugated ligand to detect gas radionuclides [8]. Metal–organic frameworks showed fast scintillation, a fluorescence yield of ∼40%, and accessible porosity suitable for hosting noble gas atoms and ions. Adsorption and detection of 85Kr, 222Rn and 3H radionuclides were explored through a newly developed device, suggesting the use of scintillating porous MOFs to fabricate sensitive detectors of natural and anthropogenic radionuclides.

[1] *Nature Chem.* **2020**, 12, 845.
[2] *Nanoletters* **2020**, 20, 7613.
[3] *J. Am. Chem. Soc.* **2021**, 143, 13082.
[4] *Angew. Chem. Int. E*d. **2023**, e202215893.
[5] *J. Am. Chem. Soc.* **2020**, 142, 9048.
[6] *Nature Photonics* **2021**, 15, 393-400;
[7] *Nature Communications* **2022**, 13, 3504.
[8] *Nature Photonics* **2023**, https://doi.org/10.1038/s41566-023-01211-2.

3D Electron diffraction (3DED) the ultimate tool for structure analysis from nano crystal?

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Many functional materials are nano crystalline or are composed of particles down to a few nanometers in size. X-ray powder diffraction, usually used for structural investigation of these materials, renders often difficult especially if the solution of a new crystal structure is involved. Features like low crystal size, large cell parameters and low symmetry or disorder as well as impurities and phase mixtures lead to uncertainties in intensity determination. Electron microscopy, especially high-resolution imaging techniques using a transmission electron microscope (HR-(S)TEM) allow visualizing structural features directly at the atomic scale but require high electron dose of several thousand e-/Å2s causing beam damage.

In the last two decades electron crystallography experienced a boost through the development of electron diffraction tomography. After the principles of data acquisition and processing strategies were developed 2007 as automated electron diffraction tomography (ADT) [1] a series of other methods has been set up slightly differing in data collection strategies. Later all methods were summarized as three dimensional electron diffraction (3DED) [2].

The major difference between the methods in imaging and diffraction strategies using TEM/SAED or STEM/NED mode will be compared for application on crystalline domains in the regime of some tens of nanometer, sometimes even strongly agglomerated or for material which is highly beam sensitive (MOFs, small organic molecules). In the case of STEM imaging special tracking routines have been developed (FAST-ADT) [3]. The potential of the FAST-ADT method for crystal structure analysis of a variety of nano-crystalline oxides like battery materials, catalysts and glass ceramics as well as the detection of metastable phases will be discussed [4,5]. The handling of special crystallographic features like twinning, intergrowth of polytypes and the quantitative analysis of defects like stacking faults will be presented.

[1] U. Kolb, T. Gorelik, C. Kübel, M.T. Otten, D. Hubert, *Ultramicroscopy*, **2007**, 107, 507

[2] M. Gemmi, E. Mugnaioli, T. E. Gorelik, U. Kolb, L. Palatinus, Ph. Boullay, S. Hovmöller and J. P. Abrahams, *ACS Cent. Sci.* **2019**, 5, 1315.

[3] S. Plana-Ruiz, Y. Krysiak, J. Portillo, E. Alig, S. Estrade, F. Peiro, and U. Kolb, *Ultramicroscopy*, **2020**, 211, 112951

[4] P. Opitz, Y. Krysiak, S. Plana-Ruiz, G. Matveeva, P. Nocon, M. Maslyk, M. Mondeshki, U. Kolb and W. Tremel, *Angew. Chem.*, **2021**, 115, 41

[5] F. Steinke, L. Gemmrich Hernandéz, S. J. I. Shearan, M. Pohlmann, M. Taddei, U. Kolb and N. Stock, *Inorg. Chem.* **2023**, 62 (1), 35

The growing community of crystallographers

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Conducting independent research, applying for funds, writing articles and reports, teaching various classes, managing research groups and labs, supervising students, dealing with bureaucracy, and popularizing disciplines among pre-academic students and the public are some common tasks that faculty members of a university have to undertake. Not to mention the service to the institution of affiliation, and to the community. And the list continues.

Whereas on one side, this may seem daunting to those young researchers dedicated to pursuing an academic career, on the other side, the various facets of the academic profession are actually key to carrying out the primary objectives of the profession itself. These goals encompass advancing science, as well as inspiring and educating the new generations, transferring knowledge, sharing expertise and innovations, encouraging global scientific cooperation, increasing public awareness. In short, a career in academia presents countless opportunities to make a lasting impact and leave a mark in the scientific community and beyond.

In this talk, I'll take you on a journey of my personal experience, culminated in coordinating the UN International Year of Crystallography 2014 and from there, continued to coordinating the outreach and education activities of the most prestigious international crystallographic society, the IUCr. This has brought me to collaborate closely with UNESCO and several other governmental and non-governmental organizations.

My interest in coordinating scientific activities at different scales was discovered through my involvement with the Italian Crystallographic Association (AIC). From my first participation in the organising committee for the SIMP-AIC Congress 2008, to serving on the AIC Commission on Teaching for two mandates and on the AIC Council for one mandate, I have particularly contributed to give an international flavour to the AIC Schools, culminating in organizing the 1st European Crystallography School in 2014.

For the last ten years, initiatives have targeted emerging countries worldwide and students of all ages, from schoolchildren to early career researchers and established crystallographers. With a strong sense of inclusiveness and an expanding geographical scope, crystallography has come to occupy a highly respected position in the global science diplomacy and advocacy debate. The scientific community's appreciation for assessing science capacity building worldwide has also significantly grown thanks to efforts dedicated to enhancing scientific research, education, and infrastructure.

Flagship activities I have initiated, like the IUCr-UNESCO OpenLab, *LAAAMP*, X-TechLab, crXstal, as well as other initiatives will be presented.

Micro symposium 1

Tailoring noncovalent interactions to design organic crystals

MS1 - Tailoring noncovalent interactions to design organic crystals

Chairs: P. Metrangolo (Polytechnic University of Milan); P. Paoli (University of Florence)

Understanding and controlling noncovalent interactions, which guide the supramolecular arrangement in crystals, is a crucial step for the bottom-up design and synthesis of materials featuring the desired properties/functions. This micro symposium welcomes contributions to using hydrogen, halogen, and chalcogen bonds, van der Waals, pi-stacking, and other supramolecular interactions in crystal engineering. The aim is to provide a forum for researchers working across different molecular-based crystalline solids such as pharmaceuticals, organic semiconductors, agrochemicals, organic pigments, organic frameworks, etc. Contributions are welcome that cover fundamental to applied research, experimental and *in-silico* approaches, and structure-property/function rationale.

Wednesday 6 September – morning 10.30-12.30

Keynote 1: 10.30-11.00
Alessia Bacchi
Department of Chemical Sciences, Life Sciences and Environmental Sustainability, University of Parma
Tweaking interactions to achieve release performances in co-crystals

Keynote 2: 11.00-11.30
C. Malla Reddy
Department of Chemical Sciences, Indian Institute of Science Education and Research, Kolkata
Crystal engineering of adaptive smart materials

Oral 1: 11.30-11.45
Giovanni Macetti
Department of Chemistry, Università di Milano
Symmetry-constrained Monte Carlo to predict the experimental crystal structure of small organic molecules

Oral 2: 11.45-12.00
Enrico Spoletti
Department of Chemical Science & Bernal Institute, University of Limerick
True Polymorphism in a Solid Solution of Tolbutamide and Chlorpropamide affords a High-Soluble Co-Drug Form

Oral 3: 12.00-12.15
Giovanni Pierri
Department of Chemistry and Biology, University of Salerno
The influence of weak interactions in the backbone conformation and solid state behavior of cyclic peptoids

Oral 4: 12.15-12.30
Luigi Renzo Nassimbeni
Department of Chemistry, University of Cape Town
A survey of Inclusion Compounds: Structure, Selectivity and Kinetics

MS1-KN1

Tweaking interactions to achieve release performances in co-crystals

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Crystal engineering is a powerful tool to design materials with high technological added value to address health and environment protection through mild and nature friendly components and methods. Some compounds relevant to human health and nutrition are liquid at ambient conditions (L-API); widely known examples are propofol, vitamin E, nicotine, and terpenoids and phenolic derivatives used as natural antioxidants such ascarvacrol, eugenol, eucalyptol, and valproic acid. A practical way to manufacture some of these compounds in a solid dosage form is to modifytheir molecular structures by synthetic derivatization, or to turn them into salts, provided that the molecule may be reacted with a convenient acid orbase, and that these are acceptable from a regulatory point of view. However, not all the molecules may become salts, and derivatization may alter molecular bioavailability. Recently, cocrystallization has proven to be a powerful method to control the release of liquid ingredients in the environment, by engineering of ad hoc intermolecular interactions which strengthen or weaken the tendency of the ingredient to be retained inside the solid matrix. [1-2]. Similarly, L-API have been encapsulated within adaptable cavities of Metal Organic Frameworks purposedly designed to uptake such guests; the evolution in time of the supramolecular arrangement of the nano-confined guests in the cavities has beenmonitored by SCXRD and related to the observed selectivity ofthe material towards different L-API guests [3].

We here present some proofs of concept that a rational design of crystalline materials capable to store and release L-API guests is feasible (Figure 1), and that the release profile can be related to the solid state arrangement of the material, offering a strong and rational tool to afford a vast range of materials capable of controlled release of L-APIs.

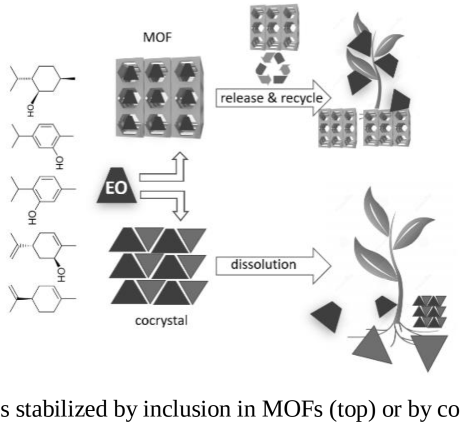

Figure 1. Example of EOs stabilized by inclusion in MOFs (top) or by cocrystallization (bottom) to customize their release profile or dissolution rate.

[1] A Bacchi, P.P. Mazzeo, *Crystallography Reviews* **2021**, *27(2)*, 1

[2] P. P. Mazzeo, C. Carraro, A. Monica, D. Capucci, P. Pelagatti, F. Bianchi, S. Agazzi, . Careri, A. Raio, M. Carta, F. Menicucci, M. Belli,M. Michelozzi, A. Bacchi, *ACS Sustainable Chem. Eng*. **2019**, *7*, 17929

[3] D. Balestri, P. P.Mazzeo, C. Carraro, N. Demitri, P. Pelagatti, A. Bacchi. *Angew. Chem. Int. Ed.*, **2019**, *58*, 17342

Crystal engineering of adaptive smart materials

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High crystallinity, although desired in materials for a wide range of high-performance engineering applications, generally comes with undesirable attributes such as high brittleness and fragility [1]. This makes crystalline materials incompatible with many future technologies, such as flexible devices and soft-robotics. Recent progress in crystal engineering has brought into light many possible opportunities to address these issues, enabling the design of adaptive crystalline materials that respond to external stimuli with exceptional qualities [1-7]. For instance, crystals that bend (elastically or plastically), twist, curl, wind, jump, exfoliate, laminate, and explode, under external stresses, such as mechanical stress, pressure, light, heat, solvent, etc., have been shown. On the other hand, until very recent time, self-healing was observed only in soft and amorphous materials, mostly involving approaches that use chemical reactions, diffusion, solvent, vapour, electricity, etc., with typical healing time scales in minutes to weeks [8]. A new self-healing mechanism that we recently introduced [9] in materials science, enables ultrafast, near 100% autonomous diffusion-less repair in crystalline materials that uses electrostatic surface potentials generated on the freshly created fracture surfaces, inherent to certain types of polar single crystals. My talk will cover structure-property correlation for crystal engineering of adaptive materials.

[1] Saha, S., Mishra, M. K., Reddy, C. M. & Desiraju, G. R. (**2018**) *Acc. Chem. Res*. 51, 2957.

[2] Reddy, C. M., Gundakaram, R. C., Basavoju, S., Kirchner, M. T., Padmanabhan, K. A. & Desiraju, G. R. (**2005**), *Chem. Commun*. 3945.

[3] Ghosh, S. & Reddy, C. M. (**2012***) Angew. Chem. Int. Ed.*, 51, 10319.

[4] Krishna. G. R., Devarapalli, R., Lal, G. & Reddy, C. M. (**2016**) *J. Am. Chem. Soc*., 138, 13561.

[5] Naumov, P., Chizhik, S., Panda, M. K., Nath, N. K. & Boldyreva, E. (**2015**) Chem. Rev., 115, 12440.

[6] Mondal, A., Bhattacharya, B., Das, S., Bhunia, S., Chowdhury, R., Dey, S. & Reddy, C. M. (**2020**) *Angew. Chem. Int. Ed.* 59 ,10971.

[7] Takamizawa, S. & Miyamoto, Y. (**2014**) *Angew. Chem. Int. Ed.* 53, 6970.

[8] Yanagisawa, Y., Nan, Y., Okuro, K. & Aida, T. (**2018**) *Science*, 359, 72.

[9] Bhunia, S., Chandel, S., Karan, S. K., Dey, S., Tiwary, A., Das, S., Kumar, N., Chowdhury, R., Mondal, S., Ghosh, S., Mondal, A., Khatua, B. B., Ghosh, N & Reddy, C. M. (**2021**), *Science,* 373, Issue 6552, pp. 321-327.

Symmetry-constrained Monte Carlo to predict the experimental crystal structure of small organic molecules

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Crystal structure prediction (CSP) of molecular materials [1] is probably the "Holy Grail" of computational crystallography [2,3] due to its paramount impact, among others, in polymorph control and tailored synthesis of solids with desired properties.

Brute force CSP algorithm share more or less the same strategy. First, a number of putative structures are generated based on a specific criterion, e.g. the packing efficiency, then the structure landscape is analyzed and the independent structures are optimized by maximizing their cohesive energies. The result is a handful of plausible structures which are ranked according to their relative energy. Unfortunately, the task is not so easy [3-4] and several CSP methods have been developed in the last two decades, with alternate success [5-6].

Most of the available algorithms work on static structures and do not explicitly take into account the thermodynamic boundaries conditions, like temperature and pressure. To go a step further, we propose a new CSP method based on a symmetry-constrained Monte Carlo (SC-MC) algorithm. The program relies on the free MiCMoS platform [7] and shares its built in force fields, which proved to successfully reproduce the packing features of several molecular crystals [7]. The idea is to set up a bunch of classical MC trajectories, where only user-defined symmetry-independent molecules are free to change, while the symmetry-dependent ones are generated by the appropriate symmetry operators (Figure 1). Relying on the degrees of freedom of the sole asymmetric unit, the algorithm is potentially very fast and can quickly explore the energy landscape of several space groups, allowing to locate the most thermodynamically favorable structures in a few hours on a standard laptop computer.

The project is ongoing, but preliminary results are encouraging and suggest that the algorithm may be easily implemented also for other applications, like the structure solution from accurate X-ray powder diffractograms.

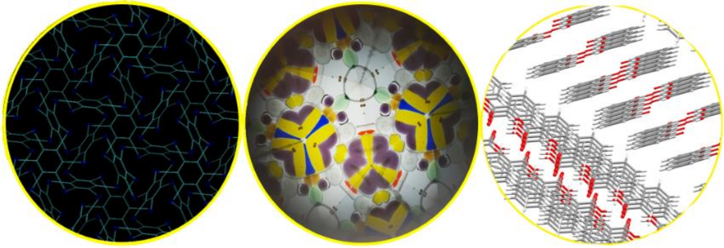

Figure 1. SC-MC evolves the lattice by reproducing a small asymmetric unit with user-defined symmetry elements, as in a kaleidoscope (center). Left: hexacyanobenzene; right: benzoic acid.

[1] A. Gavezzotti, *J. Am. Chem. Soc.* **1991**, 113, 4622-4629.
[2] S. L. Price, *Chem. Soc. Rev.* **2014**, *43*, 2098-2111.
[3] G. Macetti, L. Sironi, L. Lo Presti, in *Comprehensive Computational Chemistry*: *Chemistry, Molecular Sciences and Chemical Engineering*, Elsevier **2023**, DOI: 10.1016/B978-0-12-821978-2.00107-0
[4] S. L. Price, *Acta Crystallogr.* **2013**, B69, 313-328.
[5] D. H. Bowskill, I. J. Sugden, S. Konstantinopoulos, C. S. Adjiman, C. C Pantelides, *Annu. Rev. Chem. Biomol. Eng.* **2021**, *12*, 593-623.
[6] A. M. Reilly *et al.*, *Acta Cryst. B.* **2016**, *72*, 439-459.
[7] A. Gavezzotti, L. Lo Presti, S. Rizzato, *CrystEngComm*, **2022**, *24*, 922-930.

True Polymorphism in a Solid Solution of Tolbutamide and Chlorpropamide affords a High-Soluble Co-Drug Form

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Poor drug solubility and crystal form control are among the main challenges in the pharmaceutical industry. Traditionally crystal form screening for polymorphs and co-crystals often enables the isolation of a stable and high soluble form that improves drug stability and bioavailability [1,2,3]. In such a landscape, molecular solid solutions allow the modification of physicochemical properties and stoichiometry in continuum [4].

Tolbutamide and chlorpropamide are common oral hypoglycaemic sulfonylurea drugs that belong to Class II drugs in the Biopharmaceutical Classification System due to their high membrane permeability and low solubility. These molecules have a similar chemical structure, and both are extremely prone to polymorphism.

Solid solutions of tolbutamide (TBA) and chlorpropamide (CPA) have been synthesized by three different methods: mechanochemically (manual grinding and ball milling), crystallization from solution and crystallization from the melt. The products were characterized via single crystal and powder X-ray diffraction, and differential scanning calorimetry.

Mechanochemical synthesis affords the *Pna*2_1 polymorph, isostructural to the commercial TBA form I^L and the metastable CPA form ε (SS form 1). Crystallization from the melt results in the *Pbcn* polymorph, isostructural to the metastable forms TBA V and CPA β (SS form 2). Finally, solution crystallization produces a mixture of both the forms.

The SS form 2 is a metastable phase, converting into SS form 1 over time, but is kinetically stable, requiring from a few to several months depending on the synthetic and storage conditions. Powder dissolution tests for both SSs show faster dissolution profiles than the physical mixture of the pure drugs, which could translate into increased bioavailability.

The findings of this work point out how solid solutions could represent a viable strategy to control and enhance structural and physicochemical properties of drugs.

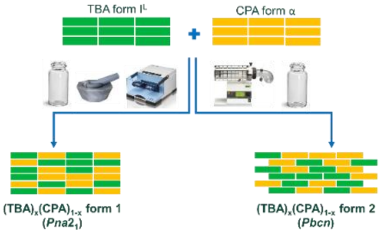

Figure 1. Representation of the solid solutions of tolbutamide (TBA) and chlorpropamide (CPA).

[1] Censi, R. and P. Di Martino. Polymorph impact on the bioavailability and stability of poorly soluble drugs. *Molecules*, **2015**. 20(10): p. 18759-18776.

[2] Bučar, D.K., R.W. Lancaster, and J. Bernstein. Disappearing polymorphs revisited. *Angewandte Chemie International Edition*, **2015**. 54(24): p. 6972-6993.

[3] Babu, N.J. and A. Nangia. Solubility advantage of amorphous drugs and pharmaceutical cocrystals. *Crystal Growth & Design*, **2011**. 11(7): p. 2662-2679.

[4] Lusi, M., A rough guide to molecular solid solutions: design, synthesis and characterization of mixed crystals. *CrystEngComm*, **2018**. 20(44): p. 7042-7052.

The influence of weak interactions in the backbone conformation and solid state behavior of cyclic peptoids

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Cyclic peptoids are *N*-substituted cyclooligomeric glycines belonging to the realm of the peptidomimetic compounds [1]. Because of the possibility to change the ring size and the side chains nature, they have proven to be an interesting building block for the formation of supramolecular structures [2]. In particular, we reported the peculiar solid state behavior of a cyclic hexapeptoid decorated with four propargyl and two methoxyethyl side chains (**1**). We obtained an acetonitrile solvate crystal form and demonstrated that by heating the crystal, we could remove the guest molecules and obtain an anhydrous crystal form *via* a reversible single-crystal-to-single-crystal transformation [3,4]. Furthermore, new pure and solvate crystal forms were obtained by modifying the crystallization solvents. We showed that it is possible to remove the guest molecules from the methanol and hydrate crystal forms and generate a permanently porous framework (Figure 1) capable of absorbing propyne and CO_2 [5,6].

Recently, we obtained the crystal structures of four cyclic dodecapeptoids decorated with a different combination of propargyl and methoxyethyl side chains showing a peculiar backbone conformation mimicking right- and left- handed polyproline type I helices [7].

Using different approaches such as lattice energy calculations, Energy Frameworks analysis, and QTAIM, we wish to shed light on how weak interactions such as CH···OC hydrogen bonds, C5 hydrogen bonds, and CO···OC might influence the solid state assembly of cyclic peptoids, their solid state dynamic behavior, and their backbone conformation.

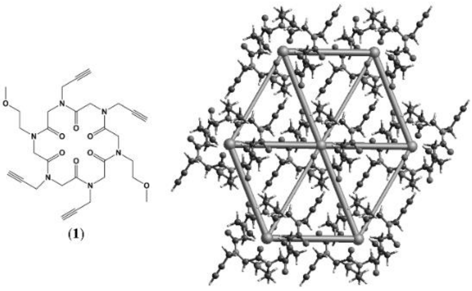

Figure 1. Left: cyclo-(Nme-Npa$_2$)$_2$ (**1**). Right: total interaction energy frameworks for the anhydrous and permanently porous crystal form of **1**.

[1] S.B.Y. Shin, B. Yoo, L.J. Todaro, K. Kirshenbaum *J. Am. Chem. Soc.* **2007**, *129*, 3218.

[2] C. Tedesco, R. Schettini, V. Iuliano, G. Pierri, A.N. Fitch, F. De Riccardis, I. Izzo *Cryst. Growth Des.* **2019**, *19*, 125.

[3] A. Meli, E. Macedi, F. De Riccardis, V.J. Smith, L.J. Barbour, I. Izzo, C. Tedesco *Angew. Chem. Int. Ed.* **2016**, *55*, 4679.

[4] G. Pierri, M. Corno, E. Macedi, M. Voccia, C. Tedesco *Cryst. Growth Des.* **2021**, *21*, 897.

[5] E. Macedi, A. Meli, F. De Riccardis, P. Rossi, V.J. Smith, L.J. Barbour, I. Izzo, C. Tedesco, *CrystEngComm* **2017**, *19*, 4704.

[6] G. Pierri, A. Landi, E. Macedi, I. Izzo, F. De Riccardis, R.E. Dinnebier, C. Tedesco *Chem. Eur. J.* **2020**, *26*, 14320.

[7] G. Pierri, R. Schettini, F.F. Summa, F. De Riccardis, G. Monaco, I. Izzo, C. Tedesco *Chem. Commun.* **2022**, *58*, 5253.

A survey of Inclusion Compounds: Structure, Selectivity and Kinetics

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We present a brief history of Inclusion Compounds, with emphasis on various types of structures, their use in separation of mixtures by selective enclathration and their solid-state kinetics of desorption and formation.

The importance of secondary interaction is highlighted and the particular problem of resolving racemates of chiral molecules is discussed. Recent results obtained with various bile acids in the separation of racemic amines will be announced.

Possible mechanism of formation and decomposition of host-guest compounds are shown, with particular reference to guest-exchange reactions.

Micro symposium 2

Combined structural methodologies to address complex biological systems

MS2 - Combined structural methodologies to address complex biological systems

Chairs: M. Milani (IBF-CNR, Milan); L. Cendron (University of Padua)

In the last ten years, Structural biology has extended its tools to extremely powerful methodologies that allow integrated approaches to address important questions about cellular complexes involved in key processes and their aberrations linked to transcription, translation, transport, modification, catalysis, protein synthesis, and degradation. This micro symposium is focused on recent examples that highlight important achievements obtained by applying structural, biophysical, and computational techniques.

Wednesday 6 September – morning 10.30-12.30

Keynote 1: 10.30-10.55
Matteo De Rosa
Institute of Biophysics-CNR
Structural bases of gelsolin-related diseases

Keynote 2: 10.55-11.20
Alessandra Magistrato
CNR-IOM
Unraveling the molecular mechanism of pre-mRNA splicing via all-atom simulations

Oral 1: 11.20-11.32
Francesco Rinaldi
Istituto Italiano di Tecnologia
Elucidating the RAD52 architecture through an integrated structural biology approach

Oral 2: 11.32-11.44
Elisa Fagnani
Department of Biosciences, University of Milano
Understanding the pro-survival role of AIF: structural and functional study of AIF-CHCHD4 complex

Oral 3: 11.44-12.06
Silvia Garavaglia
Dipartimento di Scienze del Farmaco, University of Piemonte Orientale
Using rational structural analysis for development drugs and diagnostics tools to selective targeting human ALDH1A3 in solid tumours

Oral 4: 12.06-12.18
Filippo Vascon
Department of Biology, University of Padova
Structural studies on the bacterial SOS response: how it is shaped and how to suppress it

Oral 5: 12.18-12.30
Sarita Sarita
Department of Biosciences, University of Milano
Structural and molecular features of native and fibril form of AL55 light chain protein associated with AL amyloidosis

MS2-KN1

Structural bases of gelsolin-related diseases

Matteo de Rosa

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Gelsolin is the archetype of a superfamily of multi-domain Ca^{2+}-dependent proteins responsible for the assembly, disassembly and scavenging of actin. Owing to its pivotal physiological activities, gelsolin plays a main role in a plethora of physiological processes, such as cell motility and division, organelle trafficking and apoptosis. As a consequence, alteration in gelsolin expression levels or deregulation of its activities have been observed in several diseases, cancers in particular.

While the role of gelsolin in these pathological states remains to be elucidated, the protein is directly responsible for a rare amyloidosis due to gain-of-toxic-function mutations, whose characterisation has been main focus of our research [1-4]. Integrating structural, biochemical and biophysical techniques, we aim at elucidating the molecular bases of gelsolin-related diseases and at providing a structural description of gelsolin physiological activities. In parallel, we also exploit the same approaches to design or identify small molecules potential drugs against these maladies [3,5].

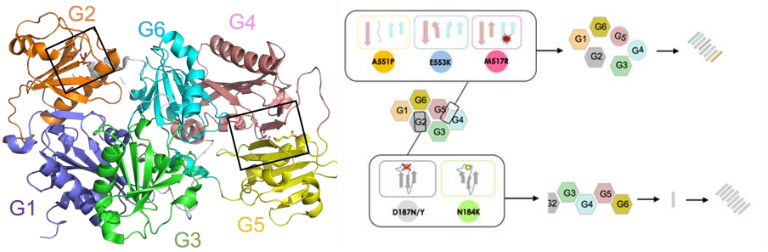

Figure 1. gelsolin amyloidosis underlying mechanisms based on our structural and biophysical data [5]

[1] Bonì F, Milani M, Porcari R, Barbiroli A, Ricagno S, de Rosa M. *Sci Rep*. **2016** 6:33463

[2] Bonì F, Milani M, Barbiroli A, Diomede L, Mastrangelo E, de Rosa M. *Hum Mol Genet*. **2018** 27(1):53-65.

[3] Giorgino T, Mattioni D, Hassan A, Milani M, Mastrangelo E, Barbiroli A, Verhelle A, Gettemans J, Barzago MM, Diomede L, de Rosa M. *Biochim Biophys Acta Mol Basis Dis*. **2019** 1865(3):648-660

[4] Bollati M, Diomede L, Giorgino T, Natale C, Fagnani E, Boniardi I, Barbiroli A, Alemani R, Beeg M, Gobbi M, Fakin A, Mastrangelo E, Milani M, Presciuttini G, Gabellieri E, Cioni P, de Rosa M. *Comput Struct Biotechnol J*. **2021** 19:6355-6365

[5] Bollati M, Peqini K, Barone L, Natale C, Beeg M, Gobbi M, Diomede L, Trucchi M, de Rosa M, Pellegrino S. *Int J Mol Sci*. **2022** 23(22):13973

Unraveling the molecular mechanism of pre-mRNA splicing via all-atom simulations

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The spliceosome, a complex protein/RNA macromolecular machinery, removes noncoding introns from precursor messenger RNAs (pre-mRNAs) and ligates coding exons, giving rise to protein coding mRNAs and functional non-coding RNAs. In this talk I will illustrate how atomic-level simulations have contributed to elucidate: (i) the function of specific protein components of the spliceosome assembly [1,2]; (ii) the mechanism of pre-mRNA selection by selected splicing factors, and the impact of cancer associated mutation on pre-mRNA recognition [3]; (iii) the chemical details of pre-mRNA splicing [4,5], and (iv) the mechanism of spliceosome helicases [6].

[1] Casalino, L.; Palermo, G.; Spinello, A.; Rothlisberger, U.; Magistrato, A. All-atom simulations disentangle the functional dynamics underlying gene maturation in the intron lariat spliceosome. *Proc. Natl. Acad. Sci. U. S. A.* **2018**, 115, 6584

[2] Saltalamacchia, A.; Casalino, L.; Borišek, J.; Batista, V. S.; Rivalta, I.; Magistrato, A. Decrypting the Information Exchange Pathways across the Spliceosome Machinery. *J. Am. Chem. Soc*. **2020**, 142, 8403.

[3] Borišek, J.; Saltalamacchia, A.; Galli, A.; Palermo, G.; Molteni, E.; Malcovati, L.; Magistrato, A. Disclosing the Impact of Carcinogenic SF3b Mutations on Pre-mRNA Recognition Via All-Atom Simulations. *Biomolecules*, **2019**, 9, 633.

[4] Casalino, L.; Palermo, G.; Rothlisberger, U.; Magistrato A. Who activates the nucleophile in ribozyme catalysis? An answer from the splicing mechanism of group II introns *J. Am. Chem. Soc*. **2016**, 138 (33), 10374

[5] Borišek, J.; Magistrato, A. All-Atom Simulations Decrypt the Molecular Terms of RNA Catalysis in the Exon-Ligation Step of the Spliceosome. *ACS Catal*. **2020**, 10, 5328

[6] Movilla, S.; Roca, M.; Moliner, V.; Magistrato, A Molecular Basis of RNA-Driven ATP Hydrolysis in DExH-Box Helicases. *J. Am. Chem. Soc*. **2023**, https://doi.org/10.1021/jacs.2c11980

Elucidating the RAD52 architecture through an integrated structural biology approach

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Human RAD52 (hRAD52) is a 47 kDa protein of 418 amino acids, which plays important functions in many DNA repair mechanisms such as HR and SSA [1, 2]. Recent studies have demonstrated that the simultaneous inactivation of hRAD52 and one of the following DNA repair proteins as BRCA1, BRCA2, PALB2, XAB2 or RAD51 paralogs leads to synthetic lethality [1, 2]. This evidence points to hRAD52 as an interesting target for drug discover studies aimed at triggering synthetic lethality in BRCA2 deficient cells [1, 2]. hRAD52 comprises two domains having different functions: the N-terminal domain (a.a. 1-208) highly similar among different species, responsible for protein oligomerization and DNA binding, and the C-terminal domain (209-418), poorly conserved, harboring the nuclear localization signal sequence (NLS), and two regions that bind hRAD51 and RPA [3]. Although the interest in hRAD52 has exponentially grown in the last decade, most information about its structure and mechanism of action is still missing [3]. In particular, no structural information is available for the C-terminal domain of hRAD52 FL, thus hampering a complete understanding of its interactions with partner interactors as hRAD51 or RPA. To get novel structural insights on this interesting target, Cryo-EM studies were performed on the hRAD52 FL. While the N-terminal region of RAD52 FL is structured in an undecameric ring and was resolved at a resolution (2.16 Å) higher than the one currently available for RAD52 N-terminal X-ray crystallographic structure, the C-terminal domain was largely absent most likely due to its pronounced mobility [4]. To face and handle the flexibility of the C-terminal domain and gain additional structural insights we coupled AlphaFold2 simulations and SEC-SAXS experiments [4]. These analyses confirmed the extreme flexibility of the RAD52 C-terminal domain, which can be described as an intrinsically disordered region. This observation further draws attention to the role played by this portion of the protein, which may fold only upon partner binding [4]. These results will substantially impact future characterizations of RAD52 mechanisms of action and inhibitors development, particularly in the context of novel approaches to synthetic lethality.

[1] M. J. Rossi, S. F. DiDomenico, M. Patel, and A. V. Mazin, “RAD52: Paradigm of Synthetic Lethality and New Developments,” *Front. Genet.*, vol. 12, no. November, pp. 1–16, 2021, doi: 10.3389/fgene.2021.780293.

[2] M. Toma, K. Sullivan-Reed, T. Śliwiński, and T. Skorski, “RAD52 as a potential target for synthetic lethality-based anticancer therapies,” *Cancers (Basel).*, vol. 11, no. 10, 2019, doi: 10.3390/cancers11101561.

[3] Balboni B., Rinaldi F., Previtali V., Ciamarone A., Girotto S., Cavalli A. “Novel Insights into RAD52’s Structure, Function, and Druggability for Synthetic Lethality and Innovative Anticancer Therapies” *Cancers (Basel),* Vol. 15(6), no. 1817, 2023, doi: 10.3390/cancers15061817

[4] Balboni B., Marotta R., Rinaldi F., Girotto S., Cavalli A. “Novel structural insights on full-length human RAD52: Cryo-EM and beyond” bioRxiv 2023.04.03.535362; doi: 10.1101/2023.04.03.535362

Understanding the pro-survival role of AIF: structural and functional study of AIF-CHCHD4 complex

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Apoptosis Inducing Factor (AIF), a highly conserved mitochondrial flavoprotein, is generally known as a caspase-independent effector in the intrinsic apoptosis pathway [1]. Beside this apoptotic function, recent studies demonstrate that AIF is also able to regulate the cell energy homeostasis by promoting the biogenesis and the function of multi-subunit respiratory complexes. Although the underlying molecular mechanisms have not been yet elucidated, it is clear that this role is played thanks to the interaction of AIF with CHCHD4, a soluble inner membrane space (IMS) protein which promotes the entrance in the IMS and the oxidative folding of substrates belonging to the respiratory complexes' subunits [2,3]. Given the interest in deeply understanding the AIF vital role in mitochondria, we decided to investigate the AIF-CHCHD4 interaction from both the functional and the structural point of view. We focused on the study of the possible impact of the 27-residues N-terminal portion of CHCHD4, which effectively mimics its binding site for AIF, on the catalytic activity and NAD+-binding ability of AIF. The peptide turned out to stimulate the DCIP-NADH reductase activity of AIF and the apparent Kd of the AIF-peptide complex was estimated in the sub-micromolar range. Another interesting finding was the ability of AIF to bind NAD+ only in the presence of the peptide. Preliminary experiments indicates that NAD+ complexation is strongly stimulated by lowering the temperature and that such effect is secondary to the AIF-peptide interaction. For the determination of relevant structural features of the complex, we used AlphaFold software to build up a model, which was then experimentally confirmed by mutagenesis experiments on AIF and mass-spectrometry analyses on the crosslinked AIF-CHCHD4 complex. Since peptide and NAD+ bindings display strong positive cooperativity, we are using this information to set up the optimal conditions for X-ray diffraction studies.

[1] Sevrioukova IF. *Apoptosis-Inducing Factor: Structure, Function, and Redox Regulation*. Antioxidant & Redox Signal. **2011** Jun 15;14(12):2545–79.
[2] Novo N, Ferreira P, Medina M. *The apoptosis-inducing factor family: Moonlighting proteins in the crosstalk between mitochondria and nuclei*. IUBMB Life. **2021**;73(3):568–81.
[3] Hangen E, Féraud O, Lachkar S, Mou H, Doti N, Fimia GM, et al. *Interaction between AIF and CHCHD4 Regulates Respiratory Chain Biogenesis*. Molecular Cell. **2015** Jun 18;58(6):1001–14.

Using rational structural analysis for development drugs and diagnostics tools to selective targeting human ALDH1A3 in solid tumours

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Elevated aldehyde dehydrogenase (ALDH) activity correlates with poor outcome for many solid tumours as ALDHs may regulate cell proliferation and chemoresistance of cancer stem cells (CSCs). Accordingly, potent, and selective inhibitors of key ALDH enzymes may represent a novel CSC-directed treatment paradigm for ALDH$^+$ cancer types. We focused our attention of two different type of tumour that have low survival rate at five years of diagnosis, Glioblastoma and malignant pleural mesothelioma (MPM), an asbestos- associated chemoresistant cancer. For both of which an effective treatments and efficient tools for an early-stage diagnosis are lacking and several studies indicate elevated expression of Aldehyde dehydrogenase 1A3 (ALDH1A3) in mesenchymal glioma stem cells as a target for the development of novel therapeutics [1]. In particular ALDH1A3 belongs to an enzymatic superfamily composed by 19 different isoforms, with a scavenger role, involved in the oxidation of a plethora of aldehydes to the respective carboxylic acids, through a NAD(P)$^+$-dependent reaction. Thanks to the structural analysis of our human ALDH1A3 model, combined with *in-silico* studies, we were able to identified specific active-site inhibitors of ALDH1A3. Indeed, we isolated lead compounds selective and competitive inhibitors of human ALDH1A3 that show poor inhibitory effect on the structurally related isoform ALDH1A1 and ALDH1A2. Our best compound NR6 show anti-metastatic activity in wound healing and invasion assays and induces the downregulation of cancer stem cell markers [2-6]. In addition, the treatment of MPM cells, cultured as multicellular spheroids with NR6 caused the accumulation of toxic aldehydes, induced DNA damage, CDKN2A expression and cell growth arrest. We observed that, in CDKN2A proficient cells, NR6 treatment induced IL6 expression, but abolished CXCL8 expression and IL-8 release, preventing both neutrophil recruitment and generation NETs. Furthermore, in response to ALDH1A3 inhibition, CDKN2A loss skewed cell fate from senescence to apoptosis. Dissecting the role of ALDH1A3 isoform in MPM cells and tumour microenvironment can open new fronts in the treatment of malignant pleural mesothelioma cancer [7]. In addition, using the same rational approach, we synthetized a curcumin-based fluorescent probe able to bind to ALDH1A3 without showing any appreciable interaction with other ALDH1A isoenzymes. Indeed, its fluorescent signal is detectable only in our positive controls *in vitro* and absent in cells that lack ALDH1A3. Remarkably, *in vivo*, our probe selectively accumulates in glioblastoma cells, allowing the identification of the growing tumour mass [8]. Taken together our results demonstrate that targeting of the ALDH1A3 enzyme is a promising approach for improving both, precise tumour diagnosis and treatments outcomes of patients affected by ALDH1A3-positive cancers.

[1] Ping M, *et al. Proc. Nat. Acad. Sci.* **2013**, *110:21, 8644-8649.*
[2] Moretti A, *et al. Sci Rep.* **2016**, *6:35710.*
[3] Jianfeng LI, *et al. Commun. Biol.* **2021**, *4:1420.*
[4*]* Quattrini L, *et al. ACS Med Chem Lett.* **2020**, 11(5):963-970.
[5] Quattrini, L, *et al. J Med Chem,* **2020**, *14;63(9):4603-4616.*
[6] Gelardi ELM, *et al. Cancers* **2021**, *19;13(2):3569.*
[7] Boumya S, *Int. J. Mol. Sci.* **2023**, *24,* 6689.
[8] Gelardi ELM *Commun. Biol.* **2022**, *5(1).*

Structural studies on the bacterial SOS response: how it is shaped and how to suppress it

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The SOS response is a widely conserved bacterial pathway elicited by genotoxic stress. DNA damage is recognized by the RecA recombinase, whose oligomerization on ssDNA stretches is the initiating event of the SOS cascade. In this activated form, RecA interacts with the bifunctional transcriptional repressor LexA, stimulating its autoproteolytic activity and thus leading to the de-repression of a species-specific set of SOS genes. The latter often include virulence factors, genes involved in biofilm formation and in the differentiation of persister populations, but the most widely conserved SOS genes correspond to error-prone DNA polymerases. Their active expression, besides allowing the repair of DNA damages, causes a sudden increase in the mutation rate, *de facto* driving the evolution of resistance to stressors, including antimicrobial agents.

The suppression of the SOS response has been proposed as a promising target for innovative anti-evolutive and anti-virulence strategies against bacterial pathogens, but known inhibitors of this pathway are still very scarce and poor in activity.

The discovery and design of new inhibitors of the SOS response require a deep elucidation of its structural and functional features, in particular in non-model organisms.

To gain insights on *Pseudomonas aeruginosa* SOS response, an integrative structural biology approach was applied. The structure of LexA autoproteolytic domain was obtained by x-ray crystallography. Conversely, the bulky RecA/ssDNA complex was difficult to crystallize, thus its structure was solved by means of Cryo-EM.

Building on these structures, computational modeling and biophysical methods were employed to study the putative binding site of RecA/ssDNA and LexA.

Besides providing information on a long-standing question in structural biology (i.e. which is the interaction site of RecA and LexA), the aforementioned structures can guide the design of inhibitors of the SOS response. In this context, we are exploiting the structure of *P. aeruginosa* LexA to computationally re-design previously discovered anti-LexA antibody fragments (nanobodies) active as SOS suppressors in *Escherichia coli* [1].

[1] L. Maso, F. Vascon, M. Chinellato, F. Goormaghtigh, P. Bellio, E. Campagnaro, L. Van Melderen, M. Ruzzene, E. Pardon, A. Angelini, G. Celenza, J. Steyaert, D. Tondi, L. Cendron. *Structure*. **2022**, *30*, 1-15.

Structural and molecular features of native and fibril form of AL55 light chain protein associated with AL amyloidosis

Sarita Puri, Tim Schulte, Angela Gadda, Ivan Polsinelli, Antonio Chaves-Sanjuan, Giulia Mazzini, Martino Bolognesi, Mario Nuvolone, Giovanni Palladini, Stefano Ricagno

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Immunoglobulin light chain amyloidosis (AL) is caused by the aberrant production of amyloidogenic light chains (LC) that accumulate as amyloid deposits in vital organs. Distinct LC sequences in each patient yield distinct amyloid structures. However different tissue microenvironments may also cause identical protein precursors to adopt distinct amyloid structures. To address the impact of the tissue environment on the structural polymorphism of amyloids, we extracted fibrils from the kidney of an AL patient (AL55) whose cardiac amyloid structure was previously determined by our group. Here we show that the 4.0 Å resolution cryo-EM structure of the renal fibril, formed mainly by the variable domain of LC, is virtually identical to that reported for the cardiac fibril. These results provide the first structural evidence that LC amyloids independently deposited in different organs of the same AL patient share a common fold.

Due to the variable domain's contribution to the amyloid fibril core, we recombinantly purified AL55 and its two domains (variable and constant) to compare the structural and molecular properties of the native proteins with their aggregation properties. Full-length AL55 X-ray crystallographic structure reveals an open conformation with two variable domains far away from each other in native dimer over the closed conformations found in other known LCs, which may lead to greater accessibility of variable domains to proteolytic digestion and ultimately, to amyloid formation. Additionally, we found that the isolated variable domain is less structured, unstable, sensitive to proteolytic digestion, and has a higher unfolding rate, which correlates well with its increased aggregation propensity under in-vitro conditions and in the body.

[1] Sarita Puri *et al.* The Cryo-EM structure of renal amyloid fibril suggests structurally homogeneous multiorgan aggregation in AL amyloidosis, 20 April 2023, PREPRINT available at Research Square [https://doi.org/10.21203/rs.3.rs-2759584/v1]

Micro symposium 3

Growth of crystalline functional materials and thin films

MS3 - Growth of crystalline functional materials and thin films

Chairs: A. Sassella (University of Milano-Bicocca); S. Rubini (CNR-IOM)

State-of-the-art technology relies on functional materials designed, grown and studied for different applications, and often integrated in devices as thin solid films. In this respect, studying and controlling the growth process, the role of interfaces and epitaxy in thin films and heterostructures, and the relationship between the growth and the properties is the goal of many research efforts. This Micro Symposium intends to collect contributions from scientists working on the growth of functional bulk crystalline materials, thin films and nanostructures, on their characterization, and on the modelization of their properties. Materials of interest span from inorganics to organics to 2D materials in thin films or integrated into more complex structures.

Wednesday 6 September – afternoon 15.00-17.00

Keynote 1: 15.00-15.30
Pasquale Orgiani
CNR-Istituto Officina dei Materiali, Trieste
Crafting the structure of materials for tailoring their quantum properties: the case of anatase TiO_2 thin films

Keynote 2: 15.30-16.00
Cristiano Albonetti
CNR-Istituto per lo Studio dei Materiali Nanostrutturati, Bologna
Identification of ultra-thin molecular layers atop monolayer terraces in sub-monolayer organic films with scanning probe microscopy

Oral 1: 16.00-16.20
Lucia Maini
Dipartimento di Chimica "G. Ciamician", Università di Bologna
Annealing and deposition procedures to access elusive polymorphs of NDI-C6 in thin film

Oral 2: 16.20-16.40
Eugenia Pechkova
Department of Experimental Medicine, University of Genova
Protein Langmuir-Blodgett Thin Films for Protein Crystallization and Structural Studies

Oral 3: 16.40-17.00
Valentina Zannier
CNR Istituto Nanoscienze and Scuola Normale Superiore, Pisa
Free-standing InSb nanostructures: growth, morphology control and electrical characterization

Crafting the structure of materials for tailoring their quantum properties: the case of anatase TiO_2 thin films

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Quantum materials continuously attract huge interest due to the widespread technologically important phenomena which can display. In this respect, the thin film technology is currently able to go beyond the single-crystals technology by allowing the investigation of the physical properties of quantum materials in the limit of single atomic layers, through the controlled deformation of the structural parameters by substrate induced strain and growth of multi-layers, thus ultimately providing key information for the development of real layered device applications. To fully exploit the potential combination of all the different quantum materials, flexible growth techniques capable of synthesizing a large variety of functional materials within the same dedicated apparatus are indeed mandatory. In this respect, the Pulsed Laser Deposition (PLD) allows a controlled growth mode at the single atomic layer on the thickness of the deposited layers of a large variety of materials [1].

As key-example, I here show a detailed investigation of surface-vs-bulk electronic properties of anatase titanium dioxide TiO_2. In anatase TiO_2, localized in-gap states, located around 1.5-2.0 eV of binding energy, have been correlated to Ti^{3+} electronic configuration triggered by the oxygen content. In addition, a 2-dimensional electron gas (2DEG) has been also observed to be stabilized at its surface and correlated to Ti^{4+} electronic configuration. Differently from other Ti-based system (e.g. the band-gap insulator $SrTiO_3$), the 2DEG appears to be decoupled by the localized in-gap states and being generated by a very local chemical doping in the near-surface region rather than in the bulk of the material. Moreover, such a 2DEG can be modulated in the k-space by different surface reconstruction of the films as well as by a structural deformation induced by the epitaxial strain. This very last structural deformation can also be used to affect the optical absorption of the TiO_2 by fine tuning the energy position of the in-gap sates. Finally, the stabilization of the 2DEG at TiO_2 surface has been also investigated as a function of the film thickness down to a single-unit-cell of anatese TiO_2 thus ruling out the request of a minimum critical thickness as shown in other oxide systems.

The case of anatase TiO_2 thin films can fully show how to refine the understanding of the surface-vs-bulk electronic properties of quantum materials by taking advantage of thin film technology. Our Dual-PLD system – which combines the use of two independent laser sources, namely, a KrF UV and a Nd:YAG IR lasers [1-2] – has allowed us to successfully grow a large number of different quantum materials, ranging from oxides to metals, to selenides, and others. During a 2017–2022 five-year period, the Dual-PLD facility has been used to grow 36 different materials in the form of thin films and/or heterostructures [1-2].

The full control of the electronic properties of quantum materials can be therefore achieved through the crafting of their structural properties by thin film technology.

[1] P.Orgiani, S.K.Chaluvadi, S.Punathum Chalil, F.Mazzola, A.Jana, S.Dolabella, P.Rajak, M.Ferrara, D.Benedetti, A.Fondacaro, F.Salvador, R.Ciancio, J.Fujii, G.Panaccione, I. Vobornik, and G. Rossi, “Dual pulsed laser deposition system for the growth of complex materials and heterostructures,” *Review of Scientific Instruments*. **2023**, *94*, 033903. https://doi.org/10.1063/5.0138889.

[2] S. K. Chaluvadi, D. Mondal, C. Bigi, D. Knez, P. Rajak, R. Ciancio, J. Fujii, G. Panaccione, I. Vobornik, G. Rossi, and P. Orgiani, “Pulsed laser deposition of oxide and metallic thin films by means of Nd:YAG laser source operating at its 1st harmonics: recent approaches and advances,” *Journal of Physics: Materials*. **2021**, *4*, 032001. https://iopscience.iop.org/article/10.1088/2515-7639/abe661.

Identification of ultra-thin molecular layers atop monolayer terraces in sub-monolayer organic films with scanning probe microscopy

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The morphology of sub-monolayer organic films has been investigated in situ and ex situ as a function of the substrate temperature of deposition. In this thickness range, monolayer terraces formed of edge-on molecules, i.e. nearly upright, are typically nucleated. Herein, the terrace height is found to be correlated to both the film morphology and the substrate surface energy. In particular, the presence of a layer of variable thickness with molecules lying face-on or side-on can be identified atop the terraces when the deposition is carried out on inert substrates. This phenomenon can be evidenced thanks to accurate height measurements made with atomic force microscopy and further data obtained with advanced scanning probe microscopy techniques operating in different environments, viz. liquid, air and vacuum. An upward displacement of molecules from the substrate to the top of the terraces is considered to be responsible for this layer formation, whose molecules weakly interact with the underlying terraces.

Annealing and deposition procedures to access elusive polymorphs of NDI-C6 in thin film

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NDI-C6 has been extensively studied for its semiconducting properties and its processability. It is known to have several polymorphs and a high thermal expansion. Here we report a full thermal characterization of NDI-C6 by combining differential scanning calorimetry, variable temperature X-ray powder diffraction, and hot stage microscopy, which revealed two different thermal behaviours depending on the annealing process. The ranking of stability was determined by the temperature and energy involved in the transitions: Form α is stable from RT until 175°C, Form β is metastable at all temperatures, Form γ is stable in the range 175-178°C and Form δ in the range 178°C-207°C followed by the melt at 207°C. We determined the crystal structure of Form γ at 54°C from powder. The analysis of the thermal expansion principal axis shows that Form α and Form γ possess negative thermal expansion (X1) and massive positive thermal expansion (X3) which are correlated to the thermal behaviour observed. We were able to isolate pure Form α, Form β, and Form γ in thin films and we found a new metastable form, called Form ε, by spin coating deposition of a toluene solution of NDI-C6 on Si/SiO_2 substrates. Preliminary exemples of devices based on the different polymorphs are shown.

[1] De Oliveira Martins, I.; Marin, F.; Modena, E.; Maini, L. On the Crystal Forms of {NDI}-C6: Annealing and Deposition Procedures to Access Elusive Polymorphs. *Faraday Discuss.* **2022**, *235*, 490–507. https://doi.org/10.1039/d1fd00100k.

Protein Langmuir-Blodgett Thin Films for Protein Crystallization and Structural Studies

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With the new generation of synchrotrons and micro- and nano-focused beamlines, great progress has been made in the area of X-ray protein crystallography. Recently, cryo-electron microscopy in microbeam electron diffraction mode (microED), X-ray nanodiffraction (nanoXRD), and serial femtosecond X-ray nanocrystallography (SFX) at X-ray free electron lasers (XFELs) have opened new ways to collect diffraction data. However, the production of the protein crystals as well as their quality remain open problems. Since this field is rapidly evolving, novel methods of macromolecule organization into diffracting arrays have come to the forefront. Nanotechnology could offer great potential in structural and functional proteomics, aiming to *ab initio* construct solid protein-based materials for these studies.

The Langmuir-Blodgett (LB) nanotemplate method, applicable to any protein (including membrane proteins), allows highly ordered 2D protein nanofilm formation on the air-water interface and their deposition onto solid supports. These nanofilms can be applied as a 2D nanotemplate for triggering 3D protein crystal growth [1]. Moreover, highly ordered solid LB multilayered protein films have been shown to be more temperature-resilient than proteins in solution [2], with long-range order increasing after heating and cooling protocols [3]. Indeed, surface ordering of the multilayered nanofilms and an improvement of the correlation between the layers during thermal annealing have been revealed by atomic force microscopy and grazing-incidence small-angle X-ray scattering (GISAX) [3].

Consequently, the information on the structural changes in the bulk of nanofilms occurring after heating up to 150 and cooling to the r.t. was obtained by means of emerging advanced techniques such as nanoXRD [4,5], microED [6], and SFX at XFEL [7]. The results suggest LB multilayers could become a potential tool for protein structural studies and applications.

[1] E. Pechkova, C. Nicolini. *Nature Protocols* **2017**, *12*, 2570.
[2] E. Pechkova, P. Innocenzi, L. Malfatti, L. et al. *Langmuir* **2007**, 23, 1147−1151
[3] E. Pechkova, S. Tripathi, C. Nicolini. *J. Synchrotron Radiat.* **2009**, *16*, 330.
[4] E. Pechkova, C. Nicolini, M. Burghammer, C. Riekel. *Appl. Phys. Lett.* **2020**, *117*, 053701.
[5] E. Pechkova, M. Burghammer, C. Nicolini, C. Riekel. *NanoWorld J* **2020**, *6*, 66.
[6] E. Pechkova, C. Nicolini, S. Fiordoro, C. Riekel. *Langmuir,* **2022**, *38*, 86.
[7] E. Pechkova, C. Nicolini, *NanoWorld J.* **2018**, *4*, 48.

Free-standing InSb nanostructures: growth, morphology control and electrical characterization

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Indium antimonide (InSb) has a narrow band gap, high carrier mobility, small effective mass, and it is a promising candidate for the implementation of topological superconducting states. Remarkably, the interest in this material has increased in recent years thanks to the possibility to overcome the limitation of its integration with lattice-mismatched substrates in nano-heterostructures. However, the realization of InSb nanostructures with a high crystal quality and a well-controlled morphology is still challenging. In this contribution, we show the growth of free-standing InSb nanostructures on InAs and InP nanowire stems by means of Au-assisted chemical beam epitaxy. We demonstrate that nanowires (1D), nanoflags (2D), and nanocubes (3D) can be obtained by tailoring growth parameters like growth temperature, precursor fluxes, sample rotation, and substrate orientation (Figure 1). Concerning the nanoflags, through morphological and crystallographic characterization we demonstrate that they are single-crystalline with a defect-free zinc blende structure and stoichiometric composition. The existence of two families of nanoflags, characterized by an aperture angle at the base of 145° and 160°, is observed and modelled [1]. Finally, we have further optimized the growth of these free-standing 2D InSb nanoflags. In fact, by employing more robust and tapered nanowire stems and precisely orienting the substrate with the help of reflection high-energy electron diffraction (RHEED) patterns, we could maximize length and width, and minimize the thickness of the nanoflags [2]. This allowed us to fabricate Hall-bar devices with suitable length-to-width ratio enabling precise electrical characterization of single nanoflags. An electron mobility of ~29,500 cm^2/Vs at 4.2 K was measured. We have also successfully fabricated ballistic Josephson junction devices with 10/150 nm Ti/Nb contacts that show gate-tunable proximity-induced supercurrent (∼ 50 nA at 250 mK) [3]. The devices also show clear signatures of subharmonic gap structures, indicating phase-coherent transport in the junction and a high transparency of the interfaces.

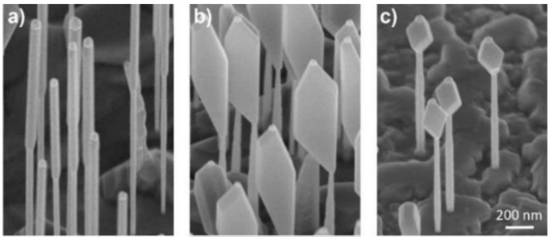

Figure 1. 45°-tilted SEM images of InAs-InSb nano-heterostructures with different morphology: (a) 1D InSb nanowires, (b) 2D nanoflags, and (c) 3D nanocubes.

[1] I. Verma, V. Zannier, F. Rossi, D. Ercolani, F. Beltram and L. Sorba. *Nanotechnology*, **2020**, 31, 384002.
[2] I. Verma, S. Salimian, V. Zannier, S. Heun, F. Rossi, D. Ercolani, F. Beltram and L. Sorba. *ACS Appl. Nano Mater.* **2021**, 4, 5825–5833.
[3] S. Salimian, et al. *Appl. Phys. Lett.* **2021**, 119, 214004

Micro symposium 4

Structural approaches to disclosing molecular recognition and targeting

MS4 - Structural approaches to disclosing molecular recognition and targeting

Chairs: A. Ilari (Institute of molecular biology and pathology-CNR); F. Sica (University of Naples Federico II)

Progress in modern-day biology requires an understanding the mode of interaction between partners of different natures. Elucidating fundamental mechanisms of molecular recognition sheds light on the basic principles responsible for cellular function and opens new opportunities to use this knowledge for various biotechnological and biomedical applications. Traditionally, X-ray crystallography, with its ability to give detailed structural information, has proven to be an invaluable tool for investigating this phenomenon. Complementary methodologies have enabled a deeper understanding of the binding between different interactors and the analysis of the dynamic aspects. The micro symposium aims to provide a collection of interesting recent results using single/multiple structural approache/s.

Wednesday 6 September – afternoon 15.00-17.00

Keynote 1: 15.00-15.24
Giuseppina De Simone
CNR-Institute of Biostructures and Bioimaging, Napoli
Carbonic Anhydrase IX as target for the design of novel anticancer drugs: an integrated biochemical, structural, and computational approach

Keynote 2: 15.24-15.48
Francesco Angelucci
Department of Life, Health and Environmental Sciences, Università degli Studi dell'Aquila
Circumventing nucleophilic active sites of thioredoxin reductases for selective inhibition

Oral 1: 15.48-16.00
Benny Danilo Belviso
CNR-Istituto di Cristallografia, Bari
Unveiling the structural effects of copper and zinc ions on K48-linked diubiquitin

Oral 2: 16.00-16.12
Eloise Mastrangelo
Department of Biosciences, University of Milano – CNR-Biophysics Institute
Retromer stabilization for Neuroprotection in Amyotrophic Lateral Sclerosis: analysis of the possible binding sites of bis-1,3-phenyl guanylhydrazones to the retromer VPS29/VPS35 interface

Oral 3: 16.12-16.24
Cecilia Pozzi
Department of Biotechnologym Chemistry and Pharmacy, University of Siena
Structural evidence of the dimerization of C-type lectin-like receptor CD93, promoting its binding to Multimerin-2 in endothelial cells

Oral 4: 16.24-16.36
Alessia Ruggiero
CNR-Institute of Biostructures and Bioimaging, Napoli

Thermotoga maritima Arginine Binding Protein as a model system for understanding protein self- and hetero-interactions

Oral 5: 16.36-16.48

Carmelinda Savino

CNR-Institute of Molecular Biology and Pathology

Novel insights into fungal catabolism of lignocellulose: structural characterization of an auxiliary enzyme that assists laccase-mediated oxidations

Oral 6: 16.48-17.00

Ilaria Silvestri

CNR-istituto di cristallografia di Caserta

Targeting the conserved active site of splicing machines with specific and selective small molecule modulators

Carbonic Anhydrase IX as target for the design of novel anticancer drugs: an integrated biochemical, structural, and computational approach

Giuseppina De Simone

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Human carbonic anhydrase IX is a tumour associated protein, since it is scarcely present in normal tissues, but highly overexpressed in many solid tumours, where it actively contributes to survival and metastatic spread of tumour cells [1]. Due to these features, it has been largely investigated for drug design purposes [2]. Aim of this presentation is to provide an overview of the biochemical, structural and computational studies [3,4,5,6], carried out in my lab, in collaboration with several national and international institutions, for the development of potent and selective inhibitors with potential as anticancer drugs.

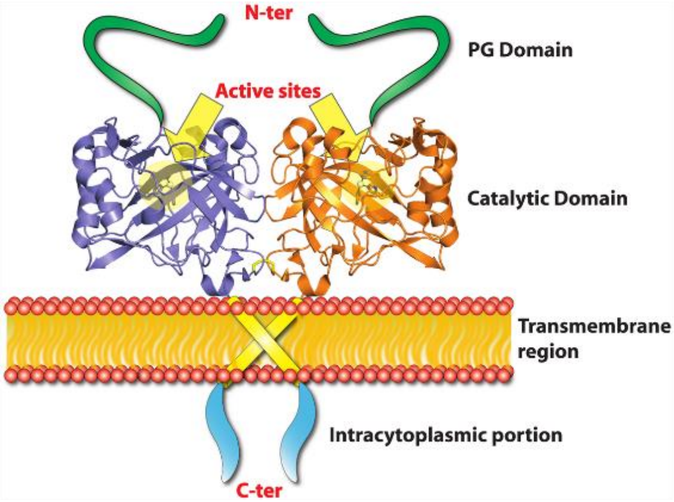

Figure 1. hCA IX dimer on cellular membrane.

[1] C.T. Supuran, V. Alterio, A. Di Fiore, K. D' Ambrosio, F. Carta, S.M. Monti, G. De Simone. *Med Res Rev.* **2018**; 38, 1799.
[2] V. Alterio, A. Di Fiore, K. D'Ambrosio, C.T. Supuran, G. De Simone. *Chem Rev.* **2012**;112, 4421.
[3] E. Langella, M. Buonanno, G. De Simone, S.M. Monti. *Cell Mol Life Sci*. **2021**;78, 2059.
[4] M. Buonanno, E. Langella, N. Zambrano, M. Succoio, E. Sasso, V. Alterio, A. Di Fiore, A. Sandomenico, C.T. Supuran, A. Scaloni, S.M. Monti, G. De Simone. *ACS Chem Biol.* **2017**;12, 1460.
[5] V. Alterio, M. Hilvo, A. Di Fiore, C.T. Supuran, P. Pan, S. Parkkila, A. Scaloni, J. Pastorek, S. Pastorekova, C. Pedone, A. Scozzafava, S.M. Monti, G. De Simone. *Proc Natl Acad Sci U S A.* **2009**; 106,16233.
[6] A. Sarnella, Y. Ferrara, L. Auletta, S. Albanese, L. Cerchia, V. Alterio, G. De Simone, C.T. Supuran, A. Zannetti. *J Exp Clin Cancer Res.* **2022**; 41,122.

Circumventing nucleophilic active sites of thioredoxin reductases for selective inhibition

Francesco Angelucci,[a] Matteo Ardini,[a] Valentina Z. Petukhova,[b] Sammy Y. Aboagye,[c] Rachel P. Lullo,[c] Francesca Fata,[a] Margaret E. Byrne,[c] Federica Gabriele,[a] Lucy M. Martin,[c] Luke N.M. Harding,[b] Nicola Demitri,[d] Maurizio Polentarutti,[d] Grégory Effantin,[e] Wai Li Ling,[e] Andrea Bellelli,[f] Rodolfo Ippoliti,[a] Gregory R.J. Thatcher,[g] David L. Williams,[c] Pavel A. Petukhov[b]

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Pyridine nucleotide-disulfide oxidoreductases are potential drug targets for numerous diseases, with selenoprotein thioredoxin reductases (TrxRs) standing out as crucial for treating cancer and infectious diseases. However, selective drug development for these enzymes is challenging, primarily due to the reliance on covalent inhibition strategies. Recently, a breakthrough, by means of an X-ray crystallography screening, allowed the identification of a novel regulatory site, the "doorstop pocket," in schistosoma's thioredoxin glutathione reductase (TGR), a TrxR-like enzyme and a validated drug target against schistosomiasis, a human parasitic infection [1,2]. To identify TGR inhibitors, the initial molecular fragments were ligated and partially optimized as first-in-class non-covalent inhibitors of TGR [3]. A first cryo-EM structure of TGR demonstrated that these inhibitors bind at the doorstop pocket, blocking enzyme function. This discovery led to the identification of new leads demonstrating superior efficacy against juvenile parasite stages, outperforming the current drug against schistosomiasis, praziquantel [3]. Since the doorstop pocket is present in the protein family, this breakthrough offers opportunities for selectively inhibiting other pyridine nucleotide-disulfide oxidoreductases essential for various pathogens and holds implications for combating cancer.

[1] Silvestri I, Lyu H, Fata F, Boumis G, Miele AE, Ardini M, Ippoliti R, Bellelli A, Jadhav A, Lea WA, Simeonov A, Cheng Q, Arnér ESJ, Thatcher GRJ, Petukhov PA, Williams DL, Angelucci F. *ACS Chem Biol.* **2018** 13, 2190-2202.
[2] Fata F, Silvestri I, Ardini M, Ippoliti R, Di Leandro L, Demitri N, Polentarutti M, Di Matteo A, Lyu H, Thatcher GRJ, Petukhov PA, Williams DL, Angelucci F. *ACS Infect Dis.* **2021** 7, 1932-1944
[3] Petukhova V, Aboagye S, Ardini M et al. *Research Square* **2022**, https://doi.org/10.21203/rs.3.rs-2002501/v1.

Unveiling the structural effects of copper and zinc ions on K48-linked diubiquitin

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Metal ion concentration in the cell is finely regulated by dedicated homeostatic processes selected by the evolution. More and more evidence is revealing that the failure of such processes could alter the degradation process performed by the ubiquitin (Ub) proteasome system (UPS) [1] because metal ions affect UPS activity and lead to modifications in the structure and dynamics of the UPS-related proteins [2], as proven in the case of the Ub. Indeed, it has been known for some time that Ub have binding sites for several heavy metal ions and that its aggregation is triggered by such ions [3]. In this study, we focused on the effect of metal ions on the structure and stability of polyubiquitin chains, which are linear polymeric Ub tags capable of marking target proteins directing them to specific pathways. Specifically, the interaction between K48 linked diubiquitin (K48-Ub_2), a simple model for polyubiquitin chains, copper and zinc ions, two cofactors of several important enzymes also playing a role in oxidative stress [4], has been investigated by circular dichroism, calorimetry, fluorescence emission, and Small Angle X-ray scattering (SAXS). Our analyses revealed that both metals can bind up to four ions to K48-Ub_2 and alter the protein structure in a different way: copper reduces protein stability compared to the case of metal-free protein or in the presence of zinc and zinc binding leads to a shift of the protein conformational dynamics toward less compact and more flexible states. The SAXS analysis unveils that the two metals slightly increase the distance between the two monomers, with a greater effect observed in the case of zinc ion. Interestingly, structural comparison among our K48-Ub_2 SAXS models and those in the Protein Data Bank revealed that the structure of the metal-free protein is similar to that observed when the protein is bound to the E2 conjugating enzyme, supporting the idea that K48-Ub_2 recruitment by other enzyme follows a conformational selection mechanism. Our findings add a new piece of the complex puzzle of the Ub chain mechanism recognition and support the idea that targeting metal-mediated disruptions of Ub signaling could have a great potential for treating a wide range of diseases associated to failure in protein degradation.

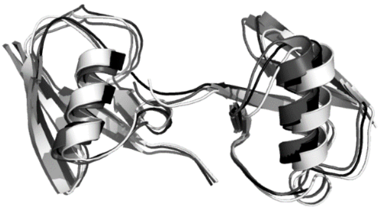

Figure 1. SAXS models of K48-Ub_2 alone (black), with copper (dark gray), and zinc (light gray).

[1] B. Zhang and R. Burke *Metallomics*. **2023**, *15*, mfad010.
[2] C.A. Ross, M.A. Poirier *Nat. Med.* **2004**, *10*, S10; D.C. Rubinsztein *Nature.* **2006**, 443, 780; K.M. Davies, J.F. Mercer, N. Chen, K.L. Double *Clin. Sci. (Colch).* **2016**, *130*, 565.
[3] F. Arnesano, B.D. Belviso, R. Caliandro, G. Falini, S. Fermani, G. Natile, D. Siliqi *Chemistry*. **2011**, *17*, 1569; G. Falini, S. Fermani, G. Tosi, F. Arnesano, G. Natile *Chem Commun (Camb).* **2008**, *7*, 5960
[4] J. Chen, Y. Jiang, H. Shi, Y. Peng, X. Fan, C. Li *Pflugers Arch.* **2020**, *472*, 1415

Retromer stabilization for Neuroprotection in Amyotrophic Lateral Sclerosis: analysis of the possible binding sites of bis-1,3-phenyl guanylhydrazones to the retromer VPS29/VPS35 interface

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Impaired endosomal trafficking leads to the accumulation of misfolded proteins. The trafficking is dependent on the retromer complex (including VPS29, VPS35 and VPS26), and its malfunctioning is implicated in the pathogenesis of several neurodegenerative diseases. For instance, VPS35 and VPS26 are deficient in the hippocampal formation of Alzheimer's disease (AD) patients, while down-regulation of the retromer complex has been identified in amyotrophic lateral sclerosis (ALS) patients. Thus, the stabilization of the complex can be effective in the treatment of different neurological disorders. Following the identification of bis-1,3-phenyl guanylhydrazones as an effective class of new compounds for the treatment of ALS, being able to **attenuate locomotion impairment in mice** and to **increase motor neurons survival** [1], we analyzed the possible binding sites of the best candidate molecule (compound 2a) to the retromer complex. Our experimental and computational results showed that the affinity of compound 2a for different sites of the VPS35/VPS29 heterodimer (Figure 1, A & B) depends on the charge state of the molecule and therefore slight changes in the cell microenvironment could induce different binding states. Moreover, by a combination of molecular dynamic simulation and crystallographic structural data, we identified a **new possible binding site** located in a deep cleft between VPS29 and VPS35 (Figure 1, A) that can be further explored to identify novel active molecules.

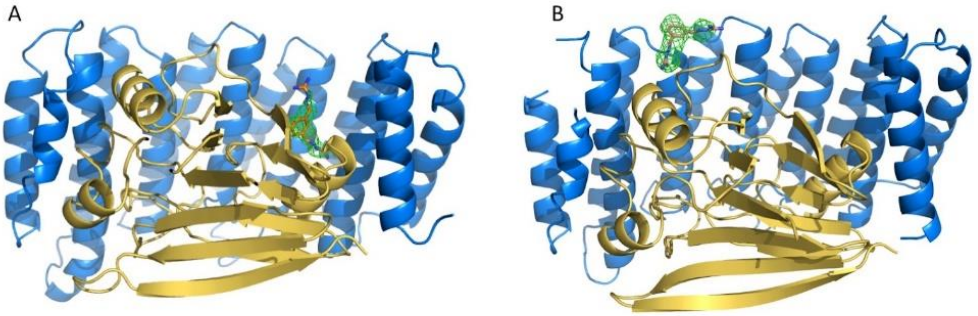

Figure 1. Crystal structures of VPS29 (in yellow) e VPS35 (in blue). In the additional electron density (in green), the molecule 2a (in orange) has been modeled, in the A) site 1 (resolution at 2.4 Å) and B) site 2 (resolution at 2.5 Å).

[1] Muzio L, Sirtori R, Gornati D, Eleuteri S, Fossaghi A, Brancaccio D, Manzoni L, Ottoboni L, Feo L, Quattrini A, Mastrangelo E, Sorrentino L, Scalone E, Comi G, Marinelli L, Riva N, Milani M, Seneci P, Martino G. Retromer stabilization results in neuroprotection in a model of Amyotrophic Lateral Sclerosis. *Nat Commun.* **2020**; 11(1):3848. doi: 10.1038/s41467-020-17524-7.

Structural evidence of the dimerization of C-type lectin-like receptor CD93, promoting its binding to Multimerin-2 in endothelial cells

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Blood vessel formation is required for development, growth, and wound healing, and its misregulation contributes to various disorders [1]. Thus, targeting blood vessels with antiangiogenic drugs is an appealing concept and the discovery of new molecular markers suitable for developing new antiangiogenic therapies is crucial [1]. CD93 is a single-pass transmembrane protein, member of the C-type lectin-like domain (CTLD) superfamily group 14, also including endosialin/CD248, thrombomodulin, and CLEC14A [2]. CD93 consists of a conserved CTLD, followed by a sushi-like domain, five EGF-like repeats, a heavily glycosylated mucin-like region, a transmembrane domain, and a short cytotail [3]. Recent evidence has shown that blocking signal activation by the plasma membrane receptor CD93 is a useful tool in antiangiogenic treatment and oncotherapy, since it regulates cell adhesion, migration, and vascular maturation in the proliferating endothelium [1-4]. The receptor activity of CD93 is supported by the evidence of its binding to the ECM pan-endothelial glycoprotein Multimerin-2 [3,5,6]. This interaction promotes EC migration and tube formation and triggers the activation of β1 integrin, thus promoting fibronectin deposition and remodeling [6]. The mechanisms by which CD93 interacts with the extracellular matrix activating signaling pathways involved in the vascular remodeling are still unclear. On this purpose, we have demonstrated that in ECs CD93 is physiologically structured as a dimer and described for the first time the structure of the CTLD-sushi region of recombinant CD93 at 1.92 Å resolution (PDB id 8A59) [7]. Our initial efforts to use the structures of other CTLDs as molecular replacement search models have been unsuccessful, reasonably for their low structural conservation with CD93. However, we have been able to solve the structure of CD93 CTLD-sushi using the structural model predicted by AlphaFold2. Crystallographic X-ray analysis has revealed a surprising CD93 dimeric arrangement, showing the crucial role played by the C-type lectin-like and sushi-like domains in arranging as an antiparallel dimer [7]. This peculiar arrangement represents the functional binding state to Multimerin-2, involvement in the cell-cell and cell-ECM adhesion phenomena. Our evidence provides key information for the future design of new drugs able to hamper CD93 function in neovascular pathologies.

[1] B. Sennino, D.M. McDonald, *Nat. Rev. Cancer* **2012**, *12*, 699–709.
[2] A.N. Zelensky, J.E. Gready, *FEBS J.* **2005**, *272*, 6179–6217.
[3] F. Galvagni, F. Nardi, O. Spiga, A. Trezza, G. Tarticchio, R. Pellicani, E. Andreuzzi, E. Caldi, P. Toti, G.M. Tosi, A. Santucci, R.V. Iozzo, M. Mongiat, M. Orlandini, *Matrix Biol.* **2017**, *64*, 112–127.
[4] K.A. Khan, J.L. McMurray, F. Mohammed, R. Bicknell,,*FEBS J.* **2019**, *286*, 3299–3332.
[5] K.A. Khan, A.J. Naylor, A. Khan, P.J. Noy, M. Mambretti, P. Lodhia, J. Athwal, A. Korzystka, C.D. Buckley, B.E. Willcox, F. Mohammed, R. Bicknell, *Oncogene* **2017**, *36*, 6097–6108.
[6] S. Barbera, F. Nardi, I. Elia, G. Realini, R. Lugano, A. Santucci, G.M. Tosi, A. Dimberg, F. Galvagni, M. Orlandini, *Cell Commun. Signal*. **2019**, *17*, 55.
[7] S. Barbera, L. Raucci, G. Tassone, L. Tinti, F. Prischi, A. Santucci, M. Mongiat, G.M. Tosi, F. Galvagni, A. Dimberg, C. Pozzi, M. Orlandini, *Int J Biol Macromol* **2023**, *224*, 453–464.

MS4-O4

Thermotoga maritima Arginine Binding Protein as a model system for understanding protein self- and hetero-interactions

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Substrate binding proteins represent a large protein family that plays a crucial role in the selective transportation of metabolites across the membrane. In the last decade, we have structurally characterized and manipulated the *Thermotoga maritima* Arginine Binding Protein (TmArgBP) that is endowed with several unusual features, which include extraordinary stability against both temperature and pressure as well as a remarkable structural versatility [1-7]. We elucidated the structural basis of domain swapping of this protein by initially characterizing its monomeric form obtained by deleting its C-terminal helix (Figure) [3]. This truncated form was further dissected into two domains (D1 and D2) that were exhaustively characterized using a repertoire of different experimental and computational techniques [4]. These analyses demonstrated that, although in the parent protein, both D1 and D2 cooperate for the arginine anchoring; only D1 is intrinsically able to bind the substrate. Interestingly, both D1 and D2 retain the remarkable thermal/chemical stability of the wild-type protein. The analysis of the structural and dynamic properties of TmArgBP and the individual domains has also highlighted possible routes of domain communication. Given the remarkable stability of TmArgBP, we also characterized the structural/thermodynamic impact of the mutation of Gly52, a residue that adopts a conformation that is considered to be strictly forbidden to other residues, with Ala or Val [8]. In recent years, we developed variants of the protein suitable for arginine sensing [8] and we characterized its interaction with chemical denaturants [9]. Currently, we are using TmArgBP and the variants here described as a scaffold for efficient epitope presentation by exploiting the protein thermostability and the helix insertion motif, which we recently identified and characterized [10] in this protein. Interestingly, the variants bearing epitopes extracted from proteins of HCV or HIV viruses tightly bind neutralizing antibodies targeting these pathogens [Ruggiero et al. in prep.].

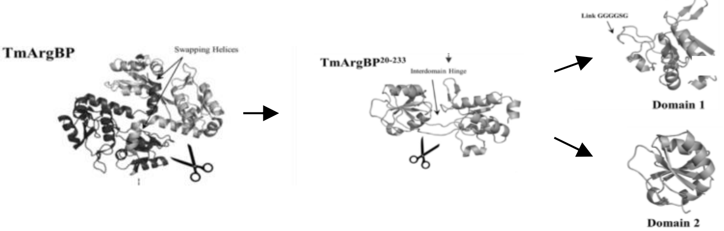

Figure. Scheme of TmArgBP dissection: from the wild-type dimer to the individual domains.

[1] A. Ruggiero, et al. *PloS One*. **2014**, *9*, e96560.
[2] G. Smaldone, et al. *Biochim Biophys Acta*. **2016**, *1864,* 814.
[3] G. Smaldone, et al. *Biochim Biophys Acta*. **2018**,*1866*, 952.
[4] G. Smaldone, et al. *Int J Biol Macromol*. **2018**, *119,* 758.
[5] N. Balasco, et al. *Sci Rep*. **2019,** *9*, 6617.
[6] G. Smaldone, et al. *Acta Cryst.*. **2019**, F*75*, 707.
[7] M.W. Jaworek et al. *Phys Chem Chem Phys*. **2020**, *22,* 11244
[8] G. Smaldone, et al. *Int J Biol Macromol*. **2020**, *21*, 7503.
[9] S. Cozzolino, et al. *Int J Biol Macromol*. **2020**, *163,* 375.
[10] N. Balasco, et al. *Int J Biol Macromol*. **2018**, *118,* 1924.

Novel insights into fungal catabolism of lignocellulose: structural characterization of an auxiliary enzyme that assists laccase-mediated oxidations

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Lignin is the third most abundant biopolymer on earth, after cellulose and chitin, accounting for up to 30% of plant biomass. It could be an inestimable source of aromatics of interest for organic syntheses, probably the primary one after petrol runs out. However, its heterogeneous, randomly assembled and extremely complex chemical structure makes its valorisation and exploitation scarce. Laccase-mediated lignin degradation *in vitro* showed that highly reactive radicals produced by laccase oxidation are prone to repolymerization into higher molecular weight intermediates, more recalcitrant to further enzymatic treatment. A solution to this problem can be found in nature: filamentous fungi stood out as efficient degraders of lignin owing to a synergistic action of secreted redox proteins, that perform an enzymatic combustion [1]. During *in vivo* degradation, fungi can prevent the massive repolymerization observed *in vitro*, because they possess mechanisms to control or redirect the pool of radicals produced. These enzymes are mostly annotated within the "Auxiliary Activities" (AA) class defined in the Carbohydrate Active enZymes (CAZy) database [2]. AA encompass enzymes with different cofactors, such as heme peroxidases (fAA2), copper laccases (AA1) and flavoenzymes (AA3). One of the current hypotheses predicts that these flavoenzymes use saccharides produced by enzymatic degradation of cellulose and hemicellulose, to fuel the reduction of phenoxy radicals deriving from laccase. One of these AA3 enzymes is oligosaccharide dehydrogenase from the Basidiomycete *Pycnoporus cinnabarinus* (PcODH) [2]. We identified the structural determinants responsible in *Pc*ODH for substrate recognition and preferential activity towards different electron donors [3]. We provide unexpected insights into its role as an auxiliary enzyme that supports laccase during the lignin degradation process. Structural analysis of *Pc*ODH in complex with electron acceptor analogues provided more details on its recognition mechanism. Functional studies performed on *Pc*ODH and *Pc*LAC allowed unveiling synergy *in vitro* and identifying reaction intermediates and products. These details pave the way to a more detailed understanding of enzyme mechanisms and synergies which are key for lignin degradation by fungi.

[1] T.K. Kirk, O. Gifford, P. Drive, R.L Farrell *Annu Rev Microbiol* **1987**, *41*, 465.
[2] F. Piumi, A. Levasseur, D. Navarro, S. Zhou, Y. Mathieu, D. Ropartz, R- Ludwig, C.B. Faulds, E. Record *Appl. Microbiol. Biotechnol.* **2014**, *98*, 10105.
[3] G. Cerutti, E. Gugole, L.C. Montemiglio, A. Turbé-Doan, D. Chena, D. Navarro, A. Lomascolo, F. Piumi, C. Exertier, I. Freda, B. Vallone, E. Record, C. Savino, Sciara, G. *Biotechnol. Biofuels* **2021**, *14*, 1.

Targeting the conserved active site of splicing machines with specific and selective small molecule modulators

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The self-splicing group II introns are bacterial and organellar ancestors of the nuclear spliceosome and retro-transposable elements of pharmacological and biotechnological importance. Integrating enzymatic, crystallographic, and simulation studies, we demonstrate how these introns recognize small molecules through their conserved active site. These RNA-binding small molecules selectively inhibit the two steps of splicing. First, they compete with the substrates of the splicing reaction, i.e., the splice junctions. Second, they prevent crucial active site conformational changes that are essential for splicing progression. This is due to their flexibility when they are bound to the active site, which allows them to adopt distinctive poses at different stages of catalysis. Our data exemplify the enormous power of RNA binders to mechanistically probe vital cellular pathways. Most importantly, by proving that the evolutionarily-conserved RNA core of splicing machines can recognize small molecules specifically and by identifying their binding mode by X-ray crystallography, our work puts solid bases for the rational design of potential novel molecules selective not only for bacterial and organellar introns, but also for the human spliceosome, which is a validated drug target for the treatment of congenital diseases and cancers.

[1] Chillón I. and M. Marcia. "Self-Splicing Group II Introns." *Ribozymes* **2021**, 1: 143-167.
[2] Marcia, M. and A. M. Pyle. "Visualizing group II intron catalysis through the stages of splicing." *Cell* **2012**, 151(3): 497-507.
[3] Marcia, M., J. Manigrasso and M. De Vivo. "Finding the Ion in the RNA-Stack: Can Computational Models Accurately Predict Key Functional Elements in Large Macromolecular Complexes?" *J Chem Inf Model* **2021**, 61(6): 2511-2515.
[4] Manigrasso, J., I. Chillon, V. Genna, P. Vidossich, S. Somarowthu, A. M. Pyle, M. De Vivo and M. Marcia. "Visualizing group II intron dynamics between the first and second steps of splicing." *Nat Commun* **2020**, 11(1): 2837.
[5] Fedorova, O., G. E. Jagdmann, Jr., R. L. Adams, L. Yuan, M. C. Van Zandt and A. M. Pyle. "Small molecules that target group II introns are potent antifungal agents." *Nat Chem Biol* **2018**, 14(12): 1073-1078.

Micro symposium 5

Challenging 3D structure: equipment, methodologies, and computing

MS5 - Challenging 3D structure: equipment, methodologies, and computing

Chairs: D. Siliqi (institute of Crystallography-CNR); A. Rosato (University of Florence)

The Micro Symposium aims to demonstrate how to cope with difficult 3D structures, from molecules to novel materials, by developing creative experimental and computational methodologies. We welcome contributions focusing on structural methods such as cryo-EM, NMR, and crystallography (x-ray, neutron, and electron diffraction). In modern practice, statistical tools are essential for all of these techniques. Applications ranging from the 3D structure of molecules (from small molecules to biopolymers) to the validation of structural results have been impacted by the availability of huge data- and knowledge bases. Machine learning and artificial intelligence tools are one field that has made significant progress recently.

Thursday 7 September – morning 10.30-12.30

Keynote 1: 10.30-11.00
Enrico Ravera
University of Florence
Integration in Structural Biology

Keynote 2: 11.00-11.30
Corrado Cuocci
CNR-Istituto di Cristallografia, Bari
Challenging structure solution of microcrystalline materials by the direct space approach in action using the EXPO software

Oral 1: 11.30-11.45
Marco Mazzorana
Diamond Light Source, Oxford
Dose-aware data collection at MX beamlines

Oral 2: 11.45-12.00
Marco Milanesio
University of Piemonte Orientale
Are modern lab powder diffractometers “*small* large scale facilities”?

Oral 3: 12.00-12.15
Linda Cerofolini
University of Florence
Application of SSNMR for Epitope Mapping and Binding Assessment of multispecific biologics

Oral 4: 12.15-12.30
Danilo Marchetti
University of Parma and Istituto Italiano di Tecnologia
Combined application of 3D electron diffraction analysis and mechanochemical synthesis to identify novel nanocrystalline reticular materials

Integration in Structural Biology

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To date, the PDB [1] hosts approximately 200,000 structures. Of these, roughly 200 are depositions of "integrative structures", and the PDB-dev [2] archiving system hosts further 100 depositions, for a total of 300. For a comparison, there are approximately 1,000 X-ray structures of lysozyme. Most often, it is the case that the structural information that can be achieved by a single technique, and the model that is obtained from this information are deemed sufficient for answering the practical questions that pertain to the system under investigation (e.g.: computational screening can be performed on structural models of any resolution), and no need for combining different techniques is perceived. It is a completely different matter when one considers the extent to which two techniques can be combined. For this, a remarkably good example is the combination between NMR and X-ray. In the first, the structural information is mostly encoded as interatomic distances and angles, therefore NMR progresses from local information to global information building up from a network of short distances [3]. In the second, the stronger reflections encode low resolution information on the overall shape of the molecule, and high quality wide angle reflections are needed for reaching atomic resolution [4]. In addition, even in the highest resolution X-ray structures, only a handful hydrogen atoms positions can be experimentally determined [5], whereas NMR preferentially reports on hydrogen positions [6]. *X-ray data and NMR intrinsically provide non-overlapping information*.

In this contribution, experimental examples of compatibility will be presented [7-8].

This work has been supported by the project "Potentiating the Italian Capacity for Structural Biology Services in Instruct-ERIC - ITACA.SB" (Project no. IR0000009) within the call MUR 3264/2021 PNRR M4/C2/L3.1.1, funded by the European Union NextGenerationEU, and the Ministero dell'Università e della Ricerca - Dipartimenti di Eccellenza 2023-2027 (DICUS 2.0) to the Department of Chemistry "Ugo Schiff" of the University of Florence.

[1] H. M. Berman, *et al.*, The Protein Data Bank. *Nucleic Acids Res.* **2000**, 28, 235–242.

[2] B. Vallat, B. Webb, J. D. Westbrook, A. Sali, H. M. Berman, Development of a Prototype System for Archiving Integrative/Hybrid Structure Models of Biological Macromolecules. *Structure* **2018**, 26, 894-904.e2.

[3] J. Cavanagh, W. J. Fairbrother, A. G. Palmer III, M. Rance, N. J. Skelton, *Protein NMR Spectroscopy. Principles and practice* (Academic Press, 2007).

[4] G. Rhodes, *Crystallography Made Crystal Clear* (Elsevier, 2006) https:/doi.org/10.1016/B978-0-12-587073-3.X5000-4 (June 23, 2019).

[5] E. I. Howard, *et al.*, Ultrahigh resolution drug design I: details of interactions in human aldose reductase-inhibitor complex at 0.66 A. *Proteins* **2004**, 55, 792–804.

[6] M. Zweckstetter, A. Bax, Evaluation of uncertainty in alignment tensors obtained from dipolar couplings. *J Biomol NMR* **2002**, 23, 127–137.

[7] A. Schirò, *et al.*, On the complementarity of X-ray and NMR data. *Journal of Structural Biology: X* **2020**, 4, 100019.

[8] E. Ravera, *et al.*, A High-Resolution View of the Coordination Environment in a Paramagnetic Metalloprotein from its Magnetic Properties. *Angewandte Chemie International Edition* **60**, 14960–14966 (2021).

Challenging structure solution of microcrystalline materials by the direct space approach in action using the EXPO software

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Among the approaches adopted for solving crystal structures from powder diffraction data, direct-space (DS) methods occupy a relevant place, as they are widely used for solving molecular organic and metallorganic structures without excluding the non-molecular compounds [1-3]. They have been developed mainly to bypass the difficulties of the reciprocal space (RS) methods and take advantage of the available supplementary information deriving from prior knowledge of the molecular geometry of a well-defined structural fragment. Based on global optimization methods, DS methods involve the generation of a random sequence of trial structures starting from an appropriate 3D model which is moved until a good match is attained between the calculated and observed patterns. Chemical information about the structure under investigation plays a relevant role because it is actively used to reduce the number of parameters to be modified: bond distances and angles are required and are usually kept fixed while torsion angles are modified during the procedure. In addition, when the quantity of information available from a powder X-ray diffraction pattern is limited (due to, for example, severe peak overlap, broad peaks, preferred orientation, presence of weak scatters) and/or the number of degrees of freedom is large, it can be necessary to add extra chemical information to the optimization process in order to obtain the correct solution. The use of restraints on bond distances and angles, the application of bond-valence restraints and the use of anti-bumping restraints all increase the likelihood of obtaining chemically plausible models.

The software *EXPO* [4], born in 1999 as the first and unique program, in the international landscape, for solving powder structure by direct methods, in its current version, can also use DS methods, in particular the simulated annealing (SA) technique.

The SA approach implemented in *EXPO* has been recently modified using a message passing interface (MPI) parallelization paradigm, aimed at speeding up the solution process using more than one processor and exploiting all available computing power [5,6]. Running the procedure in parallel permits tackling structures with great complexity in a reasonable time.

Case studies of structure solutions using DS methods based on a simulated annealing approach are discussed. Representative examples of applications of the software *EXPO* are described in detail to provide methodological and computational tools useful to face complex cases of structure solutions from powders.

[1] W. I. F. David *International Tables for Crystallography*, Vol. H, edited by C. J. Gilmore, J. A. Kaduk & H. Schenk, Chichester: Wiley, **2019**, 414.

[2] A. J. Florence *International Tables for Crystallography*, Vol. H, edited by C. J. Gilmore, J. A. Kaduk & H. Schenk, Chichester: Wiley, **2019**, 433.

[3] R. Černý, V. Favre-Nicolin *International Tables for Crystallography*, Vol. H, edited by C. J. Gilmore, J. A. Kaduk & H. Schenk, Chichester: Wiley, **2019**, 442.

[4] A. Altomare, et al. *J. Appl. Cryst.* **2013**, *46*, 1231.

[5] C. Cuocci, et al. *Comput. Mater. Sci.* **2022**, *210*, 111465.

[6] C. Cuocci, et al. *J. Appl. Cryst.* **2022**, *55*, 411.

Dose-aware data collection at MX beamlines

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Over the past few decades, Macromolecular crystallography (MX) has gradually changed from a laborious and time-consuming biophysical method into a rapid and efficient method to describe the structure of biological molecules and their interaction with substrates and modulators.

Leading the way in this advancement, synchrotron facilities have played a pivotal role in enhancing X-ray sources, sample manipulation, and data analysis capabilities. As a result, they have made cutting-edge equipment more accessible, democratizing its usage and significantly boosting the efficiency of both academic and proprietary research endeavours.

Nevertheless, the utilization of powerful and tuneable instruments has led to the emergence of a significant challenge in the form of radiation damage, which results in the ionization and deterioration of the exposed material. To address this issue, various strategies have been implemented to minimize the degradation of samples when subjected to the beam. These include the use of multiple crystals, data collection at cryogenic temperatures [1,2] and the adoption of free radical scavengers, and of data collection techniques that enable the exposure of fresh regions of the sample over time.

The wide availability of very different and rapidly changing beamlines often biases the users towards data collection strategies which might not be appropriate for their specific needs.

This is partially overcome by automated data collection methods, which use standard ‘recipes’ designed by beamline scientists to satisfy average requirements [3]. They are generally conservative and tend to preserve data crystal quality for a wide variety of samples. However, a better data collection strategy needs to be driven by dose [4] and include the properties of beamline, sample and must consider the final goal of the experiment. I will present here how the integration of live flux calculations, the Raddose3D software [5] and the user requirements can provide valuable data, giving uniformity to experiments conducted at different instruments over time.

[1] Garman E., Owen R. L. *Acta Crystallogr. D*. **2006**, *62*, 32–47.
[2] Haas, DJ. The early history of cryo-cooling for macromolecular crystallography (2020) *IUCrJ* **2020**. *7*, 148–157.
[3] https://www.diamond.ac.uk/Instruments/Mx/I03/I03-Manual/Unattended-Data-Collections.html
[4] RL Owen *Proc et al, Natl Acad Sci U S A.* **2006** Mar 28; *103(13*): 4912–4917.
[5] CS Bury *et al*. *Protein Sci.* **201**8, *27*:217–228

Are modern lab powder diffractometers “*small* large scale facilities”?

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The oxymoronic title aims at asking ourselves if modern laboratory X-ray Powder diffraction (XRPD) equipment allows facing and solving experimental problems that 20 years ago were placed within the (almost ?) exclusive realm of X-ray large scale facilities, such as crystal structure solution of organic compounds, microdiffraction, *in situ* experiments with dedicated setup, or multitechnique experiments. In this contribution, examples of these kind of experiments carried out by lab XRPD equipment are given, with details on how the setup can be modified or implemented thanks to the flexibility of the modern X-ray powder diffraction hardware and the complementary contribution of statistical tools [1].

The crystal structure solution process by powder diffraction of organic salts [2], molecular complexes [3,4] and MOF-like organometallic compounds are described. These compounds could most often be solved using the synchrotron data until recently.

In situ experiments can be carried out by standard commercial environmental chambers. An example of such experiments is the one performed on Urea/Choline deep eutectic solvent. The experiment is here reported and to show how new phases can be identified and (hopefully) crystal structure solved by combining *in situ* experiment and crystal structure solution by powder diffraction.

In some special cases (aggressive compounds and/or need of a larger sample holder), commercial chambers are not well suited for the specific case. Moreover, in standard chambers, it is often (to not say impossible) coupling complementary techniques. The study of inorganic industrial eutectics requires studying crystallization and melting in large sample holders (more representative of the real-world case), while probing the sample also from the morphological viewpoint. The flexibility of modern diffractometers, equipped with motorized xyz stages and large cabinets, allowed the design and implementation of an *in situ* setup where diffraction is coupled to imaging to probe at the same time structure (XRPD) and morphology (imaging). The coupled diffraction/imaging approach was exploited to investigate the crystallization and melting of inorganic eutectic salt/water mixtures [5]. The time resolution is of course not that of synchrotron sources but experiments with less than 1 minute per pattern can be obtained and the collected data successfully refined with high accuracies.

Microdiffraction experiments require collimated X-ray beams not easily achievable with standard laboratory X-ray sources. The use of Goebel mirrors coupled to tiny tips down to 300 μm and slits down to 0.1 mm allows obtaining spatial sub-millimetres space resolution. The setup was at first used on an oxidized magnesium alloy to identify surface brucite-like layered species and then to characterize a mineralogical sample, where a small glaucofane (a sodium amphibole) inclusion in calcite was identified, overcoming its reduced size and the presence of preferred orientations.

[1] M. Lopresti, B. et al. *Journal of Applied Crystallography*, **2022**, 55, pp. 837–850.
[2] M. Lopresti, M. Milanesio, L. Palin, *Crystals*, **2023**, *13(2)*, 261.
[3] A. Mirocki, M. Lopresti, L. Palin, A. Sikorski, M. Milanesio, *CrystEngComm*, **2022**, *24(39*), pp. 6839.
[4] A. Mirocki, E. Conterosito, L. Palin, M. Milanesio, M. Lopresti, *Crystals*, **2022**, *12(11*), 1573.
[5] M. Lopresti et al. *Crystal Growth and Design*, **2023**, *23(3)*, 1389.

Application of SSNMR for Epitope Mapping and Binding Assessment of multispecific biologics

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Structural information at atomic level of macromolecular complexes is routinely obtained by using X-ray crystallography, solution NMR and, more recently, cryo-electron microscopy. However, the flexibility of fusion-derived biotherapeutics, on one hand, and their large molecular weight, often prevent their structural characterization by most of the available techniques. Thanks to advances in the hardware and in sample preparation, solid-state NMR has reached sufficient maturity to tackle systems of large size and outstanding complexity, such as biological drugs, vaccine formulations, biomaterials and amyloid proteins.[1–3]

An interesting example of the application of solid-state NMR to these systems has been recently provided by the characterization of the complex between a multispecific fusion protein with the ectodomain of the programmed cell death ligand 1 (PD-L1). The analysis enabled us to identify the pattern of the residues of PD-L1 that are involved in the interaction with the biological drug.[4] This is possible because the large size and the intrinsic flexibility of the complexes are not limiting factors for solid-state NMR. This case study proves that the integration of solution and solid-state NMR studies can provide structural information that can be used to develop biotherapeutics with improved quality and safety profiles.

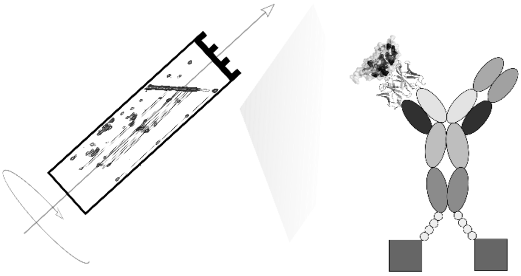

Figure 1. SSNMR spectra shed light on the binding region of a multispecific biologics on PD-L1.

[1] L. Cerofolini, S. Giuntini, E. Ravera, C. Luchinat, F. Berti, M. Fragai, *npj Vaccines* **2019**, *4*, 20.
[2] L. Cerofolini, S. Giuntini, A. Carlon, E. Ravera, V. Calderone, M. Fragai, G. Parigi, C. Luchinat, *Chemistry – A European Journal* **2019**, *25*, 1984–1991.
[3] L. Cerofolini, E. Ravera, S. Bologna, T. Wiglenda, A. Böddrich, B. Purfürst, I. Benilova, M. Korsak, G. Gallo, D. Rizzo, L. Gonnelli, M. Fragai, B. De Strooper, E. E. Wanker, C. Luchinat, *Chem. Commun. (Camb.)* **2020**, *56*, 8830–8833.
[4] D. Rizzo, L. Cerofolini, S. Giuntini, L. Iozzino, C. Pergola, F. Sacco, A. Palmese, E. Ravera, C. Luchinat, F. Baroni, M. Fragai, *J. Am. Chem. Soc.* **2022**, DOI 10.1021/jacs.2c03232.

Combined application of 3D electron diffraction analysis and mechanochemical synthesis to identify novel nanocrystalline reticular materials

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Mechanochemistry finds application in the synthesis of new organic and metal-organic materials such as molecular crystals, salts, cocrystals and polymeric structures. This method allows the formation of products, polymorphs and topologies different from those obtained in solution. However, the structural characterisation of the obtained products is one of the main challenges related to this synthetic approach, due to the presence of nanometric crystals that cannot be analysed by conventional single-crystal X-ray diffraction. Furthermore, powder diffraction methods can be extremely difficult to apply in the case of large unit cells, low symmetry and polyphasic systems. Electron crystallography, especially 3D electron diffraction (3D ED), is an emerging characterisation technique that, due to the most recent developments, can be successfully employed to obtain the structure of nanocrystalline species. This has allowed the structural characterisation of different types of materials, spanning from porous MOFs, COFs and zeolites, to pharmaceutical APIs [1,3]. The 3D electron diffraction analysis is usually performed in transmission electron microscopes (TEMs); however, the growing interest in 3D ED also prompted the development of dedicated electron diffractometers. In this contribution, we present a combined approach based on mechanochemistry and 3D ED analysis for the synthesis and structural characterisation of new reticular compounds. In particular, we studied a tetrahedral pyridyl-based SOF, zinc(II) and 2,6-pyridine dicarboxylic acid coordination polymers (CPs) [4] and a MOF based on copper(II) and protocatechuic acid. The single-crystal 3D ED analyses of metal-organic compounds were performed in a TEM, whereas the SOF was characterised in a new electron diffractometer. The comparison between 3D ED and X-ray powder diffraction data is also discussed.

[1] S. Yuan, J.-S. Qin, H.-Q. Xu, J. Su, D. Rossi, Y. Chen, L. Zhang, C. Lollar, Q. Wang, H.-L. Jiang, D. H. Son, H. Xu, Z. Huang, X. Zou, H.-C. Zhou, *ACS Cent. Sci.* **2018**, *4*, 105.
[2] Z. Huang, T. Willhammar, X. Zou, *Chem. Sci.* **2021**, *12*, 1206.
[3] I. Andrusenko, V. Hamilon, E. Mugnaioli, A. Lanza, C. Hall, J. Potticary, R. S. Hall, M. Gemmi, *Angew. Chem.* **2019**, *131*, 11035.
[4] D. Marchetti, F. Guagnini, A. E. Lanza, A. Pedrini, L. Righi, E. Dalcanale, M. Gemmi, C. Massera; *Cryst. Growth & Design* **2021**, *21*, 12, 6660.

Micro symposium 6

Understanding materials properties through in situ non-ambient and in operando studies

MS6 - Understanding materials properties through in situ non-ambient and in operando studies

Chairs: P. Lotti (University of Milan); M. Milanesio (University of Eastern Piedmont)

The instrumentation and computing improvements of the last decade significantly fostered our capabilities to perform crystallographic analyses at non-ambient and operando conditions. In situ experiments at non-ambient conditions allow to track the structural changes that control the physical properties of crystalline compounds, and in operando experiments allow us to follow reactions and transformations from a structural viewpoint at real-world conditions. For both, computational modelling provides a complementary approach. The goal of this microsymposium is to highlight how non-ambient crystallography can shed light and open new avenues in a wide range of disciplines, spanning from Earth sciences to chemistry and to biopharmaceutical fields

Thursday 7 September – morning 10.30-12.30

Keynote 1: 10.30-11.00
Georgia Cametti
University of Bern
Tracking in situ the structural transformations occurring in zeolite as a function of temperature

Keynote 2: 11.00-11.30
Heinz Amenitsch
Graz University of Technology
Operando Small Angle X-ray Scattering as a tool in energy research

Oral 1: 11.30-11.45
Andrea Bernasconi
Dipartimento di Scienze della Terra, University of Torino
Structure of Na_2O-CaO-Al_2O_3-SiO_2 glass by *in-situ* total scattering synchrotron experiments

Oral 2: 11.45-12.00
Paolo P. Mazzeo
University of Parma
Time Resolved In Situ (TRIS) monitoring by X-ray Powder Diffraction of Mechanochemical reactions: a chronical of impacts

Oral 3: 12.00-12.15
Gianfranco Ulian
Department of Biological, Geological and Environmental Sciences, University of Bologna
Elastic and thermodynamic properties of hydroxylapatite and carbonated apatite from theoretical *ab initio* simulations

Oral 4: 12.15-12.30
Rebecca Vismara
University of Granada and Universita' dell'Insubria
HR-PXRD isotherms: a tool to understand CO_2 adsorption in an iron(III) pyrazolate MOF

Tracking *in situ* the structural transformations occurring in zeolite as a function of temperature

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Zeolites are porous materials, which are exploited in a wide range of applications, spanning from catalysis, environmental remediation, nuclear-waste disposal, drug-delivery, etc [1,2]. The properties of these materials are strictly linked to their porous structure, i.e. dimension and interconnectivity of the pores, hydration level, and chemical nature of the guest species.

Variations in temperature and water-vapour pressure have a striking effect on the structural features, and as a consequence on the material properties [3,4]. The possibility to track *in situ* the structural transformations occurring under non-ambient conditions is of interest not only to determine the formation of new intermediate phases, but also to assess the chemical evolution of the metal cations inside the pores. Both aspects play a fundamental role in evaluating the range of conditions under which the material can be actually used.

In this contribution, I will focus on *in situ* high-temperature (HT) X-ray diffraction measurements. After a short introduction on the practical aspect, i.e. HT non-standard equipment for *in-house* diffractometers, I will discuss few examples, focussed on metal-exchanged zeolites.

The case studies will address the following points: i) structural transformations of the tetrahedral framework; ii) evolution of the metal species (oxide-, metallic-, and hydroxide-clusters); iii) dehydration process up to thermal collapse.

The importance of combining different experimental techniques (X-ray diffraction, X-ray absorption spectroscopy, infrared spectroscopy) with theoretical methods will also be highlighted.

[1] M. E. Davis *Nature* **2002**, *417*, 813.
[2] J. Cejka, H. VanBekkum, A. Corma, F. Schuth. In: *Studies in Surface Science and Catalysis* **2007**, *168*, 1.
[3] A. Alberti, A. Martucci *Mciroporous and Mesoporous Materials* **2011**, *141*, 192.
[4] G. Cruciani *Journal of Physics and Chemistry of Solids* **2006**, *67*, 1973.

Operando Small Angle X-ray Scattering as a tool in energy research

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Simultaneous Small and Wide Angle X-ray Scattering (SWAXS) has been proven to be a valuable tool for characterization of nanostructures in the size range from 0.1 nm till 100 nm in all states of matter generally, and in particular for materials used in energy applications.

One of its key benefits based as X-ray technique is the versatility with respect to the control of physical or chemical parameters such as temperature, chemical potential or environment, humidity, pressure etc., which is limited or not so straightforward with other structure determining methods e.g. electron microscopy. Further the availability of very intense synchrotron radiation facilitates the in operando cinematographic observation of structure forming or varying in situ/in operando providing new insights in the underlying processes.

In this presentation - besides a short introduction and outline of the general experimental possibilities at the Austrian SAXS beamline of the synchrotron radiation facility ELETTRA - an overview of the recent opportunities of the SWAXS technique in the field of energy research is given, which is highlighted in the following examples: LiO batteries [1], supercaps [2], fuel cells [3-5].

[1] C., Prehal, A. Samojlov, M. Nachtnebel, M. Kriechbaum, H. Amenitsch, S. A. Freunberger *PNAS*, **2021**,18 (14), art. no. e2021893118.
[2] C. Prehal., C. Koczwara, N. Jäckel, A. Schreiber, M. Burian, H. Amenitsch, M. A. Hartmann, V. Presser, O. Paris, *Nature Energy*, **2017**, 2 (3), art. no. 16215.
[3] M. Bogar, Y. Yakovlev, D. J. S. Sandbeck, S. Cherevko, I. Matolínová, H. Amenitsch, I. Khalakhan, *ACS Catalysis*, **2021**,11 (18), 11360.
[4] M. Bogar, I. Khalakhan, A. Gambitta, Y. Yakovlev, H. Amenitsch, *Journal of Power Sources*, **2020**, 477, art. no. 229030.
[5] I. Khalakhan, M. Bogar, M. Vorokhta, P. Kúš, Y. Yakovlev, M. Dopita, D. J. S. Sandbeck, S. Cherevko, I. Matolínová, H. Amenitsch., ACS Applied Materials and Interfaces, **2020**, 12 (15), 17602.

Structure of Na_2O-CaO-Al_2O_3-SiO_2 glass by *in-situ* total scattering synchrotron experiments

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Glasses are amorphous materials with relevant interest in both the earth science field, as they can be constituent of rocks, and in the manufacturing process, for example in the ceramics. They are defined as a solid lacking in long range order which exhibits a region of glass transition behavior [1], making these materials unique in terms of characterization approaches.

In fact, it is not possible to investigate their structure by conventional crystallographic approaches as well as their structural modification are very subtle to be detected by conventional setup.

In-situ total scattering synchrotron experiments represent a powerful tool to reveal both intermediate and short range order characteristics.

In fact, First Sharp Diffraction Peak (FSDP) analysis can provide material volume variations upon heating/cooling [2] while Pair Distribution Function (PDF) analysis can reveal bond distance details, coordination numbers and network connectivity parameters [3]. All these, by exploiting the capabilities of a high flux synchrotron beam, a fast area detector and a proper sample environment (see Figure 1).

In consideration of the abovementioned details, we investigated a Na_2O-CaO-Al_2O_3-SiO_2 glass at the ID11 Material Science beamline (ESRF, Grenoble). The sample underwent two different thermal protocols. In the former one, the sample was heated from room temperature to 1000°C at 10°C/min and then cooled down to room temperature at 20°C/min (fast cooled sample). In the latter one, the sample was heated from room temperature to 1000°C at 10°C/min and then cooled down to room temperature at 2°C/min (slow cooled sample).

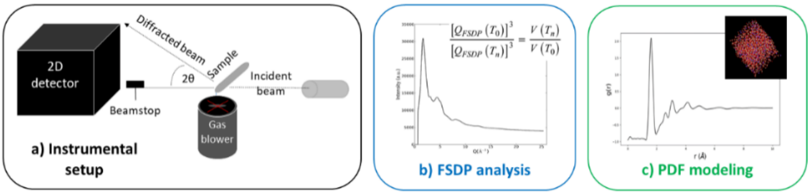

Figure 1. Scheme of experimental and data analyses flow.

FSDP analysis highlighted the presence of a region of transformation in the 400-780°C range (upon heating) as well as the importance of slow cooling pathway to achieve a more relaxed glass structure. PDF analysis, performed mostly by means of EPSR routine [4], displayed that tetrahedral units' expansion and shrinkage are independent from the intermediate range order characteristics revealed by FSDP analysis. Moreover, PDF analysis showed that coordination numbers and polymerization degree are not affected by temperature.

[1] J. Shelby. Introduction to glass science and technology, The Royal Society of Chemistry, **2005**.
[2] W. Botta, K. Ota, K. Hajlaoui, G. Vaughan, A. Yavari. *J. Non Crystalline Solids*. **2008**, 354, 325-327.
[3] A. Bernasconi, M. Dapiaggi, D. Bowron, S. Ceola, S. Maurina. *J. Mater. Sci.* **2016**, *51*, 8845-8860.
[4] A. Soper. *EPSRshell: a User's guide*, ISIS Disordered Material Group, Didcot (U.K.), **2010**.

MS6-O2

Time Resolved In Situ (TRIS) monitoring by X-ray Powder Diffraction of Mechanochemical reactions: a chronical of impacts.

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Matteo Masino,[a] Franziska Emmerling,[b] Alessia Bacchi[a]

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Time-resolved in situ (TRIS) monitoring approaches have opened the door to exceptional detail regarding mechanochemical reactions.[1,2]. Cocrystals (i.e. multicomponent crystalline molecular materials made of different chemical entities that crystallize within the same crystal structure) are typically obtained in bulk through mechanochemical protocols. Whereas the macroscopic aspects of grinding are becoming clear, the fundamental principles that underlie mechanochemical cocrystallisation at the microscopic level remain poorly understood and the description of the step-by-step mechanism of the overall cocrystallisation process are often neglected. In the present communication, a class of cocrystals between two solid coformers that proceeds through the formation of a metastable low melting binary eutectic phase is reported. 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.[3]

Ex-situ validation of the deep eutectic phase was also provided with a multi-technique approach. 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.[2,4]

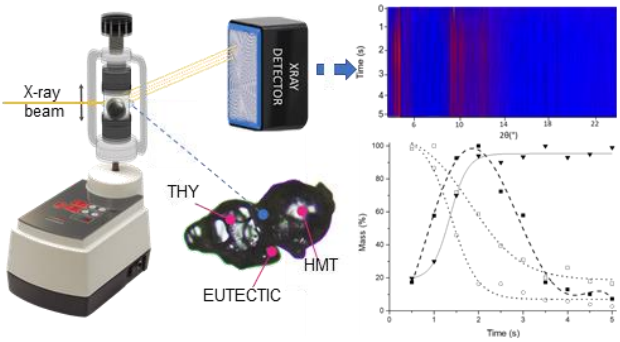

Figure 1. Schematic representation of the TRIS-XRPD experimental setup with an insight of the Rietveld Refinement data analysis.

[1] Friščić, T.; Halasz, I.; Beldon, P. J.; Belenguer, A. M.; Adams, F.; Kimber, S. A. J.; Honkimaki, V.; Dinnebier, R. E. *Nat. Chem.* **2013**, *5*, 66–73.

[2] Lampronti, G. I.; Michalchuk, A. A. L.; Mazzeo, P. P.; Belenguer, A. M.; Sanders, J. K. M.; Bacchi, A.; Emmerling, F. *Nat. Commun.* **2021**, *12* (1), 1–9.

[3] Mazzeo, P. P. M.; Prencipe, M.; Feiler, T.; Emmerling, F.; Bacchi, A. *Cryst. Growth Des* **2022**, *22* (7), 4260–4267.

[4] Mazzeo, P. P.; Lampronti, G. I.; Michalchuk, A. A. L.; Belenguer, A. M.; Bacchi, A.; Emmerling, F. *Faraday Discuss.* **2023**, *241*, 289–305.

Elastic and thermodynamic properties of hydroxylapatite and carbonated apatite from theoretical *ab initio* simulations

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Calcium apatites are important crystalline phases employed in several research and technological fields. For example, the fission-track analysis of detrital apatite and zircon is a low-temperature thermochronometric dating technique commonly adopted to reveal and quantify the spatial and temporal pattern of cooling and exhumation in many active mountain belts [1]. In addition, the inorganic component of the hard tissues of animals and humans is made of biological apatite, which is based on hexagonal hydroxylapatite [OHAp, $Ca_{10}(PO_4)_6(OH)_2$, $P6_3$ space group, see Fig.1] presenting several cationic/anionic substitutions to stabilize the crystalline phase. Among them, the carbonate ion is one of the most abundant, being able to substitute the hydroxyl groups (type-A substitution), the phosphate group (type-B substitution), or both (type AB-substitution) [2]. Hence, bio-engineering and biomaterials studies have been carried out to employ this mineral to create, just to cite some examples, fillers and coatings for prostethic implants. For all these reasons, a detailed knowledge of mechanical and thermal properties of stoichiometric hydroxylapatite and carbonated (hydroxyl)apatite is of utmost importance to calibrate thermo-chronological models and to guide biomaterial development and applications.

While some data are present in literature about the second order elastic constants (SOECs) of hydroxylapatite, both on the experimental [3] and theoretical sides [4], no data are available on the elastic and thermodynamic properties of type-A and type-AB carbonated apatite (CAp). Here, we report the thermo-chemical and thermo-physical properties of both OHAp and CAp minerals in a wide pressure range and at temperatures between 0 K and 800 K, obtained from Density Functional Theory (DFT) simulations with the B3LYP hybrid functional and all-electron Gaussian-type orbitals basis set The calculated data could be helpful for experimental researchers involved in the mechanical analysis of this kind of materials at physical conditions that are difficult to obtain during experimental procedures, and for guiding researchers interested in quantum mechanical modelling of apatite-based minerals.

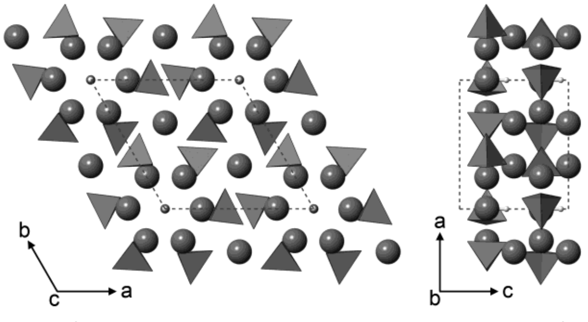

Figure 1. Crystal structure of hydroxylapatite. The dashed line is the unit cell of the mineral. PO_4 groups are shown as tetrahedra, Ca, O and H atoms are represented as balls with decreasing radii.

[1] A. Carter *Dev. Sedimentol.* **2007**, *58*, 851-868.
[2] S.V. Dorozhkin *Materials*. **2009**, *2*, 399-498.
[3] T.N. Gardner, J. C. Elliott, Z. Sklar, G. A. D. Briggs *J. Biomech.* **1992**, *25*, 1265-1277.
[4] A. Slepko, A. A. Demkov.*Phys. Rev. B*. **2011** *84*, 134108.

HR-PXRD isotherms: a tool to understand CO_2 adsorption in an iron(III) pyrazolate MOF

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Understanding adsorption processes at the molecular level, with multi-technique approaches, is at the frontier of porous materials research [1]. Hence, many efforts have been made in finding appropriate techniques to properly characterize their pore surface [2]. In the recent years, *in situ* synchrotron-radiation high-resolution powder X-ray diffraction (HR-PXRD) has emerged as a powerful tool to unveil the primary adsorption sites and main host-guest interactions in a wide range of inorganic, organic, and organic/inorganic porous materials [3]. Nonetheless, this approach has not yet been brought to the limit, going beyond crystal structure determination, framework response monitoring, host-guest interactions description, and guest quantification, to study additional properties, such as the thermodynamics of the adsorption process. Indeed, only recently, deeper efforts to model and understand the whole adsorption process, e.g. through the construction of PXRD adsorption isotherms, have been made [4].

In this work [5], we show that a plethora of hidden but easily accessible information can be extracted from underexploited PXRD data without the necessity to rely on single crystals or to recur to more sophisticated X-ray based techniques. With this aim, we performed an in-depth HR-PXRD characterization of the CO_2 adsorption process (T = 273 and 298 K, p_{CO2} = 0-8 bar) in the robust pyrazolate-based $Fe_2(BDP)_3$ [H_2BDP = 1,4-bis(1*H*-pyrazol-4-yl)benzene] metal-organic framework [6]. The behaviour of $Fe_2(BDP)_3$ at the molecular level (as retrieved by diffraction experiments and computational modelling) was compared with that depicted for the bulk (*via* adsorption experiments), aiming to show that PXRD, applied on variable gas pressure data sets, can be successfully exploited not only to localize the adsorbed guest molecules in the host framework, but also to shed light on the thermodynamics of the adsorption process.

[1] Z. Ji et al. *Adv. Funct. Mater.* **2020**, *30*, 2000238.
[2] a) C. Gropp et al. *ACS Cent. Sci.* **2020**, *6*, 1255. b) J. Marreiros et al. *J. Am. Chem. Soc.* **2021**, *143,* 8249.
[3] a) D. E. Jaramillo et al. *Nat. Mater.* **2020**, *19,* 517. b) J. Oktawiec et al. *Nat. Commun.* **2020**, *11,* 3087.
[4] a) C. Giacobbe et al. *J. Chem. Mater. A* **2017**, *5,* 16954. b) D. Lenzen et al. *Chem. Commun.* **2020**, *56,* 9628. c) J. Lill et al. *J. Phys. Chem. C* **2022**, *126*, 2214.
[5] R. Vismara et al. *Adv. Mater.* **2023**, 2209907.
[6] Z. R. Herm et al. *Science*, **2013**, *340*, 960.

Micro symposium 7

Giovani Cristallografi Italiani MicroSymposium

MS7 - Giovani Cristallografi Italiani

Chairs: R. Vismara (University of Granada); G. Pierri (University of Salerno)

We are happy to announce the first symposium dedicated to young crystallographers! The spirit of the GCI symposium is to provide a welcoming environment for young scientists to present and discuss their research and establish future collaborations and networks. All main topics of crystallography will be covered. The symposium will include oral communications and flash presentations to promote your poster!

Thursday 7 September – afternoon 14.45-16.45

Oral 1: 14.45-14.55
Marzia Dell'Aera
Department of Chemistry, University of Zurich
An overview on CrystalMApp

Oral 2: 14.55-15.10
Vincentia Emerson Agbemeh
Istituto Italiano di Tecnologia
Organic Cocrystals Structures Solved Using 3D Electron Diffraction

Oral 3: 15.10-15.25
Tommaso Battiston
Department of Earth Sciences, University of Milano
P-mediated crystal-fluid interaction in the ABC-6 zeolite group: the case of ERI, OFF and EAB topologies

Oral 4: 15.25-15.40
Martina Lippi
Department of Industrial Engineering, University of Florence
Further insights into (S)-(+)-naproxen diastereomeric salt formation from ongoing solid state

Oral 5: 15.40-15.55
Giacomo Montanari
Department of Philosophy and Communication Studies, University of Bologna
Vitriols: The Many Colors of Iron

Oral 6: 15.55-16.10
Samet Ocak
Department of Chemistry, University of Bologna
Exploring the Plastic Phase Transition Characteristics of Quinuclidinolium Salts with Diverse Counter-Anions and Their Solid Solutions

Oral 7: 16.10-16.25
Luca Sironi
Department of Chemistry, University of Milano
Study of molecular recognition of supercooled benzoic acid with MiCMoS

Flash 1: 16.25-16.30

Laura Macchietti
Department of Chemistry, University of Bologna
Application of multivariate analysis on powder diffraction data for the monitoring of a mechanochemical synthesis

Flash 2: 16.30-16.35
Michele Prencipe
Department of Chemistry, Life Sciences and Environmental Sustainability, University of Parma
Solid state transformations: a mighty approach through mechanochemistry

Flash 3: 16.35-16.40
Giusy Tassone
Department of Biotechnology, Chemistry and Pharmacy, University of Siena
Evidence of amino-thiadiazoles as innovative inhibitors of human glutaminyl cyclase, validated target for neurodegenerative disorders

Flash 4: 16.40-16.45
Gabriella Tito
Department of Chemical Sciences, University of Naples Federico II
Structural characterization of the adduct formed upon reaction of dirhodium tetraacetate with a double helix dodecamer

An overview on CrystalMApp

Marzia Dell’Aera,[a,b] Alberta Terzi,[b] Aurelia Falcicchio,[b] Nicola Corriero[b]

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'*CrystalMApp*' is a scientific dissemination App funded by the Association of Italian Crystallography (AIC) and developed within the project entitled “Progetti di Divulgazione delle Scienze Cristallografiche” 2021.

The goal of the App, whose logo is depicted in Figure 1, is to encourage relations not only among researchers in the field, but also with young people who are willing to embark on a scientific career or would like to deepen scientific contents related to the world of crystallography.

The App has indeed a dual purpose: 1) to disseminate the knowledge and importance of crystallography as it has developed over the years through a historical section, 2) the geolocation and promotion of scientists in the crystallographic sector on the Italian territory, highlighting their areas of expertise, scientific results and laboratories, also allowing to view any open positions for collaborations and promoting the transition from digital to physical interaction between individuals. The basic idea is to combine the interactive method of learning with the active search for work and scientific collaborations. In fact, it is well known that a digital application is also an educational and informative opportunity [1,2,3] for research and for the satisfaction of needs and curiosities.

In this sense, '*CrystalMApp*' is conceived as an effective tool to sensitize the general public towards crystallography, which may not be the most familiar branch of science due to its complexity, but it is undoubtedly one of the most important discipline in helping to understand the world in our daily life. Furthermore, the App represents a useful tool for scientists themselves who have the possibility of more easily establishing a collaboration with other research groups.

Figure 1. CrystalMApp Logo

[1] S. Timotheou, O. Miliou, Y. Dimitriadis, S. V. Sobrino, N. Giannoutsou, R. Cachia, A. M. Monés, A. Ioannou *Educ. Inf. Technol.* **2023**, *28*, 6695–6726.
[2] R. Tavares, R. M. Vieira, L. Pedro *Educ. Sci.* **2021**, *11*, 79.
[3] T.P. Reber, N. Rothen, *NPJ Sci. Learn.* **2018**, *3*, 22.

Organic Cocrystals Structures Solved Using 3D Electron Diffraction

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Danilo Marchetti,[a,b] Mauro Gemmi[a]

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Some Active Pharmaceutical Ingredients (APIs) have been limited in their usage for oral intake due to low bioactivity. This problem is dependent on the solubility and dissolution rate among other physicochemical properties of the drug [1]. The improvement of the physicochemical properties of APIs are important not only for exploring new drug development but also for obtaining patents for new drugs [2]. Cocrystallization is a proposed method used to improve this limitation by combining one conformer which is usually a Generally Recognized As Safe (GRAS) drugs with relatively high solubility. A cocrystal is a crystal where two different molecules (in our case one is an API and the other, a coformer) in a well-defined stoichiometric ratio are bonded by non-covalent interactions [3].
Oxyresveratrol cocrystals were synthesized and reported in a work by Sakamoto et al with coformers urea, nicotinamide, isonicotinamide and ethyl maltol but their crystal structures are not known [4].
In this work, we focus on solving these crystal structures and as a side result we obtained also a new anhydrous and hydrated structures of Oxyresveratrol using 3D electron diffraction [5].

[1] K. T. Savjani, A. K. Gajjar, J. K. Savjani, *ISRN Pharm.* **2012**, *2012*, 195727. DOI: 10.5402/2012/195727.
[2] S. Aitipamula, R. Banerjee, A. K. Bansal, K. Biradha, M. L. Cheney, A. R. Choudhury, G. R. Desiraju, A. G. Dikundwar, R. Dubey, N. Duggirala, et al., *Cryst. Growth Des.* **2012**, *12* (5), 2147–2152. DOI: 10.1021/cg3002948.
[3] R. Machado Cruz, T. Boleslavská, J. Beránek, E. Tieger, B. Twamley, M. J. Santos-Martinez, O. Dammer, L. Tajber, *Pharmaceutics*. **2020**, *12* (8), 741. DOI: 10.3390/pharmaceutics12080741.
[4] N. Sakamoto, N. Tsuno, R. Koyama, K. Gato, V. Titapiwatanakun, K. Takatori, T. Fukami, *Chem. Pharm. Bull. (Tokyo).* **2021**, *69* (10), 995–1004. DOI: 10.1248/cpb.c21-00375.
[5] M. Gemmi, E. Mugnaioli, T. E. Gorelik, U. Kolb, L. Palatinus, P. Boullay, S. Hovmöller, J. P. Abrahams, *ACS Cent. Sci.* **2019**, *5* (8), 1315–1329. DOI: 10.1021/acscentsci.9b00394.

P-mediated crystal-fluid interaction in the ABC-6 zeolite group: the case of ERI, OFF and EAB topologies

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The Pressure-mediated intrusion of molecules and solvated ions into the nano-cavities of microporous (or layered) materials is an efficent method to facilitate the mass transfer from fluids to crystalline solids. This phenomenon, which can be observed in both synthetic and natural zeolites, for example, could expand their industrial applications, develop new functional materials, and improve catalytic performance of these open-framework compounds. In addition, from a geological perspective, a comprehensive understanding of the crystal-fluid interaction induced by pressure may lead to a reassessment of the role played by zeolites as carriers of fluids during the early stages of subduction. It is worth noting that this class of open-framework silicates can contain up to 20 wt% of H_2O. In this study, we have investigated the crystal-fluid interaction, driven by pressure, in three different natural zeolites belonging to the "ABC-6 group": erionite (ERI framework, with a 6-membered ring sequence of AABAAC), offretite (OFF, sequence of AAB), and bellbergite (EAB, sequence of AABCCB). The aims of this study were twofold: 1) to determine the potential role of erionite as a fluid carrier during subduction, as one of the alteration minerals occurring in oceanic floor basalts, and 2) to compare the mechanisms adopted by structurally similar frameworks in accommodating bulk compression and adsorbing new molecules, as well as to determine the magnitude of the crystal-fluid interaction in structurally similar frameworks. Synchrotron XRD experiments were conducted on single crystals of natural erionite, offretite and bellbergite using a diamond anvil cell, both with potentially penetrating and non-penetrating pressure-transmitting fluids. The latters served as a reference for evaluating the crystal-fluid interaction, as the adsorption of new molecules reduces the bulk compressibility for the "pillar" effect exerted by the intruded guest species in the structural voids. The results revealed that erionite shows the largest adsorption capacity among the three zeolites. Moreover, the occurrence and magnitude of the crystal-fluid interaction phenomena were found to be strongly influenced by the H_2O content in the hydrous pressure-transmitting fluids used in our experiments. In the case of offretite, liquid neon acted as penetrating fluid, with intruded atoms forming weak Van der Waals interactions with the extra-framework population. Natural bellbergite, on the other hand, shows limited intrusion of guest molecules from the pressure-transmitting fluids, highlighting the significant role of "secondary factors," such as the initial extra-framework content of the mineral, on crystal-fluid interaction phenomena.

[1] G.D. Gatta, P. Lotti, G. Tabacchi. The effect of pressure on open-framework silicates: elastic behaviour and crystal–fluid interaction, *Phys. Chem. Miner.* **2018**, *45*, 115–138.
[2] D. Comboni, F. Pagliaro, P. Lotti, G.D. Gatta, M. Merlini, S. Milani, M. Migliori, G. Giordano, E. Catizzone, I.E. Collings, M. Hanfland. The elastic behavior of zeolitic frameworks: The case of MFI type zeolite under high-pressure methanol intrusion, *Catal. Today,* **2020**, *345*, 88–96.

Further insights into (S)-(+)-naproxen diastereomeric salt formation from ongoing solid state studies

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Diastereomeric salt formation in pharmaceutical industry is widely employed as purification and separation strategy. In particular, there is the constant need to obtain enantiopure APIs (Active Pharmaceutical Ingredients) in an efficient (and possibly economical) manner, since almost 60% of the drugs on the market are chiral, exerting their therapeutic effect through one of the two enantiomers.[1] For example, the pharmacological activity of non-steroidal anti-inflammatory drugs (NSAIDs) resides mainly in their S-forms whereas their enantiomers are less active or even toxic. The choice of the optically active resolving agent is of great importance to promote preferential crystallization of the enantiopure compound in high yield and is typically time-consuming and largely empirical.

In our preliminary studies, we reported the solid-state investigation of structurally related diastereomeric salts (DSs) of a series of NSAIDs belonging to the propionic acid derivate family with R- and S-phenylethylamine, with the aim of extracting useful information about the forces and the features controlling the chiral separation of the naproxen racemic mixture. Our latest findings evidenced that the enantiopure S-naproxen was not able to discriminate between the phenylethylamine enantiomers, once kept in contact with the racemic mixture of this commonly used resolving agent.[2] Hence, inspired by the promising use of aminoindanols as basic resolving agents for the diastereomeric resolution of racemic acids[3], we continued our structural studies on the diastereomeric salt formation of S-naproxen. We present here the preliminary results of experimental and *in silico* investigations of the anhydrous DS of (S)-(+)-naproxen with (1S,2R)-cis-1-aminoindan-2-ol (1) in addition to the DS of (S)-(+)-naproxen with (1R,2S)-cis-1-aminoindan-2-ol in both the anhydrous (2) and monohydrated (3) forms. The solid-state studies were performed in order to investigate the differences in the crystal packing of the diastereomeric salts, with the aim to better understand the potential chiral discrimination mechanism.

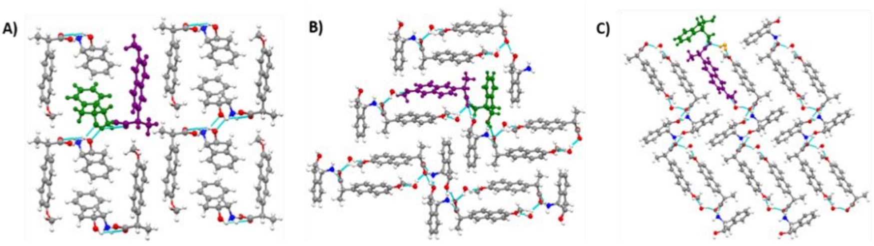

Figure 1. Crystal packing of A) 1, B) 2 and C) 3 where S-naproxen, 1-aminoindan-2-ol and water are highlighted in purple, green and orange respectively.

[1] Calcaterra, A.; D'Acquarica, I., J. *Pharm. Biomed. Anal*. **2018**, *147*, 323−340.
[2] Rossi P.; Ceccarelli J.; Milazzo S.; Paoli P.; Missina J. M.; Ciattini S.; Ienco A.; Tuci G.; Valleri M.; Giovannoni M. P.; Guerrini G.; Conti L., *Cryst. Growth Des*. **2021**, *21*, 6947-6960.
[3] Kinbara K.; Kobayashi Y.; Saigo K., *J. Chem. Soc., Perkin Trans*. **2000**, *2*, 111–119.

Vitriols: The Many Colors of Iron

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"Vitriol" is a term that appears during the Middle-Ages to indicate a panoply of ingredients widely used both in medicinal and alchemical recipes.

Commonly described only by their color, it's sometimes difficult to give a clear identification for these compounds using modern chemical terms.

Expressions such as Green, Blue, or White Vitriol are easily associated with Iron(II), Copper(II), and Zinc Sulfate respectively, thanks to the technical literature from the historical period when older, traditional names and modern chemical nomenclature overlapped [1].

However, other colors of Vitriols are attested throughout history, such as Yellow, Red, or Black. The identification of these compounds is significantly less straightforward, and often chalked up to *decknamens* or unspecified impure ores [2].

By thermal manipulation of Iron(II) Sulfate, we managed to identify several compounds that fit with historical descriptions, which were later characterized through XRPD. Moreover, by using a Kofler Bench and Variable Temperature XRPD, we were able to further investigate the transitions between these phases.

This papar shows what invaluable tool crystallography and solid state phase analysis is for Chemistry Historians, in particular when aiming to offer a modern chemical description of methods and procedures of the past.

[1] A. Campana. *Farmacopea Ferrarese*, presso Silvestro Gnoato, Venice, **1805**.
[2] V. Karpenko, J. A. Norris *Chemicke Listy*. **2002**, *96*, 997

Exploring the Plastic Phase Transition Characteristics of Quinuclidinolium Salts with Diverse Counter-Anions and Their Solid Solutions

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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 realizing various sorts 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 primary objective of this study encompasses three key aspects. Firstly, our focus is on investigating the influence of counter-anions on the plastic phase transitions within a series of R-(+)-(3)-hydroxyquinuclidinium salts [QH]X. By varying the anions' size, shape, and charge, we anticipate observing diverse behaviors in terms of plastic phase transition characteristics and types. Secondly, we aim to explore the feasibility of producing crystalline solid solutions, examining how the composition of these resultant materials further impacts the phase transition compared to the pure parent systems. Lastly, we intend to analyze the ionic conductivity behavior of these salts, particularly by comparing their conductivities in both ordered and disordered phases. To achieve this objective, 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^-), octahedral hexafluorophosphate (PF_6^-), and methanesulfonate ($SO_3CH_3^-$) by the metathesis of [QH]Cl using metal salts of the corresponding anions. A combination of solid-state techniques is employed to investigate the properties of these materials, including variable temperature X-ray diffraction (XRD), thermal analyses, multinuclear solid-state NMR spectroscopy (utilizing nuclei such as ^{11}B, ^{13}C, ^{15}N, ^{19}F, and ^{31}P, variable temperature wide-line ^{19}F T_1 relaxation measurements, micro-Raman spectroscopy, and electrochemical impedance spectroscopy (EIS). Through these analyses, we aim to gain insights into the synthesized materials' crystal structures, phase transition behavior, and ionic conductivity [3].

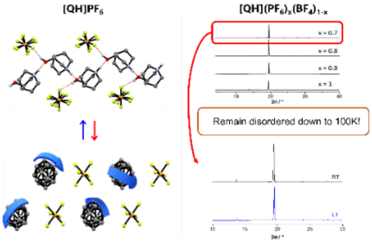

Figure 1. LT and HT structures of $[QH]PF_6$ (left), and the effect of solid solution on the phase transition behaviour (right).

[1] S. Das, A. Mondal, C. M. Reddy, *Chemical Society Reviews*. **2020**, 49, 8878-8896.
[2] S. d'Agostino, L. Fornasari, D. Braga. *Cryst. Growth & Des*. **2019**, *19*, 6266-6273.
[3] S. Ocak, R. Birolo, G. Carì, S. Bordignon, M. R. Chierotti, D. Braga, R. Gobetto, T. Salzillo, E. Venuti, O. Yaffe, and S. d'Agostino. *Mol. Syst. Des. Eng*. **2022**, *7*, 950-962

Study of molecular recognition of supercooled benzoic acid with MiCMoS

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The importance of crystal nucleation is immense. Yet, nucleation is still far from being fully understood. Despite its merits, the Classical Nucleation Theory (CNT) is being increasingly superseded by evidences that a multi-step mechanism should be explicitly considered. Unfortunately, the experimental observation of individual molecular recognition events that lead to nucleation is challenging. Accurately calibrated molecular dynamics simulations [1-4] could help to figure what is going on at the atomic level, providing a physical framework to interpret the experimental outcomes.

Here, we report on the study of pre-nucleation clusters of supercooled liquid benzoic acid (BZA) with the free Milano Chemistry Molecular Simulation (MiCMoS) platform [5,6]. The molecular recognition of BZA is governed by strong hydrogen bonds, which promote the formation of supramolecular aggregates. These aggregates vary in size, ranging from simple cyclic dimers to clusters consisting of dozens of molecules (Figure 1), with different degrees of stability. We propose a simple energy criterion to distinguish between transient aggregates and true sub-critical clusters, the latter likely lying on the path to nucleation. The influence of confinement on the clustering of BZA is also investigated: confinement increases the liquid viscosity and hampers the molecular rotational reorientation, extending the lifetime of hydrogen bonds. Polarization effects in the vicinity of barriers are also detected, with possible implications on the development of long-range order.

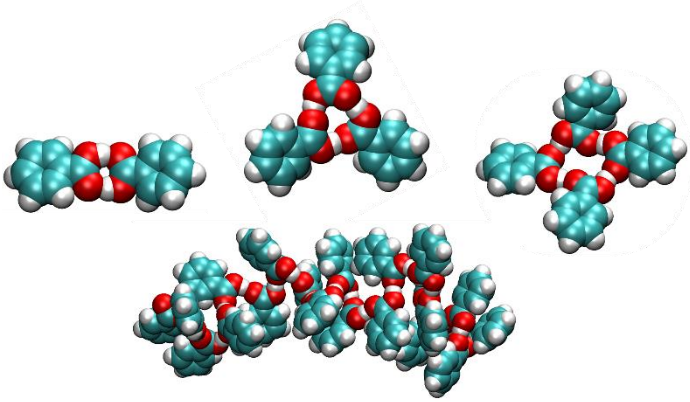

Figure 1. Selection of hydrogen-bonded clusters of benzoic acid.

[1] G. Macetti, L. Sironi and L. Lo Presti, *Classical Molecular Dynamics Simulation of Molecular Crystals and Materials: Old Lessons and New Perspectives*, **2023**, DOI: 10.1016/B978-0-12-821978-2.00107-0
[2] A. Gavezzotti and L. Lo Presti, *New J. Chem*. **2019**, *43*, 2077–2084
[3] A. Gavezzotti and L. Lo Presti, *J. Appl. Cryst*. **2019**, *52*, 1253–1263
[4] A. Gavezzotti, L. Lo Presti and S. Rizzato, *CrystEngComm* **2020**, *22,* 7350-7360
[5] L. Lo Presti, A. Gavezzotti, MiCMoS (MIlano Chemistry MOlecular Simulation) 2.1; Università degli Studi di Milano: Milano, **2022**, https://sites.unimi.it/xtal_chem_group/index.php
[6] A. Gavezzotti, L. Lo Presti, S. Rizzato, *CrystEngComm*, **2022**, 24, 922-930

Application of multivariate analysis on powder diffraction data for the monitoring of a mechanochemical synthesis

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Multivariate analysis (MA) is a strategic tool for the analysis of complex data, becoming fundamental in the application of Process Analytical Technologies (PAT) for process monitoring. Phase identification through powder diffraction data involves the analysis of complex profiles, therefore it is suited for the application of MA methods. In this work we tested the chemometric method MCR-ALS (Multivariate Curve Resolution - Alternating Least Squares) on synchrotron powder diffraction data as a tool to follow the formation, via mechanosynthesis, of the co-crystal of theophylline with malonic acid [1,2].

The MCR-ALS method applies a bilinear deconvolution that enables to extract "pure" constituents profiles, and their respective concentrations, from a series of composite signals [3], as is the case with XRD patterns of a mixture of crystallographic phases monitored over time. The concentration profiles allow to follow the kinetics of the process, and, through the comparison of these profiles in different conditions, to evaluate the effect, on the kinetics, of process variables such as milling frequency, temperature, and solvent amount. Moreover, the "pure" signals decomposition is a useful tool to monitor the behaviour of a mixture, and to detect the presence of intermediate phases.

When pure crystallographic phases are correctly separated by the calculation, the concentrations returned by the method can have a quantitative value, and we tested the results by comparing them with the phase quantification obtained via the Rietveld method.

We present here an example of the application of MCR-ALS to powder X-ray diffraction data and *in situ* monitoring, highlighting its advantages and limits.

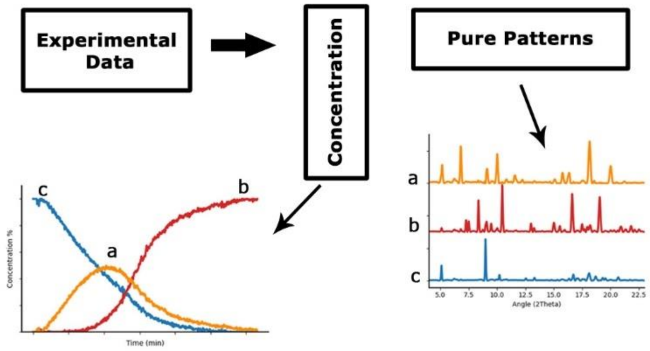

Figure 1. General scheme of the MCR deconvolution

[1] A. Trask, W. Motherwell, W. Jones, *International Journal of Pharmaceutics.* **2006**, *320*, 114–123.
[2] S.A. Stanton, J.J. Du, F. Lai, G. Stanton, B.A. Hawkins, J.A. Ong, P.W. Groundwater, J.A. Platts, *J.Phys. Chem. A.* **2021**, *125*, 9736–9756.
[3] Roma. Tauler, Bruce. Kowalski, Sydney. Fleming, *Anal. Chem.* **1993**, *65*, 2040–2047.

Solid state transformations: a mighty approach through mechanochemistry

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Mechanochemistry has become popular as sustainable and cost-effective technique for the synthesis of different classes of compounds [1]. Mechanical grinding or milling offer a way to greatly reduce or even completely avoid the solvent use, with the consequence of fast reactions and quantitative yields augmented by the absence of extensive work-up [2]. Moreover, solid state reactivity allows to run across through different reaction paths resulting in a final product often different to the ones obtained by solution chemistry [3]. The energy provided by mechanical actions, such as sharing, compression or friction, induces chemical transformations enable to break intermolecular or covalent interactions, and established novel ones. This may lead to the formation of soft materials (cocrystal, solvates, salts), new chemical compounds or activate the conversion between different polymorphic phases.

However, whereas the macroscopic aspects of grinding are becoming clear, the microscopic level of many transformations has remained poor understood due to the difficulty in identifying metastable or intermediate species which usually totally convert during the process. Therefore, cutting edge in-situ investigations are opening the way to a complete understanding of mechanistic processes by analysing the whole mechanochemical reaction with one or more techniques [4].

The purpose of this work is thus to present several examples of solid-state transformations which occur exploiting appropriate mechanochemical methods and experimental conditions. We here report cocrystallization and salt reactions performed using different mechanochemical techniques as well as polymorphic transitions which involve the formation of an amorphous intermediate.

Also, two time-resolved *in situ* experiments are proposed which were carried out using synchrotron X-ray powder diffraction to monitoring the development of inorganic and organic reactions. These investigations were performed with a suitable customized ball mill setup in order to exploit the spectral high resolution due to low energy radiation and improve the refinement of the resulting powder patterns.

[1] J. L. Howard, Q. Cao, D. L Browne, *Chem. Sci.* **2018**, *9*, 3080–3094.
[2] V. Štrukil, M. D. Igrc, M. Eckert-Maksić, T. Friščić *Chem. Eur. J.* **2012**, *18*, 8464-8473.
[3] J. G. Hernández, C. Bolm *J. Org. Chem.* **2017**, *82*, 4007-4019.
[4] G. I. Lampronti, A. A. L. Michalchuk, P. P. Mazzeo, A. M. Belenguer, J. K. M. Sanders, A. Bacchi, F. Emmerling, *Nat. Commun.* **2021**, *12* (1), 1–9

Evidence of amino-thiadiazoles as innovative inhibitors of human glutaminyl cyclase, validated target for neurodegenerative disorders

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Human glutaminyl cyclase (hQC) is a zinc-dependent enzyme belonging to the class of acyltransferases that catalyzes the intramolecular cyclization of the N-terminal glutaminyl or glutamyl of peptides and proteins into pyroglutamic acid (pGlu). This post-translational modification stabilizes and protects macromolecules from proteolytic degradation and assists them to develop the proper conformation. However, since their tendency to rapidly aggregate, pGlu-modified peptides are highly neurotoxic, promoting the insurgence and progression of various neurodegenerative pathologies, such as Alzheimer and Huntington diseases [1,2]. Former studies have reported the upregulation of hQC in these neurodegenerative disorders, thus this enzyme represents an attractive target to develop novel drugs for these pathologies, still lacking effective treatments. In this study, we have investigated a series of molecules relying on the amino-thiadiazole core as new Zn(II)-binding moiety to probe their inhibition effects on hQC. This library of amino-thiadiazole derivatives was formerly developed by us to target the parasite enzyme, *Trypanosoma brucei* pteridine reductase 1 (TbPTR1) [3]. Notably, these compounds showed a safe profile in a panel of early toxicity assay comprising cytotoxicity, mitochondrial toxicity, hERG toxicity, CYP isoforms, and Aurora B kinase. Thus, the amino-thiadiazole scaffold has a well-tolerated liability profile and it can be further explored for inhibitor development also towards other targets, such as hQC. For the present investigation, a set of twenty-four compounds have been selected from this library and tested towards hQC, leading to the identification of three inhibitors having Ki values in the high nM range. To unveil the binding mode of the most active compounds of this series, X-ray crystallography experiments have been performed using the hQC double mutant Y115E-Y117E (hQC-2X), formerly validated by us as soluble protein variant exploitable for drug discovery purposes [4]. The structural information achieved on the complexes of hQC-2X with fourteen amino-thiadiazole derivatives has allowed us to evaluate the structure-activity relationship of these inhibitors, obtaining key insights to evolve new hQC inhibitors based on this innovative Zn(II)-binding motif.

[1] Wirths, A. Hillmann, L. Pradier, W. Härtig, T. A. Bayer, *J Alzheimers Dis* **2013**, *35*, 741.
[2] M. Jimenez-Sanchez. et al. *Nat Chem Biol.* **2015**, *11*, 347.
[3] P. Linciano, A. Dawson, I. Pöhner, D. M. Costa, M. S. Sá, A. Cordeiro-da-Silva, R. Luciani, S. Gul, G. Witt, B. Ellinger, M. Kuzikov, P. Gribbon, J. Reinshagen, M. Wolf, B. Behrens, V. Hannaert, P.A. M. Michels, E. Nerini, C. Pozzi, F. Di Pisa, G. Landi, N. Santarem, S. Ferrari, P. Saxena, S. Lazzari, G. Cannazza, L.H. Freitas-Junior, C. B. Moraes, B. S. Pascoalino, L. M. Alcântara, C. P. Bertolacini, V. Fontana, U. Wittig, W. Müller, R. C. Wade, W. N. Hunter, S. Mangani, L. Costantino, M. P. Costi. *ACS Omega.* **2017**, *2,* 5666.
[4] C. Castaldo, S. Ciambellotti, R. de Pablo-Latorre, D. Lalli, V. Porcari, P. Turano, *PLoS ONE.* **2013**, *8*, e71657.

MS7-FP4

Structural characterization of the adduct formed upon reaction of dirhodium tetraacetate with a double helix dodecamer

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Since the discovery of cisplatin, metal complexes attracted a lot of attention in medicinal chemistry field [1]. In fact, there is a growing demand for cytotoxic metal complexes able to overcome the limitations associated with platinum-based therapy [2]. It has been widely demonstrated that Pt-based drug cytotoxic activity is due to their interaction with DNA [3]. Indeed, cisplatin interferes with DNA replication and transcription processes, kinking the DNA duplex by covalently binding two adjacent guanines in the major groove [4]. On the contrary, information on the interaction of non-platinum-based metallodrugs with DNA are still limited [5]. To obtain insights about the binding mechanism of other metallodrugs to DNA, X-ray crystallography could be of help. For this reason, a structural study on the interaction of a B-DNA double helical dodecamer and a metal compound of medical interest, the dirhodium tetraacetate, has been carried out coupling X-ray crystallography and mass spectrometry.

The X ray structure of the dirhodium/DNA adduct reveals a bimetallic center bound to an adenine via axial coordination (Figure 1). This result is interesting since dirhodium mode of binding to DNA is different from that of cisplatin, which generally binds guanines. This view is supported by ESI MS experiments, pointing out that, at short incubation times, adducts are formed between the DNA and $[Rh_2(\mu\text{-}O_2CCH_3)_4]$ in agreement with crystallographic results. Conversely, for longer incubation times, the dirhodium tetraacetate converts into a mono-rhodium tetraacetate fragment as the consequence of progressive cleavage of the Rh-Rh bond.

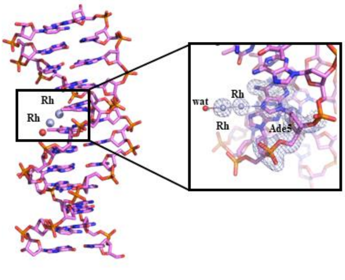

Figure 1. Metal binding site in the adduct formed upon reaction of dirhodium tetraacetate with the C-G-C-G-A-A-T-T-C-G-C-G duplex.

[1] S. M. Cohen, S. J. Lippard, *Inorganica Chimica Acta* **2001**, *67*, 93–130.
[2] B. J. Pages, D. L. Ang, E. P. Wright, J. R. Aldrich-Wright, *Dalton Trans.*, **2015**, *44*, 3505–3526.
[3] N. Z. Fantoni, T. Brown, A. Kellett, *ChemBioChem*, **2021**, *22*, 2184–2205.
[4] S. Dasari and P. Bernard Tchounwou, *European Journal of Pharmacology*, **2014**, *740*, 364–378.
[5] M. Zaki, F. Arjmand and S. Tabassum, *Inorganica Chimica Acta*, 2016, *444*, 1–22.

Micro symposium 8

Mineralogy: recent developments and applications

MS8 - Mineralogy: recent developments and applications

Chairs: P. Ballirano (Sapienza University of Rome); P. Comodi (University of Perugia)

This micro-symposium aims to show the current state-of-the-art investigation of several aspects of crystal structure, chemistry, and reactivity of minerals, glasses, melts, and fluids of interest in the Earth Sciences and their synthetic counterparts. Moreover, the link of such aspects with physical-chemical properties and, in turn, the geological and technological applications should be stressed. We encourage the submission of contributions reporting experimental and/or theoretical investigations covering different aspects of mineralogy, particularly emphasizing the green revolution-ecological transition and the interaction between minerals and biosphere.

Friday 8 September – morning 10.30-12.30

Keynote 1: 10.30-11.00
Fabrizio Bardelli
CNR-Istituto di Nanotecnologia, Roma
Combining X-ray diffraction and X-ray absorption spectroscopy to study Asbestos Bodies in human lung tissues

Keynote 2: 11.00-11.30
Rossella Arletti
Department of Chemical and Geological Sciences, University of Modena and Reggio Emilia
Secondary and alternative raw materials for ceramic tile production: a mineralogical point of view

Oral 1: 11.30-11.45
Lisa Baratelli
Department of Earth Sciences, Universiy of Milano
Crystal-chemistry and polytypism in lombardoite, $Ba_2Mn(AsO_4)_2(OH)$

Oral 2: 11.45-12.00
Ferdinando Bosi
Department of Earth Sciences, Sapienza Universiy of Rome
On the endmember composition

Oral 3: 12.00-12.15
Andrea Bisciotti
Department of Physics and Earth Sciences, Universiy of Ferrara
Rietveld QPA for imaging calibration and to predict engineering properties in recycling of construction and demolition waste

Oral 4: 12.15-12.30
Serena C. Tarantino
Department of Chemistry, University of Pavia
Transforming Biosolid Waste into Secondary Raw Materials for Sustainable Materials Production

Combining x-ray diffraction and x-ray absorption spectroscopy to study Asbestos Bodies in human lung tissues

Fabrizio Bardelli,[a,b] Paolo Ballirano,[c] Carlotta Giacobbe,[d,e] Violetta Borelli,[f] Francesco Di Benedetto,[g] Giordano Montegrossi,[h] Donata Bellis,[b] Alessandro Pacella[c]

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The asbestos bodies (AB) form in the lungs through an *in vivo* biomineralization process started by the alveolar macrophages in the attempt to isolate asbestos from the biological tissues and become the actual interface between asbestos and the host organism [1]. The AB are believed to be mainly composed of the Fe-proteins and mucopolyssaccharides. However, the presence of hydroxyapatite and Fe-(hydro)oxides, other than ferrihydrite (the mineral core of ferritin), has also been proposed [2,3]. We performed synchrotron X-ray diffraction (XRD) and absorption (XAS) measurements to unravel the mineral composition and Fe speciation in the AB, and to check the nature and crystallinity of the inner fibers. XRD revealed that the inner fiber was crocidolite, which maintained a high degree of crystallinity, despite the prolonged stay in the lungs (>10y) (Figure 1b) and revealed the presence of goethite in the Ferich coating (Figure 1c). XAS results, on the other hand, revealed the co-existence of ferrihydrite and goethite in a ~70:30 ratio (Figure 1d) [4]. The results are discussed in terms of the increased toxicity of goethite with respect to ferrihydrite.

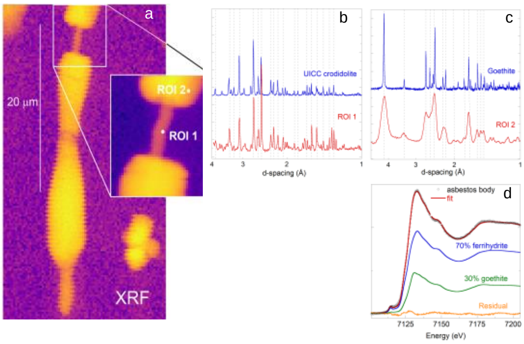

Figure 1. a) X-ray fluorescence (XRF) map of an AB (Fe-signal) showing the region of interests (ROI 1 and ROI 2) chosen for the point XRD acquisitions reported in b) and c). d) Linear combination fit of the XANES spectrum of an AB using the spectra of ferrihydrite (70 mol%) and goethite (30 mol%).

Figure 1. a) X-ray fluorescence (XRF) map of an AB (Fe-signal) showing the region of interests (ROI 1 and ROI 2) chosen for the point XRD acquisitions reported in b) and c). d) Linear combination fit of the XANES spectrum of an AB using the spectra of ferrihydrite (70 mol%) and goethite (30 mol%).

[1] A. J. Ghio, A. LeFurgey, V. L. Roggli. *J. Toxicol. Environ. Health*. **1997**, *50(2)*, 125–142.

[2] N. Bursi Gandolfi, A. F. Gualtieri, S. Pollastri, E. Tibaldi, F. Belpoggi. *J. Hazard. Mater.* **2016**, *306*, 95–104.

[3] D. Di Giuseppe et al. *Minerals*. **2019**, *9(10)*, 1–21.

[4] F. Bardelli, C. Giacobbe, P. Ballirano, V. Borelli, F. Di Benedetto, G. Montegrossi, D. Bellis, A. Pacella. *Environ. Geochem. Health* **2023**, *45*, 5039-5051.

Improving the supply chain of the ceramic sector: secondary and alternative raw materials

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The production of ceramic tiles is growing worldwide and passed in 2021 at 18.000 millions m^2. In Italy the 2022 production assessed about 540 millions of m^2, increasing 2.6 % the production of 2021. These data clearly imply a huge demand of raw materials, in particular for the production of porcelain stoneware more than four millions of tons of feldspar and clay minerals has been imported in 2021. The current supply chain is extremely articulated and the raw material sources are spread over distances up to approximately 3200Km, covered by various means of transport (truck, train, ship). In last decades, the attention of the ceramic sector, is focusing on the optimization of the resources. From one side, the progressive depletion of the main mineral deposits that this production rate imposes, and from the other the long distance to be covered is forcing the ceramic industry to look for suitable substitutes for the raw materials, able to guarantee specific technological properties to the finished product.

In this work we will present the result deriving from the exploitation of wastes from other production activities as secondary raw materials. Specifically, biomass combustion [1] ashes and product of the inertization of glass wool from building demolition [2] have been tested in substitution to feldspar. In addition, a further experiment was performed to assess the possibility of use of local clays to partially substitute Ukrainian ball clays, no longer imported from the beginning of Russian – Ukraine conflict.

Different batches containing different amount of the raw materials to be tested (i.e. inertized glass wool and biomass ashes in place of feldspar; local clays in place of Ukrainian ball clays) were realized along with standard porcelain stoneware batches to be used as benchmark. Industrial production cycle was simulated at laboratory scale for the three systems. The batch realized were fired at different T from 1000 to 1220°C in order to follow the evolution of the technological properties, phase composition (XRPD-Rietveld) and microstructure (SEM). Finished and semi-finished product were characterized to evaluate their technological properties. Results demonstrated that the substitution of the raw materials did not introduce any bottleneck in the ceramic production cycle. The introduction of both ash and waste deriving from inertization of glass wool allowed to lower the firing temperature by 20°C with respect to the benchmarck, while keeping the technological properties comparable. Moreover, the mineralogical and microstructural data revealed different sintering kinetics. The addition of the Italian red clay induced a reduction in the firing temperature (compared to the benchmark), possibly related to the higher content of iron as well as of feldspars. The most significant variations are in the color of the tiles, which results darker (compared to the benchmark) in all the tested bodies, for the presence of iron.

[1] R. Arletti, S. Conte, C. Zanelli, M. De Iuliis, D. Di Giuseppe, V., Scognamiglio, D. Malferrari, M. Dondi, A.F. Gualtieri, Recycling the Product of Thermal Inertization of Man-Made Vitreous Fibres for the Manufacture of Stoneware Tiles, *Waste Biomass Valor.* **2022**, *14*, 1-16.
[2] S. Conte, D. Buonamico, T. Magni, R. Arletti, M Dondi, G. Guarini, C. Zanelli. Recycling of bottom ash from biomass combustion in porcelain stoneware tiles: Effects on technological properties, phase evolution and microstructure, *Journal of the European Ceramic Society* **2022**, *42*, 5153–5163.

Crystal-chemistry and polytypism in lombardoite, $Ba_2Mn(AsO_4)_2(OH)$

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The brackebuschite supergroup of minerals currently has about twenty members. The minerals are monoclinic with space group $P2_1/m$ (7.5577(4) < **a** < 7.87636(18) Å; 5.97761(15) < **b** < 6.1130(6) Å; 8.7316(6) < **c** < 9.1678(2) Å; 111.785(6) < **β** < 112.930(3)°) and have general formula $A_2M^{3+}(TO_4)_2(OH)$ with A = Pb, Ba, Sr, Ca, M = Al, Fe^{3+}, Mn^{3+}, Zn, Cu, T = V, As, P, S. Among these, the arsenbrackebuschite group include minerals having As dominant at the tetrahedral sites. Lombardoite [$Ba_2Mn^{3+}(AsO_4)_2(OH)$] is thus a member of this group, described for the first time at Valletta mine, a small Fe-Mn deposit located in Valletta Valley (Canosio municipality, Maira valley, Piedmont, Italy). A crystal chemical study conducted by single crystal X-ray diffraction on Sr-rich lombardoite crystals from this locality have shown the main partitioning scheme of elements among the sites and the structural responses in terms of bond length and polyhedra geometry. Raman spectroscopy analyses on the same crystals show that chemical composition variations produce a shift of the spectra peaks wavenumber that allows distinguishing between the Ba-rich and Sr-rich members and the V-rich crystals of the solid solution. A clear relation between Sr/Ba content in lombardoite and the position of these peaks is found that allows, at first, to distinguish Sr-rich from Ba-rich samples and that could be used to calibrate the Ba-Sr content.

The diffraction studies also revealed a new polytype, having space group $C2/m$ and **a** cell parameter four times the unit base (27.832(2) < **a** < 28.1443(3) Å; 6.11680(10) < **b** < 6.1476(4) Å; 9.3705(4) < **c** < 9.4391(5) Å; 99.928(3) < **β** < 100.229(6)°; polytype 4*M*), having **a** along [101] of the brackebuschite cell (polytype 1*M*). The frequent presence of streaking in the reciprocal space along the **a*** direction in many of these crystals showed that this polytype must be intergrown with the polytype 1*M*. In fact, both structures can be described as a different stacking of the same structural unit shifted of ½ **c** (brackebuschite cell). All lombardoite crystals showing the -4*M* polytype have significant Sr amount, whereas we have observed limited solid solution of Sr in lombardoite-1*M* and of Ba in its Sr-counterpart, aldomarinoite [$Sr_2Mn^{3+}(AsO_4)_2(OH)$]. Interestingly, the cationic order of Sr in the *A*1 sites of the brackebuschite structure leads to a volume reduction of these polyhedra, whereas the cationic ordering of Ba in the larger *A*2 sites accommodates the chemical strain. This helps to reduce the strain and apparently stabilizes the polytype 4*M*. The Raman signal is not sensitive to the order of the layers within the analyzed volume, making the distinction of the polytypes intergrowths with similar composition unfeasible. Observations through Transmission Electron Microscopy, have been done with the aim of characterize the micro-syntactic (crystallographically oriented) intergrowths of both polytypes.

MS8-O2

On the endmember composition

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If the world were made of pure solid substances, our develop of the mineral properties would likely now be complete. But one of the reasons why the world is so complex it that pure substances are relatively rare (or even nonexistent). Most minerals have variable chemical composition because of isomorphic substitution of chemical elements in their structure. The range of compositions produced by this substitution is known as a substitution series or solid solution series. The compositional extremes of a substitution series are known as the end members. Thus, we need to develop a method to define the endmember compositions: we have to be able to get the dominant endmember composition in a mixed crystal. Endmembers are important in a thermodynamic sense because the thermodynamic properties of endmembers can be determined, regardless of whether they exist as stable minerals. Thermodynamic properties are important for modeling the behavior of solid solutions in petrological and geochemical processes [1].

What an *end member* is? It is not a mineral, but an ideal concept that it may be used to identify minerals. According to Hawthorne [2], an endmember composition must be conformable with the structure type of the mineral, must be electroneutral (*i.e.* not carry an electric charge) and irreducible within the system considered (*i.e*. it cannot be factorized into two or more simpler compositions that are compatible with the mineral crystal structure). This definition implies that endmembers can have more than one constituent at only one site in the structure, and only two constituents at that site. If more than one cation or anion is introduced to another site in the structure, or a third species is introduced to a site, the resulting composition is reducible and may be resolved into two endmember compositions.

However, Hawthorne [3,4] modified this endmember definition by stating that the atomic arrangement of an end member must be capable of existence: *i.e*. some atomic arrangements cannot exist for some chemical endmember formula as they strongly violate the valence-sum rule of the bond-valence theory [5]. Consequently, *i*) some endmember compositions cannot exist as the corresponding arrangement of ions is not stable with regard to the bond-valence theory, and *ii*) an endmember formula can have more than one site that contain more than one constituent ion. To test *i*) and *ii*), two hypothetical endmembers, $\square Ca_2Al_5(Si_3Al_5)O_{22}F_2$ and $\square Ca_2Mg_5(Si_6Al_2)O_{22}\square_2$, of the $C2/m$ amphibole and the hainite mineral of approximate formula $Na(NaCa)Ca_2(CaY)Ti(Si_2O_7)_2(OF)F_2$ [6] were used by Hawthorne, respectively.

Within the framework of the bond-valence theory, I will show that the hypothetical amphibole endmembers above are stable as well as that the hainite formula can be split into the endmembers $NaCa_2Ca_2(CaY)Ti(Si_2O_7)_2O_2F_2$ and $NaNa_2Ca_2(CaY)Ti(Si_2O_7)_2F_2F_2$ (with only two constituents at only one structural site) whose atomic arrangements are stable.

[1] D. Henry, M. Novák, F.C. Hawthorne, A. Ertl, B.L. Dutrow, P. Uher, F. Pezzotta *Am. Mineral.*, **2011**, *96*, 895

[2] F.C. Hawthorne *Can. Mineral.* **2002**, *40*, 69.

[3] F.C. Hawthorne *Can. Mineral.* **2021**, *59*, 159.

[4] F.C. Hawthorne *Mineral. Mag.*, **2023,** doi.org/10.1180/mgm.2023.8.

[5] I.D. Brown Eds. *The chemical bond in inorganic chemistry: the bond valence model*, Oxford University Press, UK, **2002**.

[6] L. Lyalina, A. Zolotarev, E. Selivanova, E. Savchenko, D. Zozulya, S. Krivovichev, Yu. Mikhailova *Mineral. Petrol.*, **2015**, *109*, 443.

Rietveld QPA for imaging calibration and to predict engineering properties in recycling of construction and demolition waste

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Construction and demolition wastes (CDW) account for more than a third (37.1%) by weight of total waste generated in the EU (about 2.2 billion tonnes for EU-27 in 2020). With about 292 million tonnes, the non-hazardous mineral fraction constitutes more than 98% of the total CDW [1]. This fraction includes concretes, cements, mortars, bricks, hollow bricks, tiles, and natural stones. Effective recycling of CDW is one of the highest priorities of EC to comply with the paradigms of circular economy and sustainability of primary resources for aggregates [2].

A methodology which combines image analyses, augmented by artificial intelligence, with Quantitative Phase Analysis (QPA) by the Rietveld method has been developed to improve the quality of recycled aggregates (RAs). A well-known issue which strongly affects the mechanical performances and workability of concretes prepared with recycled aggregates (RACs) is the occurrence of residual adhered mortar paste (AM) attached on the surface of RAs. Developing a fast automated screening technique to be implemented in CDW recycling plants is a priority to achieve RAs with quality comparable to that of natural aggregates, thus making the concrete sector truly circular. We have tested the feasibility of such a technique on 300 RAs which have been preliminary divided into 30 groups of 10 individual clasts by digital image analysis. Using the ImageJ software [3], comparable values of superficial area coverage have been estimated based on specific thresholding. The starting dataset has been then classified in three groups: i) clean RAs (C), almost comparable to natural aggregates, ii) mortar-covered RAs (M) with just partial areas of surface mortar paste attached and iii) mortar-rich RAs (D), this latter mainly equivalents to pure hydrated cement paste. By performing Rietveld QPA of the AM detached from RAs within a rotating mill drum the ratio between powder mass from mechanical detachment and a weighted mean density product for the mineral phases gave a volumetric quantitative phase information on AM within each group. Aggregates mean volume reconstruction was then performed by bidimensional image analyses measurements of the RAs total areas.

While the physical, mechanical, and engineering properties of new concretes prepared using recycled aggregates (RACs) have been widely investigated (e.g., [4]), very little attention has been paid so far to application of accurate QPA to predict the performances of RACs. To fill this gap, we have performed Rietveld-QPA of recycled aggregates from earthquake-generated CDW and of RACs prepared form the same RAs in a previous study [5]. QPA results were used to calculate average pseudo-properties (density, hardness, and mass absorption coefficient) which were correlated to results of physical and mechanical tests. The good correlations found allows to predict several physical and mechanical properties of concrete made from recycled CDW.

[1] https://ec.europa.eu/eurostat/databrowser/view/env_wasgen/default/table?lang=en

[2] https://www.eea.europa.eu/publications/construction-and-demolition-waste-challenges

[3] Schneider C. A., Rasband W. S., Eliceiri K. W. (2012) - NIH Image to ImageJ: 25 years of image analysis. Nature Methods, (9) 7, pp. 671–675. https://doi.org/10.1038/nmeth.2089

[4] Pacheco-Torgal, F., Ding, Y., Colangelo, F., Tuladhar, R., Koutamanis, A. (2020) *Advances in Construction and Demolition Waste Recycling*. Woodhead Publishing.

[5] Galderisi A., Bravo M., Iezzi G., Cruciani G., Paris E. & de Brito J. *Materials*, **2023**, 16, 2855.

Transforming Biosolid Waste into Secondary Raw Materials for Sustainable Materials Production

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The path to a more sustainable future is through efficient use of resources (energy, water, land, minerals), optimization of waste management, and value creation. Increasing the use of secondary and renewable resources will likely be the key to achieving sustainable use of materials. Although there is general agreement that recycled minerals alone cannot sustain global demand by 2050, all agree that recycling could play a greater role in meeting demand to provide a low-carbon transition while reducing disturbance to natural ecosystems.

This talk addresses examples of the transformation of biosolids waste into secondary raw materials. Sound chemical-physical mineralogical and crystal-chemical knowledge are essential to design and develop processes to recover and recycle materials while reducing environmental impact through sustainable practice.

Through a hydrothermal process (LIFE19 ENV/IT/000165, https://life-freedom-project.eu/), sewage sludge can be converted into secondary raw materials, which in turn can be used to produce ceramics that meet the challenges of sustainability and environmental responsibility.

Hydrothermally treated sewage sludge (cake) have been mixed in different proportions to a natural illitic clay to form the ceramic body. The obtained raw ceramics have been fired in an industrial brick kiln at 900 °C. The ceramics obtained, including those with the highest percentage of added cake, have good chemical and physical characteristics. All samples have been characterized by X-ray powder diffraction, X-ray fluorescence, and scanning electron microscopy. Na-K substitution in feldspars can be related to the firing process. In the ceramic samples alkaline feldpsars are zoned, showing a Na-rich core and a K-feldspar-like rim due to the clay mineral breakdown and reaction with the original albite. In addition, from a textural point of view, a marked primary porosity is observed due to the degradation of the organic matter contained in the added waste material, and a secondary porosity is due to the mica's degradation with the temperature.

Concluding, it is possible to add a large quantity of cake waste as a substitute for a primary raw material. In this way it is possible to release the pressure on natural resources and use waste material as secondary raw material in a circular economy perspective, in complete accordance with European legislation and directives.

Micro symposium 9

Structural aspects of metal-based systems for the sustainable development

MS9 - Structural aspects of metal-based systems for the sustainable development

Chairs: V. Colombo (University of Milan); L. Marchiò (University of Parma)

This micro symposium will focus on structural aspects of metal based-systems relevant to improving the efficient use of resources. The systems of interest will comprise mono-, poly-nuclear entities and extended frameworks. Discussion topics will be related to materials and compounds for energy storage and conversion, catalysis, recycling of materials, and any other issue relevant to sustainable development.

Friday 8 September – morning 10.30-12.30

Keynote 1: 10.30-11.00
Elisa Borfecchia
Department of Chemistry, University of Torino
Understanding local structure and reactivity of copper-based catalysts for the valorization of light alkanes: from Cu-zeolites to Cu-MOFs

Keynote 2: 11.00-11.30
Lorenzo Malavasi
Department of Chemistry, University of Pavia
Structure-property correlations in metal halide perovskites: a route to design optimized and novel materials for energy applications

Oral 1: 11.30-11.45
Mauro Coduri
Department of Chemistry, University of Pavia
Beyond entropy: understanding the phase stability of high entropy oxide $Mg_{0.2}Co_{0.2}Ni_{0.2}Cu_{0.2}Zn_{0.2}O$

Oral 2: 11.45-12.00
Andrea Daolio
Department of Materials Science, University of Milano
Dipolar molecular rotors in fluorinated MOFs and CO_2 capture

Oral 3: 12.00-12.15
Dario Giovanardi
Department of Chemical Sciences, Life Sciences and Environmental Sustainability, University of Parma
From Essential Oils to Active Food Packaging: two ML-MOFs compared

Oral 4: 12.15-12.30
Simona Galli
Universita'dell'Insubria
Mercury sequestration-driven phase transition of a luminescent Zn-MOF: a multi-technique study

MS9-KN1

Understanding local structure and reactivity of copper-based catalysts for the valorization of light alkanes: from Cu-zeolites to Cu-MOFs

Elisa Borfecchia[a]

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Valorisation of light alkanes to oxygenates represents an ongoing challenge in heterogeneous catalysis, with a huge impact on chemical industry and energy sector. In particular, a direct process to convert methane into methanol (DMTM) under mild conditions would be a spectacular achievement leading to massive energy savings and a pivotal contribution to sustainable development [1]. Crucially, Nature is able to achieve DMTM conversion at ambient conditions, using Cu-based methane mono-oxygenase (MMO) enzymes. In the last decade, attempts were made to insert Cu sites in zeolites, inspired by MMOs. As an encouraging proof-of-concept, activation of methane to the corresponding alcohols was demonstrated, yet mostly using a step-wise approach [2, 3], implying that high specificity and selectivity of man-made catalysts is yet to be achieved. In this context, Cu-functionalized MOF are envisaged as promising candidates, ensuring a higher flexibility in engineering Cu ligands, cavity confinement and structural motif around the active site compared to the more conventional zeolites [3].

To keep advancing the field, a thorough understanding of local structure and electronic/chemical properties of Cu ions hosted - often without long-range order - in zeolitic or MOF frameworks is of utmost importance. In the present contribution, I will highlight the role of in *situ/operando* X-ray spectroscopy in unravelling structure-activity relationships for the step-wise DMTM conversion over the Cu-zeolites, focusing on the MOR topology [4]. I will also present preliminary results on Cu-UiO-67 MOFs, in which the diphenyl linkers are partially (10%) replaced by thoughtfully modified bipyridine ones, showing an interesting redox cyclability under model conditions while preserving their crystallinity. An emphasis will be put on the use of advanced data analysis approaches, aimed at quantitatively determining Cu-speciation in both zeolite- and MOF-based catalysts, while deciphering the details of the local coordination environment for the formed Cu-species. These will include, for instance, statistical/multivariate analysis of large XAS datasets, to resolve spectral signatures/concentration profiles of different Cu-species, and EXAFS Wavelet Transform, to unambiguously assess their nuclearity.

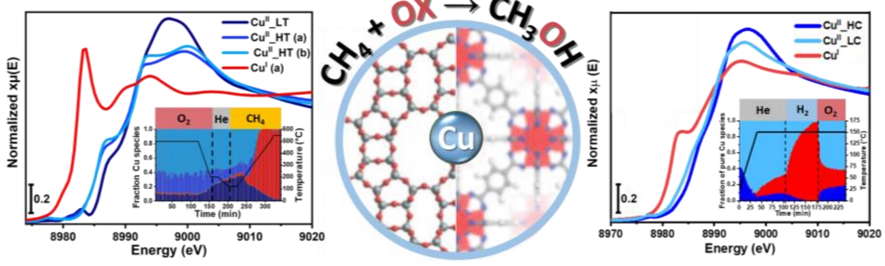

Figure 1. Cu K-edge pure XAS spectra and concentration profiles of different Cu^{II} and Cu^{I} species identified by MCR-ALS analysis of a Cu-MOR zeolite (left) and a Cu(bpy)-UiO-67 MOF (right), monitored under model redox conditions, relevant to the DMTM conversion (middle).

[1] M. Ravi *et al.*, *Angew. Chem. Int. Ed.*, **2017**, *56*, 16464.
[2] E. Borfecchia *et al.*, *Chem. Soc. Rev.*, **2018**, *47*, 8097.
[3] Ikuno, T. *et al.*, J. Am. Chem. Soc. 2017, *139*, 10294.
[4] D. K. Pappas *et al.*, *J. Am. Chem. Soc.*, **2018**, *140,* 15270; A. Martini *et al.*, *Phys. Chem. Chem. Phys.*, **2020**, *22*, 18950; K. Kvande *et al.*, *Chem. Sci.*, 2023, under revision.

Structure-property correlations in metal halide perovskites: a route to design optimized and novel materials for energy applications

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Metal halide perovskites (MHPs) are attracting a huge interest for their potential use in different applicative fields ranging from photovoltaics to photocatalysis. The most investigated MHPs possess the architepal ABX_3 crystal structure, where A= protonated monotopic amine or monovalent inorganic cation, B= Pb, Sn or Ge, and X = Cl^-, Br^-, or I^-. By playing with the nature of the different chemical constituents on the different perovskite sites, it is possible to tune and modulate the optoelectronic properties of the final material and provide materials suitable for different applications. Moreover, by changing the dimensionality of the perovskite structure, *i.e.* moving towards low-dimensional perovskite such as 2D systems, an immense playground for materials chemistry and structural chemistry can be accessed.

In the present contribution, we will present some selected examples in the filed of MHPs where, through a rigorous structure-property correlation approach, it was possible to design novel materials with tailored functional properties. This aim requires to devise, synthetise, and characterize rational series of samples to unveil the role of the various chemical degree of freedoms on the optoelectronic properties. We will show how it is possible to design photocatalytically active and water-stable MHPs to be used in the photogeneration of hydrogen and in the photofixation of nitrogen. This was achieved by selecting suitalbe amine ligands which imparts a significant degree of hydrophobicity to the final material thus allowing their use in aqueous environment as well as by understanding the role of central metal ion [1-3]. The reaction mechanism at the basis of their photocatalytic activity will be also presented, including the role of defect chemistry on the redox activity. Finally, some preliminary results in the area of chiral perovskites for sustainable electronics will be presented.

[1] L. Romani, A. Speltini, F. Ambrosio, E. Mosconi, A. Profumo, M. Marelli, S. Margadonna, A. Milella, F. Fracassi, A. Listorti, F De Angelis, L. Malavasi, *Angew. Chem. Int. Ed.*, **2021**, *60,* 3611.

[2] L. Romani, A. Speltini, C. N. Dibenedetto, A. Listorti, F. Ambrosio, E. Mosconi, A. Simbula, M. Saba, A. Profumo, P. Quadrelli, F. De Angelis, L. Malavasi, *Adv. Funct. Mater.*, **2021**, *31*, 2214428.

[3] L. Romani, A. Speltini, R. Chiara, M. Morana, C. Coccia, C. Tedesco, V. Armenise, S. Colella, A. Milella, A. Listorti, A. Profumo, F. Ambrosio, E. Mosconi, R. Pau, F. Pitzalis, A. Simbula, D. Ricciarelli, M. Saba, M. Medina-Llamas, F. De Angelis, F. Malavasi, *Cell Reports Physical Science,* **2023**, *4,* 101214.

Beyond entropy: understanding the phase stability of high entropy oxide $Mg_{0.2}Co_{0.2}Ni_{0.2}Cu_{0.2}Zn_{0.2}O$

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High entropy oxides (HEOs) are a recently discovered class of materials where a particular crystal structure, which in general is different from that of the parent compounds, is stabilized in a multicomponent system, characterized by a large amount of configurational entropy [1]. In the recent years, these materials are gathering increasing attention for many technologically relevant applications. In particular, they have been employed as electrodes for Li and Na-ion batteries, for catalysis, and they present interesting properties such as colossal dieletric constant and enhanced mechanical properties [2,3].

The main driver for the growing interest in HEOs is the potential to obtain novel properties by exploiting the enormous number of possible elemental combinations. However, most investigations on HEOs assume that these systems present their optimal characteristics in the proximity of an equimolar composition, where the configuration entropy is highest. Overall, the study of phase stability and of the optimization of the functional properties in HEOs presents significant challenges. In fact, conducting a study using the traditional approach of uniformly sampling the compositional space is not feasible due to the high number of compositional parameters involved.

Here we present a chemometric approach based on the Design of Experiment (DoE), that we employed as a simple and time-saving strategy to predict the phase stability of the prototypical high entropy oxide (Cu,Zn,Mg,Ni,Co)O with a rock salt structure. This approach allowed to extract a polynomial function able to predict, for every combination of the 5 elements, the fraction of the single rocksalt phase that could be obtained, allowing therefore to draw an isothermal phase diagram at 1000 °C for this multicomponent system. It was observed that the stability region of this HEO extends well beyond the equimolar composition $Cu_{0.2}Zn_{0.2}Mg_{0.2}Ni_{0.2}Co_{0.2}O$. In particular, significantly lower and higher fractions of Cu^{2+} and Zn^{2+} can be inserted and still lead to a single phase. By combining these thereotical findings with X-ray diffraction, we observed that a high content of Cu^{2+} induces a tetragonal distortion, associated to the strong Jahn-Teller effect of this cation.

Moreover, it was clearly observed that the overall quantity of single-phase RS that can be formed is not strictly dependent on the configurational entropy of the resulting compositions, but rather on the type and content of the cations involved [4]. This points towards the fact that configurational entropy does not have a central role in the phase stability of this HEO.

[1] C. Rost, E. Sachet, T. Borman, A. Moballegh, E. C. Dickey, D. Hou, J. L- Lones, S. Curtarolo, J. Maria, *Nat. Commun.* **2015**, *6* 8485.

[2] P. Ghigna, L. Airoldi, M. Fracchia, D. Callegari, U. Anselmi Tamburini, P. D'Angelo, N. Pianta, R. Ruffo, G. Cibin, D. Oliveira de Souza, E. Quartarone, *ACS Appl. Mater. Interfaces* **2020**, *12*, 50344-50354.

[3] M. Fracchia, P. Ghigna, T. Pozzi, U. Anselmi-Tamburini, V. Colombo, L. Braglia, P. Torelli, *J. Phys. Chem. Lett.* **2020**, *11*, 9, 3589-3593.

[4] M. Fracchia, M. Coduri, M. Manzoli, P. Ghigna, U. Anselmi Tamburini, *Nat. Commun.* **2022**, *13*, 2977.

Dipolar molecular rotors in fluorinated MOFs and CO_2 capture

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Within the ever-expanding field of porous materials, Metal-Organic Frameworks (MOFs) are well-known for their synthetic versatility and ability to capture greenhouse gases such as CO_2. MOFs have also been shown to be able to support extensive dynamics without disrupting their primary architecture. Lately, MOFs were successfully employed to insert bicyclopentane-based rotors in the frameworks as ligands bridging the metal ions or cluster nodes, demonstrating extremely fast dynamics down to 2 K. [1]. The next step of the study would be to impose or modulate the properties of the material by controlling the rotation of said ligands inside the framework. [2]

MOFs containing dipolar molecular rotors as linkers are emerging as an attractive class of compounds for their ability to interact with static or oscillating electric fields. Therefore, we built a bicyclopentane dicarboxylate-based (FTR) aluminum MOF (Al-FTR) and its dipolar, fluorinated analogue (Al-FTR-F2) (Figure 1, A), explored the rotor dynamics and CO_2 capture ability. [3] To solve the crystal structures, we considered the arrangements of the CF_2 dipoles as determined by the combination of molecular mechanics and PW-DFT *in tandem* with Rietveld refinement. Computationally-informed structural analysis of the two MOFs reveals very fast dynamics down to temperatures as low as 4 K, reminiscent of liquid state mobility, with strong agreements between ^1H T_1 spin-lattice NMR relaxation times and computational analysis. Notably, the mobility in Al-FTR-F2, especially at those extreme temperatures, is due to a concerted rotation of dipoles prompted by the interactions among nearest-neighbor rotors, interconverting into each other thanks to a cascade mechanism (Figure 1, B). The subsequent analysis of the CO_2-filled Al-FTR-F2 reveals that gas filling can induce a coherence switch of the dipolar rotors, drastically impacting the overall configurational landscape (Figure 1, C).

Similar compounds endowed with such controllable motional phenomena may find application in sensing or switching, the translation of light irradiation into movement and the control of solid-state dynamics with electrical fields minimizing energy dissipation.

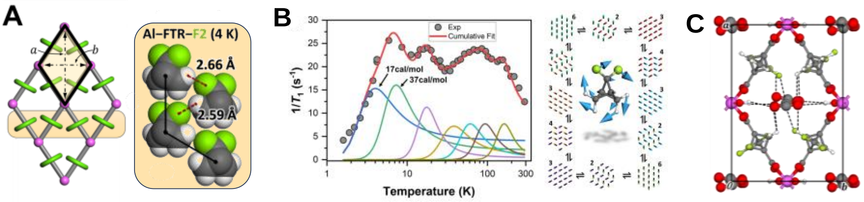

Figure 1. A) Diagrammatic structure of Al-FTR-F2 with CF_2 dipoles conformation; B) interconversion of the dipoles conformations; C) details of the interaction between the MOF and CO_2.

[1] J. Perego et al. *Nature Chem.* **2020**, *12*, 845.
[2] J. Perego et a. *J. Am. Chem. Soc.* **2021**, *143*, 13082.
[3] J. Perego et al. *Angew. Chem. Int. Ed.* **2023**, *62*, e202215893.

From Essential Oils to Active Food Packaging: two ML-MOFs compared

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Essential oils (EOs) are natural bioactive compounds with intriguing properties in terms of antibiotic, antimicrobial and antifungal activity[1]. Although their application in material sciences has grown rapidly in the last years, especially in the field of food active-packaging, their low melting points and high volatility can represent important drawbacks for real applications. It is then important to find out suitable porous materials for their immobilization and long-time release. In this regard, porous Metal Organic Frameworks (MOFs) can be considered a valid alternative.

In this communication, two pillared Mixed-Ligand Metal Organic Frameworks (ML-MOFs), namely PUM168[2,3] and PUM210[4] are compared as potential porous materials for the fabrication of active packaging. The two MOFs derive from the solvothermal reaction of N,N'-(1,1'-biphenyl)-4,4'-diylbis-4-pyridinecarboxamide with 4,4'-biphenyldicarboxilic acid and 2,6-naphtalenedicarboxilic acid, respectively. Despite the similarity of the synthetic approach and of the involved ligands, the two ML-MOFs are characterized by different architectures: PUM168 features a triple interpenetration, where the SBUs are typical paddle-wheels, while PUM210 adopts a polycatenated structure, where the frames contain two different types of SBUs (complete and truncated paddle-wheels). The guest uptake capacity and long-time guest release profiles towards different EO-components, such as eugenol, carvacrol and thymol, will be shown and correlated with the framework flexibility, porosity, type of SBU that feature the two MOFs and with the supramolecular organization that the guests adopt once included in the host framework, as inferred by single crystal X-ray analyses.

[1] E. Spisni, G. Petrocelli, V. Imbesi, R. Spigarelli, D. Azzinnari, M. D. Sarti, M. Campieri, M. C. Valerii, *Int J Mol Sci* **2020**, *21,* 1–27.

[2] P. P. Mazzeo, D. Balestri, A. Bacchi, P. Pelagatti, *CrystEngComm* **2021**, *23*, 7262–7269.

[3] D. Balestri, P. P. Mazzeo, C. Carraro, N. Demitri, P. Pelagatti, A. Bacchi, *Angewandte Chemie - International Edition* **2019**, *58*, 17342–17350.

[4] D. Balestri, I. Bassanetti, S. Canossa, C. Gazzurelli, A. Bacchi, S. Bracco, A. Comotti, P. Pelagatti, *Cryst Growth Des* **2018**, *18*, 6824–6832.

Mercury sequestration-driven phase transition of a luminescent Zn-MOF: a multi-technique study

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In its elemental, inorganic or organic forms, mercury is one of the most toxic heavy metals [1]. Largely present in surface and ground waters as a result of anthropogenic activities, it reaches the human body through the food chain and bio-accumulates, leading to numerous diseases. Despite several methods have been exploited, to date, to sequestrate and/or sense mercury from (waste)waters, effective strategies development is still a challenge [2].

The tailorable crystallochemical nature of metal-organic frameworks (MOFs) [3] has recently triggered research activities focused on their use to detect or sequestrate mercury [4]. In this context, the present contribution [5] reports on the role of interpenetration polymorphism between the two MOFs Zn(BPE) and Zn(BPE)·*n*DMF [interpenetrated i-Zn and non-interpenetrated ni-Zn·DMF, respectively; H_2BPE = 1,2-bis(1*H*-pyrazol-4-yl)ethyne; DMF = dimethylformamide] on $HgCl_2$ sequestration from water.

By means of a multi-technique approach which combined laboratory powder X-ray diffraction (PXRD) with *in silico* modelling, N_2 adsorption, X-ray fluorescence, UV-vis absorption, excitation and fluorescence spectroscopy, we carried out a comprehensive study of the $HgCl_2$/Zn(BPE) system at the molecular level. As unveiled by PXRD, a phase transition from i-Zn to ni-Zn takes place upon suspending the former in $HgCl_{2(aq)}$ solutions. To the best of our knowledge, this is the first example of disruption of a water-stable MOF, with metal-ligand coordinative bonds breaking, followed by the self-assembling, around a specific guest, of a different 3-D architecture. Non-bonding interactions between Hg^{II} and the carbon-carbon triple bond of the on-purpose designed BPE^{2-} linker characterize the primary adsorption sites and act as driving force for the phase transition. PXRD also allowed to quantitatively describe the process: the quantity of recovered $HgCl_2$@ni-Zn is directly proportional to the $HgCl_{2(aq)}$ concentration up to 500 ppm, while it tends to saturate for higher concentrations. In addition to this, UV-vis absorption, excitation and fluorescence spectroscopy unveiled a spectral benchmark, for the two MOFs, at a specific (excitation and emission) wavelength. This occurrence enabled us to *i*) qualitatively and quantitively confirm the results disclosed by PXRD, thus providing a fast and readily accessible path for $HgCl_2$ sensing and quantification, and *ii*) real-time monitor the phase transition kinetics at different $HgCl_{2(aq)}$ concentrations.

Overall, this investigation unravelled an intriguing and previously unobserved molecular-level mechanism, enabling the sequestration of a mercury-containing pollutant and its concomitant quantification. Such a case of study might open the way to new cutting-edge strategies, based on metal-organic frameworks, to achieve real-time sensing and/or sequestration of pollutants in (waste)waters.

[1] R.A. Bernhoft, *J. Environ. Public Health* **2011**, *2012*, e460508.
[2] E.M. Nolan, S. Lippard, *J. Chem. Rev.* **2008**, *108*, 3443.
[3] (a) O.M. Yaghi, M.J. Kalmutzki, C.S. Diercks, Introduction to Reticular Chemistry. Wiley-VCH, 2019. (b) S. Kaskel Ed., The Chemistry of Metal-Organic Frameworks: Synthesis, Characterization, and Application. Wiley-VCH, **2016**.
[4] X. Yan, P. Li, X. Song, J. Li, B. Ren, S. Gao, R. Cao, *Coord. Chem. Rev.* **2021**, *443*, 214034.
[5] M. Moroni, L. Nardo, A. Maspero, G. Vesco, M. Lamperti, L. Scapinello, R. Vismara, J.A.R. Navarro, D. Monticelli, A. Penoni, M. Mella, S. Galli, *J. Mater. Chem.* **2023**, *35*, 2892.

Posters

P1 - Laura Chelazzi **-** Ranolazine: crystal structure determination and investigation of its metastable polymorphs

P2 - Michele Prencipe **-** Triggering the release of essential oil-based cocrystals

P3 - Sofia De Felice **-** Crystal structure of human serum albumin in complex with Alb1 Megabody

P4 - Emanuele Fornasier - Symmetric and asymmetric dimers of the SARS-CoV-2 Main protease

P5 - Alice Pancaldi **-** Tuning the morphology of Nickel-tetraphenylporphyrin thin films

P6 - Meriem Goudjil **-** Crystal structure and magnetic properties of a new mono-bridged binuclear copper (II) complex with amino-hydroxy-naphthalene ligand

P7 - Giovanni Barra **-** The high-resolution structure of the human Annexin IV: insight into calcium-binding sites

P8 - Romualdo Troisi **-** Structural features of the highly effective anti-thrombin aptamer M08s-1

P9 - Silvia Fanti **-** Crystal structure and potential application of NAD(P)H Quinone Oxidoreductase (NQR) from *Arabidopsis thaliana*

P10 - Martina D'Auria **-** Characterization of homo- and heterodimer equilibria in human 14-3-3 ζ and ε isoform

P11 - Michele Saviano **-** The European Research Infrastructures and the Italian PNRR **-** The Project *ITACA.SB*, Potentiating the Italian Capacity for Structural Biology Services in Instruct-ERIC

P12 - Maddalena Paolillo **-** Interaction of the pharmacologically active $V^{IV}O$−Pyridinone drug with the model protein lysozyme

P13 - Nadia Curetti **-** Natural Mn and V dioxides: structural details and HT transformations

P14 - Sabrina Nazzareni **-** High-pressure and phase transitions in dalyite, a Zr-silicate

P15 - Marco Ambrosetti **-** Understanding the electrochemical features of $ZnFe_2O_4$, as anode for LIBs, by multiple physical-chemical techniques

P16 - Rossella Arletti **-** Structural investigation of high pressure intrusion of ternary aqueous solution in pure silica chabazite

P17 - Tommaso Battiston **-** High-pressure behaviour of jadarite: a promising lithium-boron natural commodity

P18 - Davide Comboni **-** The anomalous high-pressure phase transition of inderite, $MgB_3O_3(OH)_5 \cdot 5H_2O$

P19 - Lisa Baratelli **-** Elastic geobarometry applied to omphacite: a Raman spectroscopy approach

P20 - Giovanni Valdrè **-** Nanotopography and nanospectroscopy of the chlorite surface

P21 - Laura Contini **-** Synthesis and characterization of complexes of Bismuth(III) as novel urease inhibitors

P22 - Beatrice De Bonis **-** Production and characterization of metal substituted human Carbonic Anhydrase II for artificial photosynthesis

P23 - Chiara Marchini **-** New materials by mechanochemistry on calcium carbonate from waste seashells

P24 - Angelica Mucaria **-** Oxidized β-chitin hydrogel

P25 - Alessandro F. Gualtieri **-**The crystal structure of asbestiform erionite from New Zealand

P26 - Beatrice Celata **-** Chromium diffusion in synthetic $MgAl_2O_4$ spinel at High Temperature and High Pressure conditions

P27 - Paola Comodi **-** High-pressure synchrotron single crystal behaviour and structural evolution of jamesonite ($FePb_4Sb_6S_{14}$)

P28 - Paolo Lotti **-** (P,T)-behavior of an intermediate scapolite of unusual $I4/m$ symmetry

P29 - Giulia Marras **-** An in-situ experimental study of Cinnabar (HgS) stability and liquid structure at HP-T

P30 - Daniela Mauro **-** Batoniite, $[Al_8(OH)_{14}(H_2O)_{18}](SO_4)_5{\cdot}5H_2O$, the first mineral with $[Al_8(OH)_{14}(H_2O)_{18}]^{10+}$ polyoxocation clusters

P31 - Marta Morana **-** Toward the understanding of inclusions trapped in a diamond from Rio Soriso, Juina (Brazil): a multi-technique approach

P32 - Andrea Sala **-** Novel sustainable MOFs: mechanochemical synthesis, structural characterization, and applications

P33 - Silvano Geremia **-** Crystal Structures of Metal-Porphyrin-Calixarene Complexes: Microporous Materials with Diverse Architectures

P34 - Luca Angelo Betti **-** Structure-Property Investigation of Lanthanum-based Perovskites Oxides for Thermocatalytic Green Hydrogen Production

P35 - Delia Blasi **-** Water stable Cu(II)-based porous Metal-Organic materials for CO_2 capture and environmentally application

P36 - Clarissa Coccia **-** Development of Lead-Free Chiral Perovskites

P37 - Marco Moroni **-** Low dimensional systems of chiral perovskites: unveiling the role of composition and crystal structure in the photophysical properties

P1

Ranolazine: crystal structure determination and investigation of its metastable polymorphs

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Ranolazine (RNL) is an anti-anginal drug widely used in treating cardiovascular diseases, which shows advantages over other anti-anginal agents because it exhibits an anti-ischemic effect [1,2]. Unfortunately, its bioavailability is limited by its low aqueous solubility [3]. Moreover, there is scarcity of scientific results regarding the solid-state forms of RNL.

Within this framework, we investigated the polymorphism and the amorphization of RNL using both Single Crystal (SCXRD), Powder (PXRD) and Variable Temperature Powder (VT-PXRD) X-ray Diffraction and micro-tomography on different RNL preparations. All these techniques are available at the CRIST - Crystallographic Service Centre of the University of Florence.

Single crystals of RNL were produced by solvent evaporation from PEO-acetonitrile gel, allowing to solve the crystal structure for the first time. RNL crystallize in the monoclinic system, space group $P2_1/n$, with one molecule of RNL in the asymmetric unit and four molecules of RNL in the unit cell. The analysis of the packing structure shows that two molecules of RNL are linked by a hydrogen bond forming a dimer at the center of the unit cell. The formation of the dimer between the two adjacent, symmetry related, molecules can occur with two different intermolecular hydrogen bonds: N···H-O and O···H-O atoms. Each dimer is related to the adjacent by stacking interactions forming a zig-zag chain along the *c* axis.

RNL amorphous phases with T_g values lower than room temperature was obtained by cryo-milling and quench-cooling. New forms of RNL (II and III), were identified by PXRD from the relaxation of the ranolazine amorphous phase produced by cryo-milling, which takes place within several hours after grinding. At room temperature, these metastable polymorphs relax to the lower energy polymorph I, which correspond to the one obtained from SCXRD characterization. Finally, the thermal behavior of cryo-milled RNL sample was investigated by VT-XRPD experiments, which showed a partially amorphous material that increases crystallinity when subject to heating from 20 to 100 °C.

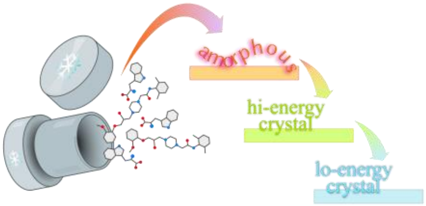

Figure 1. Relaxation process of RNL amorphous phase to lower energy polymorph I.

[1] L. Ren, X. Chen, B. Nie, H. Qu, J. Ju, Y. Bai, *Front. Mol. Biosci.* **2022**, *9*.
[2] E. Rayner-Hartley, T. Sedlak, *J. Am. Heart Assoc.* **2016**, *5*, e003196.
[3] D. R. Telange, S. A. Ukey, A. T. Hemke, M. J. Umekar, A. M. Pethe, P. S. Kharkar, *J. Pharm. Innov.* **2021**, *16* (4), 643–658.

Triggering the release of essential oil-based cocrystals

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Essential oil (EOs) 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 rule 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 crystallization to drive the release of EOs and control their availability. We here report several examples of cocrystals where the release of the active components is triggered by UV radiation. To this end, XRPD and Raman measurements were performed before and after the triggering and were compared between the individual conformer and its cocrystals. The release of each cocrystal was further tested by headspace–gas chromatography–mass spectrometry (GC–MS) analysis, evaluating different irradiation doses and the effectiveness of the treatment. Crystals structures were characterized through SCXRD and physical properties were opportunely described by calorimetric measurements (DSC, TGA).

Figure 1. Schematic view of cocrystal based on essential oils activated by UV radiation.

[1] M. B. Isman, *ACS Symp. Ser.* **2014**, *1172*, 21–30.

[2] P. P. Mazzeo, C. Carraro, A. Monica, D. Capucci, P. Pelagatti, F. Bianchi, S. Agazzi, M. Careri, A. Raio, M. Carta, F. Menicucci, M. Belli, M. Michelozzi, A. Bacchi, *ACS Sustain. Chem. Eng.* **2019**, *7*, 17929–17940

[3] F. Montisci, P. P. Mazzeo, C. Carraro, M. Prencipe, P. Pelagatti, F. Fornari, F. Bianchi, M. Careri, A. Bacchi, *ACS Sustain. Chem. Eng.* **2022**, *10*, 8388–8399.

Crystal structure of human serum albumin in complex with Alb1 Megabody

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In this work, we exploited the unique features of megabody (Mb), a small nanobody (Nb) grafted onto a large molecular weight protein scaffold, to determine the crystal structure of a Nb in complex with human serum albumin (hSA) and map their interactions. Previously proposed for Cryo-EM applications, here we have explored the versatility of Mb in the context of X-ray crystallography. The structure of hSA in complex with Mb has been determined at 3.3 Å maximum resolution. Interestingly, Mb revealed a unique hSA mode of binding, where the Nb contacts a conserved epitope located in a peripheral region of hSA domain II, not yet explored by any known hSA binders. Given the low nanomolar affinity and highly conserved nature of the contacted epitopes, Nb and its engineered versions display a reactivity toward mouse serum albumin, highly relevant for pharmacokinetic studies, as confirmed by means of yeast surface display studies. Furthermore, size exclusion chromatography experiments revealed that Mb can also recognize novel in silico designed hSA mutants. This result paves the road for the structural investigation of these hSA mutants, being their binding to Mb a feasible tool for promoting the formation of good quality crystals.

Symmetric and asymmetric dimers of the SARS-CoV-2 Main protease

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The SARS-CoV-2 Main protease (M^{pro}) is an essential enzyme for viral replication, and as such became immediately attractive as a drug target during the COVID-19 pandemic[1,2].

We produced and crystallized the double mutant H41A, C145A (M^{pro}DM) that is catalytically incompetent but structurally very similar to the wild-type M^{proWT}. We succesfully crystallized M^{pro}DM in *apo* condition and in co-crystallization with three 11-residues-long peptides corresponding to three endogenous recognition sites of M_{pro}. Additionally, we were able to obtain a crystal structure of M^{pro}DM with one of the aforementioned peptides by soaking.

The structures of M^{pro}DM in *apo* conditions and the one obtained by soaking were both in the *C2* spage group. In these structures, which are comparable to previous literature reports[3], only one molecule of M_{pro} is present in the asymmetric unit. As a consequence, the two molecules which constitute the dimer of M^{pro} are identical (symmetric dimer).

By contrast, the three structures obtained by co-crystallization in different spage groups all contained two molecules of M^{pro} per asymmetric unit, indicating that the two monomers are structurally different (asymmetric dimer). This finding is coherent with previous reports which indicate that M^{pro} is catalytically active with only one monomer at the time and that the binding on the active site on one monomer perturbs the other monomer[4]. Since the vast majority of the reported structures of M^{pro} with its peptide recognition sequences are obtained by soaking, we suggest that an important amount of information is lost whith this type of experiment. Details on the structures of the symmetric and asymmetric M^{pro} dimers will be presented and discussed during the presentation.

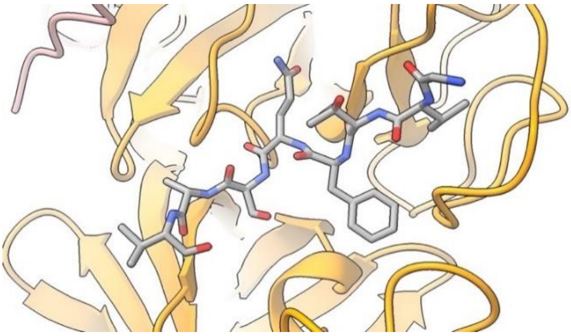

Figure 1. Peptide NSP5/6 in complex with M_{pro}DM.

[1] Jin, Z. *et al.* Structure of Mpro from SARS-CoV-2 and discovery of its inhibitors. *Nature* **582**, 289–293 (2020).

[2] Zhang, L. *et al.* Crystal structure of SARS-CoV-2 main protease provides a basis for design of improved α-ketoamide inhibitors. *Science* **368**, 409–412 (2020).

[3] Shaqra, A. M. *et al.* Defining the substrate envelope of SARS-CoV-2 main protease to predict and avoid drug resistance. *Nat Commun* **13**, 3556 (2022).

[4] Chen, H. *et al.* Only One Protomer Is Active in the Dimer of SARS 3C-like Proteinase *. *Journal of Biological Chemistry* **281**, 13894–13898 (2006).

Tuning the morphology of Nickel-tetraphenylporphyrin thin films

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The control on the growth of organic semiconductor thin films is one of the most intriguing challenges in the field of organic electronics, in view of understanding film properties and improving device performances. Many efforts have been devoted to the comprehension of the growth mechanisms [1,2], found to be highly dependent on the growth technique and the deposition conditions, in view of obtaining samples with a specific morphology and, therefore, desired properties. Among conjugated organic semiconducting systems, tetraphenylporphyrins (TPPs) are chosen for their potential in many technological fields, such as gas and chemical sensing, light harvesting or photocatalysis.

Here, we present a comparative study of Nickel-TPP thin films deposited, by means of Organic Molecular Beam Epitaxy, onto potassium acid phthalate (KAP) and highly oriented pyrolytic graphite (HOPG), following different growth protocols. The monitoring of film morphology performed ex-situ by Atomic Force Microscopy reveals the formation of nanoaggregates, in most cases accompanied by an evolution of the island structure from amorphous to crystalline. By properly adjusting the growth parameters, in particular increasing the substrate temperature and storing the sample in a controlled environment after the deposition, one crystalline stable phase can be selected and its structure and properties studied. In addition, when Nickel-TPP is deposited on KAP the selected crystalline phase is observed to display a precise orientation.

[1] L. Raimondo, S. Trabattoni and A. Sassella *Phys. Chem. Chem. Phys.*, **2019**, 21, 8482.
[2] A. Pancaldi, L. Raimondo, A. Minotto, and A. Sassella, *Langmuir*, **2023**, 39, 3266.

P6

Crystal structure and magnetic properties of a new mono-bridged binuclear copper (II) complex with amino-hydroxy-naphthalene ligand

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The design and synthesis of polynuclear covalently bridged transition metal complexes is of major interest in coordination chemistry. In particular, metal complexes of the first series containing bi- or tri-dentate ligands [1]. Such molecules are expected to exhibit peculiar magnetic features such as single-molecule magnetism (SMM), permanent magnetism, magnetic anisotropy, spin crossover (SCO) transition, paramagnetism and magnetic ordering [2,3].

Here we report a study on a binuclear copper complex of a polydentate amino-hydroxy-naphthalene ligand carried out by means of single-crystal X-ray diffraction (SC-XRD) method, Hirshfeld surface (HS) analysis and magnetic characterizations.

The copper complex crystallizes in the $P2_1/n$ space group and displays a unique mono-μ-X dimeric $[Cu_2(\mu\text{-}X)(L)_2(H_2O)_2]$ structural motif with two symmetrically non-equivalent Cu^{II} cations. Each Cu^{II} centre is penta-coordinate and adopts a distorted square-pyramidal geometry with the bridging polyanion, with a $Cu^{II}\cdots Cu^{II}$ distance of 4.72 Å.

The intermolecular interactions and their contributions to the crystal structure packing in the dimeric complex were verified and quantified through HS analysis. Indeed, the coordination moieties are linked by strong intermolecular C–H···O hydrogen bonds with 22.3% contribution to the total HS, in addition to moderate C—H···π (21.8%), and weak π···π (35.8%) stacking interactions to afford a 3D supramolecular network (see **Figure 1.a**).

The magnetic properties were investigated by temperature dependence magnetic susceptibility and magnetization measurements, performed in the direct-current (dc) mode over the *T*-range: 2–300 K. The $\chi_M \cdot T$ *vs* *T* plot, shown in **Fig.1.b**, has a curve shape characteristic of a weak antiferromagnetic coupling between Cu^{II} dimeric units [4] with a coupling constant $J = 0.83$ cm^{-1}. Further investigations are under way to explore the magnetic relaxation properties of the studied compound.

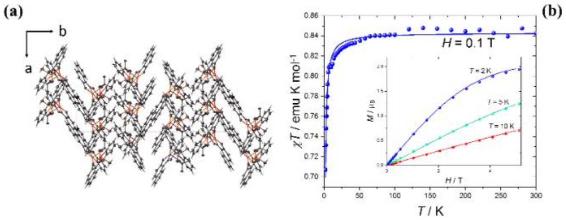

Figure 1. (a) View of the crystal packing down [001] and **(b)** temperature dependence of the $\chi_M \cdot T$ product of the $[Cu_2(\mu\text{-}X)(L)_2(H_2O)_2]$ complex. Inset of **(b)** shows low-temperature magnetization curves.

[1] J. Klingele, S. Dechert, F. Meyer *Coord. Chem. Rev.* **2009**, *253*, 21-22, 2698-2741.
[2] K.S. Murray *Eur. Inorg. Chem.* **2008**, *20*, 3101-3121.
[3] N. Motohiro, H. Oshio *Chem. Soc. Rev.* **2011**, *40*, 6, 3239-3248.
[4] M. Du, Y.M. Guo, X.H. Bu, J. Ribas, M. Monfort *New Jour. Chem.* **2002**, *26*(*7*), 939-945.

The high-resolution structure of the human Annexin IV: insight into calcium-binding sites

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The molecular mechanisms of how cancer cells promote their own survival and avoid apoptosis in response to commonly used chemotherapeutics are multiple and consist of a set of signaling pathways, which can be activated by a large number of stimuli to promote chemoresistance [1]. Chemoresistance is thus becoming a serious problem that cancer research seeks to understand and overcome.

In this context, Annexin IV (ANXA4) is an interesting oncoprotein being its overexpression involved in chemoresistance [2]. ANXA4 belongs to the family of annexins, a class of proteins that can bind calcium ions and phospholipids and contribute to biological processes such as endocytosis, exocytosis, cell division, apoptosis, and growth regulation [3, 4]

Recently, a chemoresistance model after paclitaxel treatment has been reported. In particular, in this model FHIT protein can bind and delocalize ANXA4 from plasma membrane to cytosol in paclitaxel-resistant lung cancer cells, thus restoring their chemosensitivity to the drug [5-7].

To gain structural insights into this process and of developing bioactive molecules able to modulate it, we have undertaken crystallographic studies on human ANXA4. The absence of literature reports on high resolution structure of human ANXA4 and some controversial indications on its calcium binding compared to the bovine counterpart prompted us to collect diffraction data on the crystal of this protein by using the Grenoble ESRF synchrotron radiation. Crystallographic structures obtained at different calcium concentrations provide a clear picture of the binding of calcium ions to the protein and of the role that flexible regions play in the recognition. Isothermal titration calorimetry (ITC) experiments corroborate our crystallographic data. Moreover, the analysis of the crystal structure unravels a network of contacts among charged arginine side chains, in line with the recently reported propensity of the guanidinium group to self-interact [8] (Ruggiero et al. in prep.).

[1] K. Bukowski, at al. *Int. J. Mol. Sci*. **2020**, 21, 3233.
[2] T. Mogami, et al. *PloS one* **2013**, 8, e80359.
[3] V. Gerke, et al. *Nat. Rev. Mol. Cel. Biol.* **2005**, 6, 449.
[4] S. Mussunoor, et al. *J. Pathol*. **2008**, 216, 131.
[5] E. Gaudio, et al. *Oncotarget* **2016**, 7, 29927.
[6] E. Gaudio, et al. *PloS one* **2013**, 8, e78610.
[7] M.C. Scala, et al. *Front. Mol. Biosci*. **2021**, 8, 715263.
[8] S. Cozzolino, *Int. J. Biol. Macromol.* **2020**, 163, 375.

Structural features of the highly effective anti-thrombin aptamer M08s-1

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DNA or RNA aptamers are extensively used to modulate the function of most of the factors involved in the coagulation pathway [1]. During the last decades, particular attention has been paid to the study of anticoagulant aptamers that are able to recognize human α-thrombin [2], the coagulation factor that maintains blood haemostasis by balancing procoagulant and anticoagulant actions. Among the anti-thrombin aptamers, the most studied are TBA, a 15mer oligonucleotide that adopts an antiparallel G-quadruplex structure [3], and the 26mer NU172, the only anti-thrombin aptamer evaluated in Phase II of clinical trials. The latter adopts a mixed structure formed by both a duplex and a quadruplex domain [4]. Recently, some of us selected, by using the MACE-SELEX approach, a new anti-thrombin DNA aptamer having a guanine-rich sequence of 43 nucleotides and showing an enhanced anticoagulant activity with respect to both TBA and NU172 [5].

Here we present the X-ray structure of the complex between thrombin and a truncated form of M08s-1 (named M08s-1_41mer, Figure 1), which provides a reasonable explanation of the improved properties of this oligonucleotide. The study of the interaction between M08s-1 and thrombin has been complemented by surface plasmon resonance and circular dichroism experiments. Furthermore, spectroscopic and electrophoretic analyses have been performed in order to investigate the conformational behaviour of this aptamer in the free state. Details will be discussed at the Meeting.

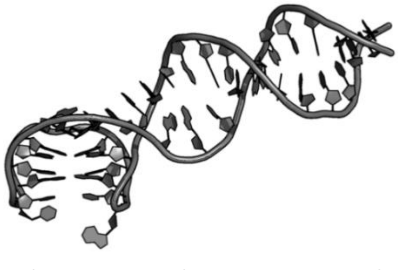

Figure 1. Cartoon representation of the structure of M08s-1_41mer as found in the crystal structure of its complex with thrombin.

[1] M. Liu, K. Zaman, Y.M. Fortenberry *Int. J. Mol. Sci.* **2021**, *22*, 3897.
[2] R. Troisi, N. Balasco, I. Autiero, L. Vitagliano, F. Sica *Int. J. Mol. Sci.* **2021**, *22*, 10803.
[3] I. Russo Krauss, A. Merlino, A. Randazzo, E. Novellino, L. Mazzarella, F. Sica *Nucleic Acids Res*. **2012**, *40*, 8119.
[4] R. Troisi, V. Napolitano, V. Spiridonova, I. Russo Krauss, F. Sica *Nucleic Acids Res*. **2018**, *46*, 12177.
[5] K. Wakui, T. Yoshitomi, A. Yamaguchi, M. Tsuchida, S. Saito, M. Shibukawa, H. Furusho, K. Yoshimoto *Mol. Ther. Nucleic Acids*. **2019**, *16*, 348.

Crystal structure and potential application of NAD(P)H Quinone Oxidoreductase (NQR) from *Arabidopsis thaliana*

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NAD(P)H quinone oxidoreductase (NQR) is a crucial enzyme involved in maintaining cellular redox balance and facilitating detoxification processes. It regulates redox signaling pathways, contributing to the generation and transmission of reactive oxygen species (ROS) signals [1]. The active enzyme is a flavoprotein which reduces short-chains quinones to hydroquinones by a two-electron reaction mechanism using nicotinamide cofactors [2]. By modulating the redox state of quinones, NQR exerts influence over various cellular responses, including gene expression, cell growth, and development [1]. Understanding the role of NQR in oxidative stress can provide insights into developing strategies to alleviate oxidative damage and maintain cellular health.

To contribute to this understanding, our work focuses on studying the structure of NAD(P)H quinone oxidoreductase from the land plant *Arabidopsis thaliana* (AtNQR) using X-ray crystallography. Notably, the structure of these enzyme is not present in Protein Data Bank (PDB). By obtaining crystals of AtNQR, we successfully determined its structure at a resolution of 1.9 Å. Analysis revealed that the monomer of AtNQR exhibits a catalytic site characterized by an α/β structure typical of flavoproteins, in which a central core consists of a β-sheet surrounded by 5 α-helices. The prosthetic group FMN is noncovalently bound to the protein and it is located at the interface between the two monomers forming the homotetramer corresponding to the quaternary structure of the protein (Figure 1). Within the binding site, the FMN phosphate group finds stabilization, while the flavin moiety remains exposed to the surrounding solvent. Moreover, considering the enzyme redox activity, we also tried to prepare a biocompatible film with antioxidant properties to potentially prevent or reduce cell damage in human skin. The films were prepared by solvent casting using carboxymethylcellulose (CMC) as soluble biopolymer and glycerol as humectant. The activity of AtNQR was evaluated showing good activity retention, even after some months.

Figure 1. Homotetrameric quaternary structure of AtNQR.

[1] Ross D, Siegel D. The diverse functionality of NQO1 and its roles in redox control. *Redox Biol.* **2021** May; 41:101950.

[2] Foster C, Bianchet M, Talalay P, Faig M, Amzel LM. Structures of mammalian cytosolic quinone reductases. *Free Radical Biology and Medicine*.Volume 29, Issues 3–4, **2000**

Characterization of homo- and heterodimer equilibria in human 14-3-3 ζ and ε isoform

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Human 14-3-3 proteins (h14-3-3s) are a highly conserved and ubiquitous family of seven proteins, named β, γ, ε, η, σ, τ, and ζ [1]. These proteins play a key role in a wide variety of signaling pathways, being involved in several functions, such as signal transduction, protein trafficking, metabolism, and regulation of apoptosis [2]. Among them, h14-3-3ζ is involved in the onset and progression of different human diseases, including various types of cancer, making it an attractive target for the development of novel anticancer treatments [3]. h14-3-3ζ exploits its function as homo- or heterodimer by binding to a huge number of different partner proteins in a phosphorylation-dependent manner [4]. To date, the structural characterization of h14-3-3ζ heterodimers and the comprehensive investigation of h14-3-3 dimerization equilibria are missing. Former studies on h14-3-3ζ have reported that Ser58, located at the dimer interface, plays a crucial role in the protein dimerization; indeed, the monomeric state is stably reached through its enzymatic phosphorylation by protein kinase A (PKA) [5]. To further investigate the role of this residue on h14-3-3ζ dimerization, two variants, S58E and S58A, have been generated and studied. The replacement of Ser58 with a glutamic acid has been studied as a phospho-mimic, whereas the variant S58A fully prevents phosphorylation at this site [5]. In this research project, the two h14-3-3ζ variants have been generated by site-directed mutagenesis and the stability of the protein quaternary assembly have been evaluated through size-exclusion chromatography and X-ray crystallography. The characterization of the protein assembly by size-exclusion chromatography has suggested that both variants adopt a dimeric structure, showing the same elution profile. The structures of both mutants have been determined and compared to that of wild type protein, also produced by us, highlighting a slight aperture of the S58E homodimer. On the other hand, no meaningful differences in the quaternary assembly have been observed in the S58A variant. A further purpose of this project was to attempt isolating the recombinant heterodimer formed by the ζ and ε isoforms. To pursue this objective, we have developed an innovative and reliable protocol for the co-expression and co-purification oh h14-3-3ζ/ε heterodimers and crystallization trials are ongoing. The results achieved by this work contribute to expand the current knowledge on h14-3-3ζ dimerization and its ability to heterodimerize with the ε isoform, giving new perspective to investigate the 14-3-3 homo/heterodimer equilibria and novel clues for the development of PPI modulators exploitable as anti-cancer treatments.

[1] Mhawech, P. 14-3-3 proteins--an update. *Cell Res.* **2005**, 15, 228–236.

[2] Masters, S. C. & Fu, H. 14-3-3 proteins mediate an essential anti-apoptotic signal. *J Biol Chem.* **2001**, 276, 45193–45200.

[3] Neal CL, Yu D. 14-3-3ζ as a prognostic marker and therapeutic target for cancer. *Expert Opin Ther Targets.* **2010**

[4] Aitken, A. 14-3-3 proteins: A historic overview. *Seminars in Cancer Biology* **2006**, 16, 162–172.

[5] Woodcock JM, Murphy J, Stomski FC, Berndt MC, Lopez AF. The dimeric versus monomeric status of 14-3-3zeta is controlled by phosphorylation of Ser58 at the dimer interface. *J Biol Chem.* **2003**

The European Research Infrastructures and the Italian PNRR - The Project *ITACA.SB*, Potentiating the Italian Capacity for Structural Biology Services in Instruct-ERIC

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European research infrastructures provide a plethora of experimental techniques and expertises open to the European scientific community. In the field of Life Science, Instruct-ERIC is an example of European distributed infrastructure that offers access to a wide palette of Structural Biology techniques, from the sample preparation all the way to the final structure (https://instruct-eric.org/). Access is on a peer-reviewed basis and those accepted can access to the infrastructure free of charge. Italy is a key member of Instruct-ERIC.

However, in order to access to Instruct-ERIC centers, users are required to provide robust and solid preliminary data – with instrumentations they often need to pay for. Such a short circuit makes prohibitive for many research groups to access to the above mentioned opportunities.

The project *ITACA.SB* (https://www.itaca-sb.it) aims at potentiating and implementing new facilities so as to provide the Italian Structural Biology community with methodologies to meet the high standard required. More in details, *ITACA.SB* will potentiate the sample production capacity with protocols specific to several complementary techniques and will offer free of charge access to new X-ray, cryo-EM, NMR, BioSAXS, and other biophysical instruments in order to evaluate the sample quality to successfully access to the European facilities. A centralized computing facility to ensure Structural Biology data storage, curation, and distribution (when appropriate) according to FAIR principles will be installed as well.

Finally, the project will contribute to the upgrade of the flagship NMR instrumentation at CERM/CIRMMP – Italian center of Instruct-ERIC – including the reduction of its carbon footprint.

Through *ITACA.SB* we expect to improve the ability of Italian researchers in Life Sciences to perform top-level research thereby improving the international visibility and appreciation of Italian research in general.

The project *"Potentiating the Italian Capacity for Structural Biology Services in Instruct-ERIC - ITACA.SB"* (Project no. IR0000009) within the call MUR 3264/2021 PNRR M4/C2/L3.1.1 is funded by the European Union NextGenerationEU

Interaction of the pharmacologically active $V^{IV}O$−Pyridinone drug with the model protein lysozyme

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Transition metals are the most widely used in the pharmaceutical industry [1,2]. Among those, vanadium has had a great appeal for the development of oxidovadium(IV) complexes with a medicinal potential. Vanadium compounds (VCs) show a wide range of pharmacological properties, including antiviral, antiparasitic, and antituberculosis activities, even if the most important application in medicine is for the treatment of cancer and diabetes [2,3]. However, vanadium-based drugs development is limited by the lack of knowledge on the formation of the active species in target organs. Indeed, the interaction of VCs active species with biological macromolecules such as proteins is of great importance for their pharmacological activity. Among the most promising VCs, the class of $V^{IV}O^{2+}$ complexes formed by pyridinone derivatives deserves to be mentioned [4]. In this work the binding of $[V^{IV}O(empp)_2]$ (where Hempp is 1-methyl-2-ethyl-3-hydroxy-4(1H)-pyridinone), an antidiabetic and anticancer VC, with the model protein hen egg white lysozyme (HEWL) was studied by X-ray crystallography coupled to electrospray ionization-mass spectrometry (ESI-MS), and electron paramagnetic resonance (EPR).

Crystallographic data, collected under three different experimental conditions (Figure 1), show covalent binding of $[V^{IV}O(empp)(H_2O)]^+$ to the side chain of Asp48, and noncovalent binding of *cis*-$[V^{IV}O(empp)_2(H_2O)]$, $[V^{IV}O(empp)(H_2O)]^+$, $[V^{IV}O(empp)(H_2O)_2]^+$, and of an unusual trinuclear oxidovanadium(V) complex, $[V^V{}_3O_6(empp)_3(H_2O)]$ with accessible sites on the protein surface. These results agreed with spectrometric/spectroscopic data and could open new perspectives in the understanding of the transport and mechanism of action of vanadium but also of metal-based drugs, promoting the development of new compounds as potential therapeutic agents.

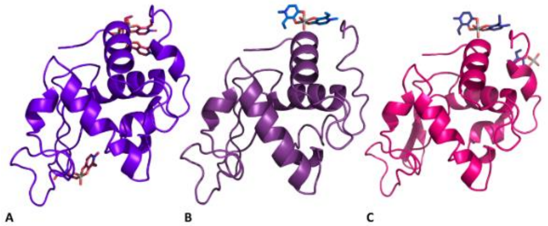

Figure 1. Overall structures of the adducts formed upon reaction of $[V^{IV}O(empp)_2]$ with HEWL under different experimental conditions: A) structure A; B) structure B; C) structure C.

[1] K. D Mjos, C. Orvig, *Chem. Rev*. **2014**, *114*, 4540−4563
[2] V.M. Miranda, *Rev. Inorg. Chem.* **2022**, *42*, 29-52
[3] J. Costa Pessoa, I. Tomaz, Curr. *Med. Chem.* **2010**, *17*, 3701-3738
[4] H. Sakurai, H. Yasui, Y. Adachi, *Expert Opin. Invest. Drugs* **2003**, *12*, 1189-1203

Natural Mn and V dioxides: structural details and HT transformations

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Mn and V are multivalent transition metals, forming a large number of different oxides. Interest for Mn and V has recently grown in relation to the increasing sensitivity to environmentally sustainable energy solutions. In fact, they have chemical-physical features making them suitable for use in many technological applications including catalysis, batteries, solar windows, supercapacitors. The need arises to characterize in detail the raw-materials extracted in mines and to explore their stability under high temperature conditions.

Ramsdellite and paramontroseite are natural Mn- and V-dioxides sharing the structural framework (S.G. *Pbnm*). The building unit is the metal-centered octahedron, wherein the atom is surrounded by four equatorial (O_{eq}) and two axial oxygens (O_{ax}). Each octahedron shares three edges with as many building units, and pairs of octahedral chains develop parallel to *z*. Double-chains are interconnected by sharing corners and originate channels, parallel to *z*.

The investigated *ramsdellite* [1] comes from Mistake Mine (Arizona) and shows a pure MnO_2 composition; it is found to be associated with its polymorph pyrolusite (MnO_2; rutile-type structure) and a small portion of groutellite ($(Mn^{4+}_{0.5}\,Mn^{3+}_{0.5})\,O_{1.5}\,(OH)_{0.5}$; ramsdellite structure). We explored the thermal range from 25 to 492 °C by *in situ* XRPD; at ~213 °C, groutellite disappears transforming into ramsdellite, as suggested by an increase of the latter. Such a transformation results from a combination of Mn-oxidation ($Mn^{3+} \rightarrow Mn^{4+}$) and O-H bond collapse (mobilization of H^+), as it is documented in a previous work. This reaction does not require recrystallization. The phase proportions change negligibly up to about 327 °C; beyond, one appreciates an increase of pyrolusite and at ~383 °C ramsdellite's diffraction peaks disappear, and an amorphous phase develops, into which ramsdellite has at least partially been converted. Our data show that the ramsdellite to pyrolusite transformation (well known in literature) takes place passing through an amorphous state followed by subsequent recrystallization [2]. The total transformation results in a balance of ramsdellite amorphization and pyrolusite crystallization; both reactions can be described with the "decelerator" model of the universal equation of solid-solid transformation at constant T. The activation energy values of the two reactions are comparable to one another (Ea= 167.7 and 146.5 kj/mol); conversely, the pre-exponential factors differ by two orders of magnitude ($A = 5.2 \times 10^{11}$ and 4.72×10^{9} min^{-1}). As a consequence, the reaction rate of pyrolusite crystallization is smaller than amorphization's, thus inducing an "accumulation" of amorphous phase.

The *paramontroseite* under study comes from Prachovice mine (Czech Republic). It contains a meaningfully amount of Fe and the average chemical formula is $V_{0.84}\,Fe_{0.19}\,Al_{0.03}\,O_2$. Single crystal XR data show that V and Fe are not vicariant of one another, as V occupies the octahedral site at (0.09 0.14 0.25), whereas Fe enters a tetrahedral site at (0.41 0.06 0.25), the latter expected to be empty in the ideal structure [3]. *In situ* XRPD data show that thermal expansion is anisotropic, leading to the following β coefficients: -2.0, 3.0, 0.8 and 1.8 $\times 10^{-5}$ °C^{-1} for *a*, *b*, *c* and *V*, respectively. At *T* higher than 350°C, V undergoes oxidation, from [4+] to [5+], and paramontroseite decomposes into Fe-tetrapolyvanadate ($Fe_2V_4O_{13}$) and V-pentoxide (V_2O_5). There is no evidence for the formation at high T of a rutile-type phase, as we observed for iso-structural ramsdellite MnO_2.

[1] N. Curetti, M. Merli, S. Capella, P. Benna, A. Pavese *Phys. Chem. Miner.* **2019**, *46*, 987-1002.
[2] N. Curetti, D. Bernasconi, P. Benna, G. Fiore, A. Pavese *Phys. Chem. Miner.* **2021**, *48*, 11.
[3] N. Curetti, A. Pavese *Eur. J. Miner.* **2023**, *35*, 373-382.

P14

High-pressure and phase transitions in dalyite, a Zr-silicate

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Dalyite, Sp. Gr. P (a = 7.37 Å, b = 7.73 Å, c = 6.91 Å, α = 106.2°, β = 111.5°, γ = 100.0°), is a rare potassium zirconium silicate, firstly discovered in pyroclastic sequences and later found in a limited variety of rocks, such as peralkaline granites and syenites, late-stage pegmatites, charoitites, lamproites, lamprophyres, fenites and carbonatites ([1] and references within). The chemical composition, physical properties, unit-cell parameters and diffraction data of dalyite were first provided by [2]. Dalyite, ideally K2ZrSi6O, is known to provide useful insides on the geochemical composition of magmatic systems and is an indicator of oversaturated K_2O systems. At ambient pressure, the crystal structure of dalyite consists in corrugated sheets of SiO_4 tetrahedra organized in distorted β-wollastonite chains, almost parallel to the (010) crystallographic plan. Such chains are connected one to the other by the O1 and O2 oxygens hinges forming 4-, 6- and 8-mRs rings, whereas the sheets are linked through Zr-octahedrons and irregular K/Na polyhedrons which forms complex pillar running along the [001] crystallographic direction. To date, the pressure and temperature stability range, and the thermodynamic parameters (namely the bulk modulus and its thermal expansion coefficient) of dalyite are still unknown. Here, we report the results of a high-pressure *in-situ* synchrotron X-ray single crystal experiment. Into details, we were able to: (*i*) identify two high-pressure polymorphs, named dalyite-II and -III (**Figure 1**); (*ii*) solve the crystal structure of dalyite-II and dalyite-III; (*iii*) obtain the elastic parameters of dalyite and its high-pressure polymorphs by fitting with Birch-Murnaghan equation-of-state and (*iv*) describe the high-pressure deformation mechanisms in dalyite and its high-pressure polymorphs.

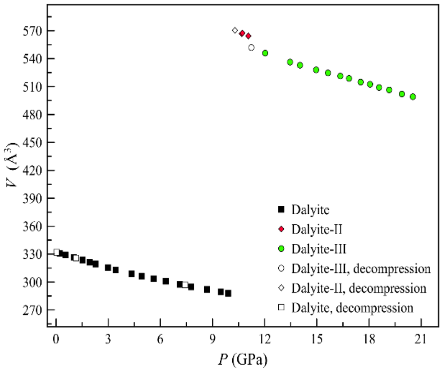

Figure 1. Evolution of the normalized unit-cell volume of dalyite with pressure: dalyite in *black squares*, *dalyite-II* in *red diamonds, dalyite-III in green spheres*. Empty symbols: decompression data.

[1] A.J. Jeffery, R. Gertisser, R.A Jackson., et al *Mineral Mag*, **2016**, *80*, 547–565.

Understanding the electrochemical features of $ZnFe_2O_4$, as anode for LIBs, by multiple physical-chemical techniques

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The search for new anode materials for lithium-ion batteries (LIBs) is a hot topic thrilling the researchers. $ZnFe_2O_4$ (ZFO) is a cubic spinel, with peculiar functional properties for various applications [1] that was proposed for the first time in 2004 as anode for LIBs [2]. ZFO, unlike other oxides, has a lithium insertion mechanism that involves both conversion and alloying reactions, so providing high capacity. After the conversion reaction of ZFO with lithium ions and the formation of metallic Zn, Fe, and Li_2O, the obtained Zn can further react with lithium to form a LixZn alloy, thus contributing additional capacity. The most intriguing ZFO characteristics are its low cost, abundance and environmental friendliness of both Zn and Fe elements, high surface-to-volume ratio, relatively short path for Li-ion diffusion, low working voltage of about 1.5 V for lithium extraction and, most importantly, high theoretical specific capacity (1072 mA h g^{-1}). Its drawbacks are represented by a first-cycle irreversibility and fast decay in the capacity after cycling, mainly due to poor electrical conductivity and large volumetric changes. To improve the electrochemical performances, it is mandatory to deeply known its physical-chemical properties. In this work, ZFO was prepared by co-precipitation (CP) and template (OX) syntheses, obtaining samples with different morphologies and crystallite sizes (Fig. 1). The sample purity was demonstrated by combining X-ray powder diffraction with more sensitive techniques such as Micro-Raman, Electron Paramagnetic Resonance and Mössbauer spectroscopies. In both samples, a high purity level was demonstrated, with only traces of hematite in the OX one. The electrochemical features were interpreted on the basis of the determined physical-chemical features, by using conventional electrochemical measurements, but also *operando* X-ray diffraction experiments.

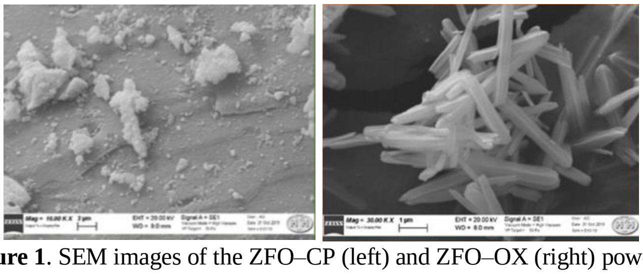

Figure 1. SEM images of the ZFO–CP (left) and ZFO–OX (right) powders

The higher electrode area of ZFO-OX with smaller particles is responsible for the better electrochemical reactivity in the first cycles but, in the long term, a lower crystallinity of active material, leading to nano-crystalline reaction products, could produce a better reversibility.

[1] G. Gazzola et al. *Mat. Chem.Phys.* **2021**, *273*, 125069.
[2] M. Bini et al. *Appl. Sci.* **2021**, *11*, 11713

Structural investigation of high pressure intrusion of ternary aqueous solution in pure silica chabazite

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Heterogeneous lyophobic systems (HLS), *i.e.* systems composed by a nanoporous solid and a nonwetting liquid, have attracted much attention as promising candidates for innovative mechanical energy storage and dissipation devices [1]. In these systems, mechanical energy (*i.e.* an external pressure) is required to force the intrusion of a non-wetting liquid into the pores of material. The penetration of the liquid inside the pores strongly increases the liquid-solid interface area leading to a conversion of mechanical energy into the breaking of intermolecular bonds of the liquid. When the external pressure is released, the liquid can be extruded, completely or partially, or can remain trapped into the solid. Therefore, the whole or a part of the initial energy is restored, or it is entirely absorbed. Consequently, the system can display a *spring* or *shock absorber* or *bumper* behaviour or a combination of them.

In this work a new HLS based on a pure silica chabazite and a ternary electrolyte solution ($KCl+CaCl_2$) is studied from porosimetric and crystallographic point of view. The combined approach of this study is fundamental to unravel the properties of the system, in fact thanks to porosimetric experiments it has been possible to determine the energetic behavior, while HP *in-situ* crystallographic analyses will help in the understanding of the mechanism of intrusion involved and ruling the phenomenon.

The results are compared with those obtained for the systems involving the same zeolite but intruded with solution containing only single salts ($CaCl_2$ or KCl). Porosimetric results of the three Si-CHA systems intruded by simple and complex electrolyte solutions (KCl 2M, $CaCl_2$ 2M and the mixture KCl 1M + $CaCl_2$ 1M) suggest that the intrusion pressure is mainly influenced by the nature of the cations. Indeed, $CaCl_2$ 2M shows the highest intrusion pressure, KCl 2M the lowest one whereas the mixture KCl 1M + $CaCl_2$ 1M is almost in the middle. These differences are probably related to the higher hydration enthalpy and Gibbs energy of Ca^{2+} compared to the one of K^+. In fact, it has been demonstrated that a partial ion desolvation is needed to promote the penetration of the species and a higher solvation energy requires higher pressure. The “intermediate value” of the intrusion pressure, shown by the complex electrolyte solution, arises from the fact that, statistically, the second/third solvation cation shells can be assumed to be partially shared between K^+ and Ca^{2+}. The stronger interaction of Ca^{2+} with H_2O molecules influences thus also the desolvation of K^+ increasing the pressure needed to activate the process compared to the one of the pure KCl 2M solution. This is confirmed by structural investigation, which shows that at the beginning of intrusion only K^+, Cl^- and H_2O penetrates the pores, whereas the intrusion of also Ca^{2+} required higher pressure in agreement with the hydration enthalpies of the two cations.

[1]. A. Eroshenko, *Entropie*, **1997**, *202/203*, 110.

High-pressure behaviour of jadarite: a promising lithium-boron natural commodity

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Over the past few decades, there has been a significant increase in global demand for lithium, driven by the growing need for advanced power storage systems (e.g., lithium-ion batteries) and electric devices (e.g., smartphone, tablets, electric vehicles). In this context, the discovery of jadarite, a mineral species found in the Jadar Basin, Serbia, has raised considerable attention. Jadarite, with an ideal chemical formula of $LiNaSiB_3O_7(OH)$ and space group $P2_1/c$, could become a valuable commodity, being both a Li- and B-bearing mineral, two elements listed as "critical" by the EU Commission [1]. One of the distinctive features of jadarite, from a marketable standpoint, is its remarkably high content of Li (~7.3 wt% Li_2O) and B (~47.2 wt% B_2O_3). Moreover, recent estimates have revealed the presence of a massive 1.5 Mt ore-deposit of jadarite in the Jadar basin, indicating the potential for future exploitation of this mineral [2]. Despite its significance, no experimental studies have been conducted on jadarite under non-ambient conditions. In addition, its crystal structure was investigated by X-ray powder diffraction only.

In this study, we present a comprehensive investigation of the crystal structure of jadarite using single-crystal synchrotron X-ray diffraction data. Additionally, we examine its compressional behavior under hydrostatic conditions, up to P=20 GPa. Notably, our findings reveal that jadarite undergoes a reconstructive, first-order, iso-symmetric phase transition between 16.57(5) and 17.04(5) GPa. This phase transition, characterized by a volume change of approximately 3%, primarily involves a rearrangement of the Li- and Na-coordination environments within the crystal structure. Furthermore, we provide an analysis of the elastic properties of jadarite, leading to a refined bulk modulus of 55.0(5) GPa (with a K_V' value of 3.84(9)). These results contribute to a better understanding of the behavior of jadarite under extreme pressure conditions and improve the thermodynamic database of hydrated borates.

[1] Whitfield PS, LePage Y, Grice JD, Stanley CJ, Jones GC, Rumsey MS, etal. *Acta Crystallogr Sect B.* **2007,** *63,* 396–401
[2] Vikström H, Davidsson S, Höök M. *Appl Energy*. **2013,** *110,* 252–66

The anomalous high-pressure phase transition of inderite, $MgB_3O_3(OH)_5{\cdot}5H_2O$

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Inderite, ideally [$MgB_3O_3(OH)_5{\cdot}5H_2O$], is a hydrated borate discovered in the Inder deposit (Kazakhstan) in 1937 and structurally characterized for the first time by Boldyreva [1]. Inderite is a Na-free hydrated borate and, unlike others common Na-bearing minerals like ulexite ($NaCaB_5O_6(OH)_6{\cdot}5H_2O$) or borax ($Na_2B_4O_5(OH)_4{\cdot}8H_2O$). Therefore, inderite would not promote any deleterious Alcali-Silica Reactions (ASR, triggered by Na-bearing phases), if used as an aggregate in Portland cements. In the last years, phase transitions occurring at different pressures were discovered in a plethora of hydrous borates, including kurnakovite and meyerhofferrite [2,3] which share the same polyion unit $[B_3O_3(OH)_5]^{2-}$. The high-pressure stability field of this kind of hydrated borates, having polyions in isolated units, appears to be directly correlated with the total H_2O content of the mineral itself. In this light, the high-pressure behaviour of inderite was investigated by an *in-situ* single-crystal X-ray diffraction (up to 17.4 GPa) under hydrostatic conditions. Results show: 1) inderite undergoes a first order phase transition between ~6.15 and ~6.45 GPa marked by a sudden 7.0 % volume decrease; 2) the structure of the high-pressure polymorph, inderite-II, was solved (Fig. 1); 3) as response to the phase transition, the boron site in planar-triangular coordination bonds to a H_2O molecule, forming a tetrahedron; 4) inderite was found to be a highly anisotropic mineral.

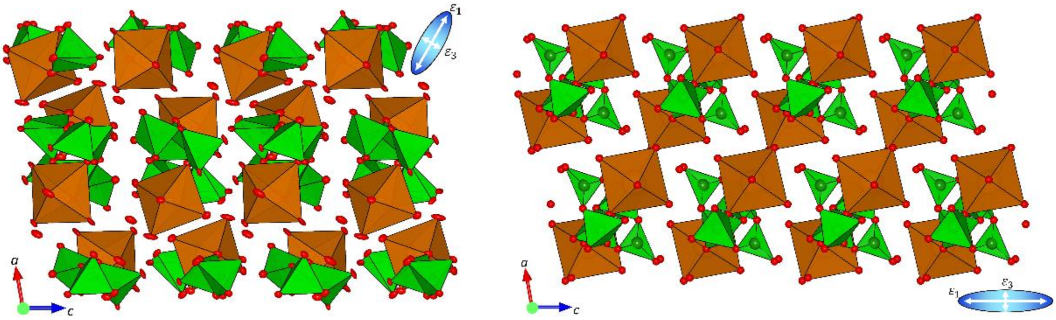

Figure 1. Low (left) and (high) pressure polymorph of inderite viewed along the [010] crystallographic direction

[1] Boldyreva A.M. *Mem Soc russe Min*, **1937**, *2*, 651–671
[2] Comboni D., Poreba T., Pagliaro F., et al. *Acta Crystallographica Section B*, **2021**, *6*, 940-945.
[3] Pagliaro F., Lotti P., Battiston T., et al. *Construction and Building Materials*, **2021,** 121094.

Elastic geobarometry applied to omphacite: a Raman spectroscopy approach

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The widespread occurrence of omphacitic clinopyroxenes (a solid solution of jadeite, augite and aegirine, with the general chemical formula $(Ca,Na)(Mg,Fe^{2+},Al,Fe^{3+})Si_2O_6$ in several geological settings and rock-types (e.g. high pressure eclogites, mantle xenoliths etc.), make them attractive to be exploited for Raman elastic geothermobarometry applications. Raman elastic geobarometry uses the deformation recorded by a mineral inclusion trapped in its host to retrieve the pressure and temperature conditions at which the inclusion has been entrapped [1], because Raman scattering is very sensitive to structural deformations in crystal structures developed upon heating or compression. Several host-inclusion systems have been studied so far, but clinopyroxene inclusions have not been thoroughly investigated yet. Therefore, the application of Raman elastic geobarometry to omphacites in various mineral hosts requires an accurate calibration of the Raman-peak positions against hydrostatic pressure. However, the Raman-peak positions and their pressure evolution depend also on the chemical composition. Besides, natural omphacite crystals can show a significant degree of cationic order related to the crystallization temperature, which can also affect the elastic behavior of omphacite.

To give an insight into the relation between the chemical order and pressure dependence of atomic dynamics, we have studied by in situ high-pressure Raman spectroscopy a series of crystals of omphacite from Münchberg Massif, Bavaria, Germany (peak conditions $P > 2$ GPa, $T = 600\text{-}650$ °C; [2]). The samples were free of iron, with compositions ranging between $Jd_{45}Di_{55}$ and $Jd_{52}Di_{48}$ and various degrees of cationic order achieved via isothermal annealing at different temperatures and for different times. We show that the pressure dependence of the wavenumber of the strongest Raman peak near 680 cm^{-1} is insensitive to the degree of chemical order, whereas the width of the same peak increases with cationic disorder and thus is indirectly related to closure temperature. To better understand the elastic behavior of the modes best suitable for elastic geobarometry, the Raman spectrum of a completely ordered omphacite of composition $Jd_{50}Di_{50}$, has been simulated at variable pressures with *ab initio* Hartree-Fock/Density Functional Theory simulations and compared with experimental spectra. The calculated data resulted to be in a good agreement with experiments and allowed us to understand changes in the pressure dependence of some modes. The experimentally obtained wavenumber-against-pressure trends can be potentially used to estimate the entrapment pressure of omphacite inclusions, assuming that they have the same chemical composition as the samples studied here. The dependence of Raman shifts on composition is planned as future work.

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[1] R.J. Angel, M.Murri, B. Mihailova, M. Alvaro *Z Kristallogr Cryst Mater*. **2019**, *234(2)*, 129-140.
[2] P.J. O’Brien *Lithos.* **1997**, *41*, 119-133.

Nanotopography and nanospectroscopy of the chlorite surface

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Nanotopography and nanospectroscopy at the surface of minerals and materials can be obtained and derived by using Scanning Probe Microscopy (SPM) methodologies. In the present work, we employed SPM to acquire simultaneously both the surface nanotopography and specific nanospectroscopic information of cleaved chlorite samples. More specifically, we measured the thickness of the TOT and brucite-like layers and correlated their topography with the specific electrostatic surface potential.

The use of spatially resolved techniques to characterize the local chemical and physical properties of mineral surfaces is of paramount importance to know their reactivity to the surrounding environment. Besides surface morphology, nowadays, recent advancements of Scanning Probe Microscopy have made available a wide range of surface investigations at the nanoscale. These include for example mechanical, rheological, magnetic and electrical properties of the surface. As mentioned, in the present work specific SPM-based methods for surface potential nanocharacterization of mineral surfaces have been developed and applied to chlorites. The interaction of micro and nanoparticles between themselves and with extended surfaces is driven by several forces, among which for instance, adhesion, hydrophilicity/hydrophobicity, magnetic forces and surface-related electrostatic potential. Chlorite is a well-suited mineral standard for surface electrostatic potential studies because it is a layer silicate where a positively charged octahedral brucite-like layer, about 0.4 nanometer thick, is sandwiched between two negatively charged TOT layers by means of weak electrostatic forces [1]. In the present work, the SPM observations were conducted at RT (22°C), atmospheric pressure and relative humidity of about 40%. After cleavage, chlorite presented simultaneously on the same specimen surface zones of brucite-like layer and zones of siloxane with lateral sizes ranging from a few nanometer to microns. TOT layers were found negatively charged, whereas brucite-like layers were found positively charged with a potential difference ranging between 100-500 mV, depending on the surface crystal chemistry and the environmental conditions.

[1] D. Moro, G. Ulian, G. Valdrè *Journal of Microscopy*. **2020**, *280(3)*, 204-221.

P21

Synthesis and characterization of complexes of Bismuth(III) as novel urease inhibitors

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Antimicrobial resistance poses an escalating danger to human health, steadily growing in its threat [1]. Metal complexes, especially those incorporating bismuth, present an appealing substitute to commonly employed organic compounds, for which bacteria resistance is frequently observed. Bismuth-based complexes have a long history of use in medicine, dating back to the late 18th century. One of these preparations, Pepto-Bismol (bismuth subsalicylate, BSS), is still used to treat H. Pylori infections. Its bactericidal activity is attributed to the inhibition of urease activity carried out by Bi(III) [2]. The capability of bismuth to inhibit urease is also of interest for the agrochemical field, where the enzyme operates within the nitrogen cycle; however, the use of bismuth complexes in this field is prevented by their poor water solubility, which limits their environmental availability [3].

In this context, crystal engineering can play a significant role in paving new ways to sustainably synthesize novel soluble coordination complexes of Bi(III). By exploiting sustainable synthetic methodologies, such as mechanochemistry, crystal engineering can guide solid-state modifications, allowing the preparation of new chemicals with improved physical-chemical properties in a green fashion [4]. Novel bismuth complexes have thus been prepared using GRAS as organic ligands and in the form of heterobimetallic systems. Solid state characterization has been performed via XRD and thermal analysis (DSC and TGA). Solubility and inhibition activity toward Jack Bean Urease have been tested. An intriguing case of ambiguous structural solution via powder diffraction concerning [Bi(Hedta)(DL-Histidine)]2H_2O has also been investigated.

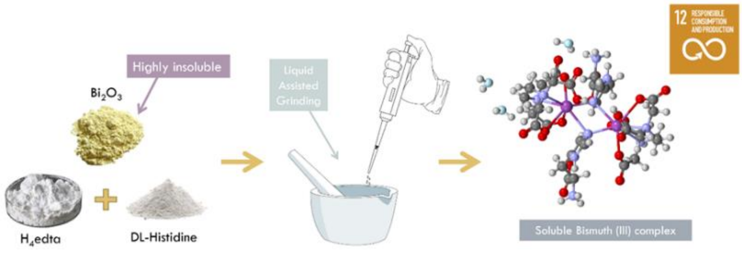

Figure 1. Synthesis of soluble Bi(III) based complexes via Liquid Assisted Grinding (LAG).

[1] Ferri, M.; Ranucci, E.; Romagnoli, P.; Giaccone, V. Antimicrobial Resistance: A Global Emerging Threat to Public Health Systems. *Critical Reviews in Food Science and Nutrition* **2017**, *57*, 2857–2876.
[2] Zhang, L.; Mulrooney, S. B.; Leung, A. F. K.; Zeng, Y.; Ko, B. B. C.; Hausinger, R. P.; Sun, H. Inhibition of Urease by Bismuth(III): Implications for the Mechanism of Action of Bismuth Drugs. *BioMetals* **2006**, *19*, 503–511.
[3] Keogan, D. M.; Griffith, D. M. Current and Potential Applications of Bismuth-Based Drugs. *Molecules* **2014**, *19*, 15258.
[4] Grepioni, F.; Casali, L.; Fiore, C.; Mazzei, L.; Sun, R.; Shemchuk, O.; Braga, D. Steps towards a Nature Inspired Inorganic Crystal Engineering. *Dalton Transactions* **2022**, *51*, 7390–7400.

Production and characterization of metal substituted human Carbonic Anhydrase II for artificial photosynthesis

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According to recent evaluations, the increasing exploitation of fossil fuels for energy production is strictly linked to increased CO_2 release into the atmosphere, with climate change as the main consequence [1]. Natural photosynthesis inspired the development of artificial systems to convert solar energy into chemical energy. Artificial photosynthesis (AP) might lead to more sustainable energy production based on light-driven water splitting, thereby reducing emission of not-polluting gases (O_2 and H_2) [2]. The present project aims at developing and optimizing novel biological catalysts for their application in AP.

Human carbonic anhydrase II (hCAII) is a ubiquitous enzyme catalysing the reversible hydration/dehydration of carbon dioxide/bicarbonate [3]. Zn(II) is an essential cofactor, in the process, and is present in the active site of the protein. Various groups reported that its substitution with different metal ions (e.g., Co, Ni, Fe) retains catalytic activity [4]. Others used different metals to modify the type of the reaction catalysed by hCAII. The most interesting for this project is Ir(III) which displays water splitting capabilities.

This project aims to screen the effect of metal and further optimization to exploit Ir(III)-substituted hCAII to efficiently produce O_2 from H_2O [5].
So far, the gene encoding for hCAII, has been used to express the recombinant enzyme in E. coli, and the active protein was obtained from multiple chromatographic stages (direct and reverse affinity, and size exclusion). To remove Zn from the active site, various chelating agents were tested and crystals of the apo- and of various metal-substituted forms were obtained, all of which diffracting X-rays to high resolution. We are now analysing the structural effect of the various metals and testing their water splitting activity. Based on the results, we expect to optimize the enzyme, increasing the turnover of oxygen production and its long-term stability, making it suitable for large scale application.

[1] Peters, G. P.; Andrew, R. M.; Canadell, J. G.; Friedlingstein, P.; Jackson, R. B.; Korsbakken, J. I.; Le Quéré, C.; Peregon, A. *Nat. Clim. Change* **2020**, *10*, 3−6.
[2] Andreiadis, E. S.; Chavarot-Kerlidou, M.; Fontecave, M.; Artero, V. *Photochem. Photobiol.* **2011**, *87*, 946–964
[3] Krishnamurthy, V. M., Kaufman, G. K., Urbach, A. R., Gitlin, I., Gudiksen, K. L., Weibel, D. B., and Whitesides, G. M. Chem. Rev, **2008**, *108*, 946–1051
[4]. Bertini I, Luchinat C, Scozzafava A. Structure and Bonding **1982**, 48, 45–92.
[5] Kim, M. C.; Lee, S. Y. *Chem. - An Asian J.* **2018**, *13*, 334–341.

New materials by mechanochemistry on calcium carbonate from waste seashells

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Amorphous calcium carbonate (ACC) and low crystallinity calcium carbonate ($CaCO_3$) are materials of increasing technological interest. Nowadays, ACC is mainly synthetically produced by wet reactions starting from calcium and carbonate reactants in the presence of stabilizers [1]. Recently, it has been discovered a sustainable and green alternative to produce ACC by ball milling calcite [2,3]. Calcite and/or aragonite are the mineral phases of mollusk shells, which formed from ACC precursors [4-6]. Here we investigated the possibility to convert, on a potentially industrial scale, the biogenic $CaCO_3$ (bCC) from waste mollusk shells in ACC and low crystallinity $CaCO_3$. For this aim the shells from aquaculture species, namely the oyster (*Crassostrea gigas*, low Mg-calcite), the scallop (*Pecten jacobaeus*, medium Mg-calcite) and the clam (*Chamelea gallina*, aragonite) were used. The ball milling process was optimized exploring the use of previously reported dispersing agents and ACC stabilizers. The obtained materials have been mainly characterized by powder X-ray diffraction, high-resolution electron microscopies, selected area electron diffraction, granulometry, infrared spectroscopy, induced coupled plasma and thermo-gravimetrical analysis. The results showed that the amorphization process occurs by a reduction of the crystalline domain sizes up to the nano-meter scale and the parallel formation of ACC domains. These two entities co-exist in micro-sized aggregates. Interestingly, such bCC behaves differently from the geogenic $CaCO_3$ and upon long milling times (24 h) the ACC reconverts in crystalline phases. The aging in diverse environments of amorphized bCC produced a mixture of calcite and aragonite in a species-specific mass ratio, while the amorphized geogenic $CaCO_3$ produced only calcite. In conclusion, this research showed that the use of bCC offers the possibility to obtain ACC and low crystallinity $CaCO_3$ having species-specific features. This is particularly relevant when $CaCO_3$ materials with diverse chemical and physical features are requested.

[1] K. Lee, W. et al. Self-assembly of amorphous calcium carbonate microlens arrays, *Nat. Commun.* **2012**, *3,* 725.

[2] H.J. Fecht, E. Hellstern, Z. Fu, W.L. Johnson, Nanocrystalline metals prepared by high-energy ball milling, *Metall. Trans. A.* **1990**, *2333*, 2337.

[3] A.W. Weeber, H. Bakker, Amorphization by ball milling. A review, *Phys. B Condens. Matter.* **1988**, *93*, 135.

[4] G. Magnabosco. et al. New material perspective for waste seashells by covalent functionalization, *ACS Sustain. Chem. Eng.* **2021** *6203,* 6208.

[5] L. Addadi, S. Weiner, Biomineralization: Mineral formation by organisms, *Phys. Scr.* **2014**, 098003.

[6] H. Pesenti, M. Leoni, P. Scardi, XRD line profile analysis of calcite powders produced by high energy milling, *Zeitschrift Fur Krist. Suppl.* **2008**, *143,* 150.

Oxidized β-chitin hydrogel

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Chitin has attracted great interest in the scientific and technological community due to its massive abundance in nature and the chemical features which makes it a potential material among others for the preparation of hydrogels.

In nature chitin, the polymer of the 1,4-N-acetyl-D-glucosamine, has crystalline domains in three polymorphs: α, β, and ɣ, which differ for the arrangement of the polymer chains that are anti-parallel, parallel, and alternating, respectively.(1) The strong intra- and inter-molecular hydrogen bonds among the polymeric chains make chitin insoluble in both conventional organic solvents and water, representing a relevant challenge for the production of hydrogels. (2)

In our research, we successfully optimized the oxidation reaction of the two most common chitin polymorphs (α and β) with the aim to preserve their crystalline structure and obtain water-soluble fibers.

Initially, the micronization of starting material was performed by grinding with a ball mill and the optimal condition was defined having the goal to obtain the smallest particles that preserved as much as possible the starting material's crystallinity. This was done by comparing the FWHM of the main peaks in diffractograms of the obtained powders. The particle size between 600 and 150 µm was chosen.

This chitin powder was oxidized by reaction with a 45 wt.% ammonium persulfate solution at different times. β-chitin reacted for 3, 6, 9 or 24 hours, while for α-chitin 9, 24, 48 or 120 hours. The choice of the best reaction time was done according with FTIR, XRD and solid-state NMR analyses, compromizing between the crystallinity and the yield of oxidation. β-chitin gave the best reaction product after 24 hours of reaction.

Under these reaction conditions, a β-chitin powder with about 10% functionalization is obtained. This oxidized chitin, when redispersed in water, leads to the formation of transparent hydrogels. The hydrogel obtained has properties that can be modulated based on the pH and the addition of ions capable of coordinating the charge of the carboxyls obtained (Ca^{2+}). These properties have been confirmed by preliminary rheological tests.

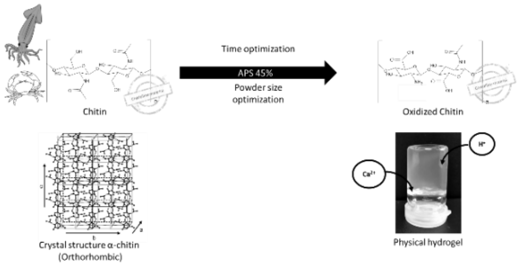

Figure 1. Oxidation reaction of chitin and the obtained physical hydrogel.

[1] Ahmad, S. I., Ahmad, R., Khan, M. S., Kant, R., Shahid, S., Gautam, L., ... & Hassan, M. I. Chitin and its derivatives: Structural properties and biomedical applications. *International Journal of Biological Macromolecules*, **2020**, *164*, 526-539.

[2] Liu, L., Wang, R., Yu, J., Jiang, J., Zheng, K., Hu, L., ... & Fan, Y. Robust self-standing chitin nanofiber/nanowhisker hydrogels with designed surface charges and ultralow mass content via gas phase coagulation. *Biomacromolecules,* **2016**, *17*, 3773-3781.

The crystal structure of asbestiform erionite from New Zealand

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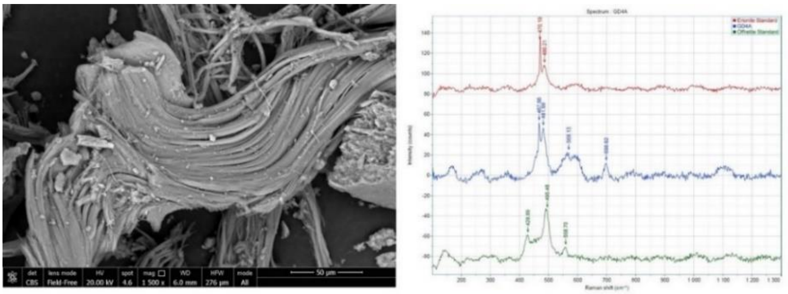
Erionite is a widespread natural zeolite originating from sedimentary or hydrothermal alteration of volcanic rocks. The crystalline habit is extremely variable (prismatic, acicular, needles, rods, fibrous, fibers, hair-like, woolly, bundles, radiating clusters … [1]). The erionite ideal chemical formula is $K_2(Ca_{0.5},Na)_7[Al_9Si_{27}O_{72}]\cdot 28H_2O$ [2]. The symmetry is hexagonal with S.G. $P6_3/mmc$ and unit-cell parameters a ~13.15 Å, c ~15.05 Å. Like asbestos, inhalation of asbestiform erionite may cause malignant mesothelioma. The International Agency for Research on Cancer (IARC) has classified erionite as a Group 1 carcinogen [3,4]. In this scenario, research related to the characterization of erionite has become increasingly important [5]. Our work describes the crystal chemistry of an asbestiform erionite from Gawler Downs, New Zealand using a multi-analytical approach. The crystal habit of this erionite sample is asbestiform (Figure 1a). The measured external surface area is 20.6 m^2/g and an amount of zeolitic water of 17.7 wt%. The formula calculated by EPMA is $K_{2.63}Ca_{1.27}Na_{0.37}Ba_{0.03}Sr_{0.01}[Al_{7.6}Si_{28.43}O_{72}]\cdot 29.07H_2O$. Micro-Raman data (Figure 1b) confirmed that the fibres are erionite and not offretite.



(a) (b)

Figure 1. Asbestiform shape of the erionite from Gawler Downs, New Zealand as observed by FEG-SEM (a) and micro-Raman data (b) that confirm its crystal-chemical classification as erionite.

The toxicity/pathogenicity potential of this mineral fibre has been predicted from its crystal-chemical-physical parameters.

[1] M. Giordani, M. Mattioli, M. Dogan, A.U. Dogan. *Journal of Toxicology and Environmental Health, Part A*. **2016**, *79(18)*, 808-824.
[2] E. Passaglia, R.A. Sheppard. *Reviews in mineralogy and geochemistry*. **2001**, *45(1)*, 69-116.
[3] IARC. **1997**, *42*, 225–239.
[4] B.S. Van Gosen, T.A. Blitz, G.S. Plumlee, G.P. Meeker, M.P. Pierson. *Environmental Geochemistry and Health*. **2013**, *35(4)*, 419-430.
[5] J. Patel, M. Brook, D. Di Giuseppe, V. Scognamiglio, A.F. Gualtieri, *EGU General Assembly Conference Abstracts*. **2012**, EGU21-13686.

Chromium diffusion in synthetic $MgAl_2O_4$ spinel at High Temperature and High Pressure conditions

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Minerals belonging to spinel supergroup are cubic (*Fd3m* space group), highly refractory phases occurring not only in the Earth's deep interior, but also in the outer space where they constitute stardust material. Their general formula is AB_2X_4, where A and B are cations in tetrahedral and octahedral coordination, respectively, and X is commonly represented by O (and minorly by S and Se).

The $MgAl_2O_4$ spinel is extensively recorded in circumstellar dust grains, while Cr represents the most abundant transition metal in cosmic systems and its incorporation into the spinel structure is extremely easy through Cr-Al solid state interdiffusion. Consequently, the cationic substitution Cr-Al is of interest in mineralogy, astromineralogy and even materials science.

In this work, a solid-state diffusion model for Cr in the $MgAl_2O_4$ spinel is provided, paying particular attention to the diffusion interface details and surface defects. Diffusion experiments were performed on synthetic single crystals of $MgAl_2O_4$ spinel [1, 2, 3] immersed in Cr_2O_3 powder at 2 GPa and 1100-1250 °C.

To obtain a detailed picture of the diffusion process and the local phenomena induced at micro- and nanoscale, both crystal core and diffusion interface were studied with a multi-analytical approach. Images were acquired with *Scanning Electron Microscopy* (SEM), chemical composition was analyzed with SEM/EDS and *Electron MicroProbe* (EMP), structural information was obtained through *Electron BackScatter Diffraction* (EBSD), and surface topography of an untreated $MgAl_2O_4$ crystal was studied with the *Atomic Force Microscopy* (AFM) to check if and how the pre-existing surface defects could have affected the diffusion process.

The Cr abundance trend is markedly decreasing inwards, showing a downfall after a few microns; nonetheless the maximum penetration of Cr inside spinel is about 50 µm for the run at 1250 °C. The diffusion interface was found to be made of Cr-Al spinel, occasionally containing microcavities up to 20 µm large filled by several sub-micrometric up to micrometric, second-generation, Cr-rich spinel crystals.

[1] G.B. Andreozzi. *Periodico di Mineralogia*. **1999**, *68*, 43–51.
[2] G.B. Andreozzi, F. Princivalle, H. Skogby, A. Della Giusta. *American Mineralogist*, **2000**, *85*, 1164–1171.
[3] G.B. Andreozzi, F. Bosi, F. Garramone. *Periodico di Mineralogia*. **2001**, *70*, 193–204.

High-pressure synchrotron single crystal behaviour and structural evolution of jamesonite ($FePb_4Sb_6S_{14}$)

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In mineralogy sulfosalts shall be considered metals and semi-metals compounds with chalcogens. Chalcogenides, because of their distinctive characteristics, are in wide abundance for next-generation materials, such as thermoelectric photoelectric, photovoltaics, optical data storage and solid-state electrolytes. The versatility of sulphosalts results from their chemical and structural components and their adjustable band gap, which can vary from almost 0 eV to over 2.0 eV. This property allows them to be used in various semiconductor materials. Some of the sulfosalts investigated at high pressure showed interesting pressure-induced structural phase transitions (Comodi et al. 2018), and the pressure may be an important parameter which could be used to tune the transport and structural properties of these thermoelectric materials (Olsen et al. 2008). In this study the high-pressure behaviour of jamesonite ($FePb_4Sb_6S_{14}$, a = 4.08(3), b = 19.08(3), c = 15.67(3) Å, space group $P2_1/c$), a natural antimony sulfosalt, has been investigated using in-situ HP-synchrotron X-ray single crystal diffraction up to 16.6 GPa with a diamond anvil cell under hydrostatic conditions. Axial and volume isothermal Equation of Sate (EoS) of Jamesonite were determined. Fitting the P-V data with a third order Birch-Murnaghan (BM) EoS we obtained the following values: V_0 = 1214(6) Å, K_0 = 35(3) GPa, and K'= 4.4(5). K_0 becomes equal to 37.0(9) fitting the data with a second order BM-EoS. The compressibilities of the lattice parameters, up to 16.6 GPa, was studied by fitting the data with a third-order BM-EoS and the following values were found: M_{0a} = 55GPa, M'_a = 19, M_{0b} = 130 M'_b = 11.0, M_{0c} = 147 and M'_c = 10; by using second-order BM-Eos the data were Ma = 81, Mb = 122, Mc = 133. Axial and volume Eulerian-finite strain (f_e) at different normalized stress (F_e) were calculated. Structural refinements comparison at different *P* indicates that Fe do not change their coordination number over the whole investigated *P* range: Fe has a 6 coordination with a increase of the distortion of the Fe polyehdra, related to different compressibility of unshared and shared edges, which reduce the approaching of Fe-Fe atoms. The three Sb polyhedra mantain the 5+2 coordination in the whole pressure range, because the Sb sterochemical activity of lone electron pairs. Moreover, the strongly distorted quadratic bases of the Sb square based pyramids, became more regular at high pressure, and strong reduction of the longest Sb-S distance direct along *a* axis explain the higher compressibility measured along this direction compared to the *b* and *c* axes. On the other hand, both Pb polyhedra increase their coordination around 12 GPa: Pb1 passes from 6+1 to 7 coordination (with 7 bond lengths lower than 3.2 Å) whereas Pb2 passes from 7+1 to 8 coordination. No phase transitions were identified in the pressure range investigated.

[1] Comodi P., Guidoni F., Nazzareni S. Balic-Zunic T., Zucchini A. Makoviky E., Prakapenka V. A high-pressure phase transition in chalcostibite, $CuSbS_2$ *Eur. J. Mineral.* **2018**, *30*, 491–505.

[2] Olsen L.A., Balic-Zunic T., Makovicky E. High-pressure anisotropic distortion of $Pb_3Bi_2S_6$: a pressure-induced reversible phase transition with migration of chemical bonds. *Inorg. Chem.*, **2008**, *47*, 6756–6762.

(P,T)-behavior of an intermediate scapolite of unusual $I4/m$ symmetry

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Scapolites are a group of open-framework aluminosilicates with general formula $M_4T_{12}O_{24}A$, where M are monovalent or divalent cations (usually Na, Ca and minor K), T are trivalent or tetravalent cations (mostly Al and Si) in tetrahedral coordination, and A are anionic elements or groups such as Cl, CO_3 and SO_4. Samples with a composition closer to the $Na_4Al_3Si_9O_{24}Cl$ and $Ca_4Al_6Si_6O_{24}CO_3$ end-members are usually reported to crystallize with a structure described in the $I4/m$ space group, whereas intermediate members are reported to show a $P4_2/n$ symmetry. Scapolites are usually formed under metamorphic conditions in the presence of fluids, but are also reported as constituents of upper mantle xenoliths [1, 2]. Scapolites form a complex non-binary solid solution as a function of the (NaCl)-($CaCO_3$)-($CaSO_4$) substitutions, which couples with Al-Si re-arrangements [3, 4]. The variable crystal chemistry and symmetry of these minerals influences their elastic and structural response to pressure and temperature variations and, consequently, their stability fields. In this study, we have investigated the behavior of an intermediate scapolite of the composition $(Na_{1.86}Ca_{1.86}K_{0.23}Fe_{0.01})(Al_{4.36}Si_{7.64})O_{24}[Cl_{0.48}(CO_3)_{0.48}(SO_4)_{0.01}])$ and its unusual symmetry $I4/m$, by means of in situ X-ray and neutron diffraction at high-T (from -100 to +1000 °C), high-P (up to 17.8 GPa) and combined high-T and P (up to 650 °C and 16 GPa). Experimental data show that the unusual I-centered lattice is always preserved, whereas a phase transition towards a triclinic polymorph, that can be described according to an unconventional I-1 symmetry, was found to occur at 9-10 GPa, with a modest influence from temperature. The deformation mechanisms, acting at the atomic scale, that lead to the structural instability and phase transition have been described on the basis of a series of single-crystal structure refinements. A comparison with data from literature allows to model the elastic response of scapolites as a function of their crystal chemistry, whereas a model of the thermo-elastic behavior is less straightforward on the basis of the available data, suggesting that a thorough re-investigation of the thermal behavior of the complex scapolite solid solution is desirable.

[1] J.K. Porter, H. Austrheim *Terra Nova*. **2017**, *29*, 29-35.
[2] L. Torró, R.F. Martin, D. Schumann, J. Cox, S. Galì Medina, J.C. Melgarejo Draper *Eur. J. Mineral.* **2018**, *30*, 45-59.
[3] D.K. Teerstra, B.L. Sheriff *Chem. Geol.* **1997**, *136*, 233-260.
[4] E.V. Sokolova, F.C. Hawthorne *Can. Mineral.* **2008**, *46*, 1527-1544.

An in-situ experimental study of Cinnabar (HgS) stability and liquid structure at HP-T

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Cinnabar (HgS) is a hexagonal mineral phase the importance of which is due to extraction of pure Hg and its toxicity. It has two polymorphic structures, the zinc blende structure between 0.3-1.7 GPa and 950-1350 °C [1], and a rock salt structure reported to be stable along with cinnabar within the range of 16-24 GPa and 570-900 °C [2 and references therein]. A typical feature is represented by the negative Clapeyron-slope of the cinnabar-rock salt structure phase transition resulted both from HP-T experiments and theoretical simulations. However, to date, no data are known on the melting behavior and liquid structure of HgS at HP-T, that would have implications for the speciation of Hg from Earth's interior, as well as the atomic rearrangement inherited by the crystalline polymorph.

In this study, we performed in-situ synchrotron HP-T experiments to constrain the stability and phase transitions of HgS up to 20 GPa and 1500°C and its liquid structure up to 6 GPa and 1600 °C. Natural cinnabar crystals were selected from the MUST collection (Sapienza University of Rome, Italy), observed by scanning electron microscopy and, then, used as starting material. Experiments were conducted at beamline ID06 LVP of ESRF (Grenoble, France) using the Voggenreiter press coupled with angle dispersive X-ray diffraction at ~55 keV to investigate HgS behavior at HP-T upon cold and hot compression and decompression. The melting behavior and liquid atomic structure were investigated through experiments performed using the VX5 Paris-Edinburgh press combined with angle dispersive X-ray diffraction at beamline 13-ID-C of GSECARS at the Advanced Photon Source (Chicago, USA).

The preliminary results show no cinnabar phase transition to rock salt structure in the investigated P-T range in contrast to previous studies. The results of the liquid structure measurements were compared with data of liquid Fe-S, S and Hg and help understanding the compressibility as function of P-T both in the intermediate-range ordering (i.e., the structure factor, S(q)) and in the local structure (i.e., pair distribution factor, G(r)) Our preliminary data are discussed in terms of possible mechanisms of Hg mobilization from the Earth's upper mantle with possible implications for the Hg emissions to the atmosphere during large magmatic events.

[1] Tedenac, J. C., Record, M. C., Ayral-Marin, R. M., Brun, G., Jun, J., Grzegory, I., Bockowski, M. *Japanese journal of applied physics* **1993**, *32*(S1), 26.
[2] Da-Wei, F., Wen-Ge, Z., Cong-Qiang, L., Fang, W., Yin-Suo, X., Jing, L., Hong-Sen, X. *Chinese Physics Letters* **2009**, *26*(4), 046402.

Batoniite, $[Al_8(OH)_{14}(H_2O)_{18}](SO_4)_5\cdot 5H_2O$, the first mineral with $[Al_8(OH)_{14}(H_2O)_{18}]^{10+}$ polyoxocation clusters

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In the framework of a systematic investigation of sulfate mineral assemblages from Tuscany (Italy), the new mineral species batoniite, $Al_8(SO_4)_5(OH)_{14}(H_2O)_{18}\cdot 5H_2O$, from the Cetine di Cotorniano mine (Chiusdino, Siena) was identified and characterized through electron microprobe analysis and single-crystal X-ray diffraction.

Chemical data pointed to the empirical formula $(Al_{7.98}Fe_{0.01})_{\Sigma 7.99}(SO_4)_{5.01}(OH)_{13.95}\cdot 23H_2O$, based on Al + Fe + S = 13 atoms per formula unit and recalculating H_2O on the basis of structural data. Batoniite is triclinic, space group P-1, with unit-cell parameters a = 9.1757(6), b = 12.0886(9), c = 20.9218(15) Å, α = 82.901(3), β = 87.334(3), γ = 86.999(3)°, V = 2297.8(3) Å^3. The crystal structure was solved and refined to R_1 = 0.0964 for 8118 reflections with $F_o > 4\sigma F_o$ and 679 parameters. The crystal structure can be described as bipartite, showing a structural unit and an interstitial complex, in agreement with [1,2].

The structural unit is represented by the polyoxocation $[Al_8(OH)_{14}(H_2O)_{18}]^{10+}$ (Fig. 1). Two symmetry-independent clusters occur in the crystal structure of batoniite. Every cluster is formed by a tetrameric unit forming a flat core of edge-sharing Al-centered octahedra, with two central $Al(OH)_6$ and two peripheral $Al(OH)_5(H_2O)$ polyhedra. The cluster is completed by four additional $Al(OH)_2(H_2O)_4$ octahedra, bonded to the core through corner-sharing. Such a polyoxocation was previously known only in synthetic compounds [3] and it represents a novel aluminate polyoxocation after those reported in caseyite and protocaseyite [4,5].

The interstitial complex is composed by five independent SO_4 groups and five "free" H_2O groups. A system of H-bonds connect the structural unit with the interstitial complex.

Taking into account the results of the structural investigation, the crystal chemical formula of batoniite can be written as $[Al_8(OH)_{14}(H_2O)_{18}](SO_4)_5\cdot 5H_2O$.

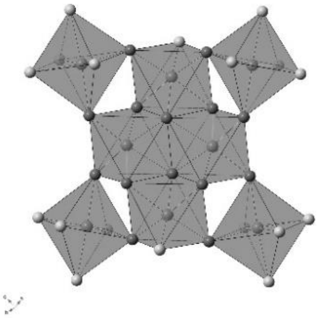

Figure 1. The polyoxocation $[Al_8(OH)_{14}(H_2O)_{18}]^{10+}$ occurring in batoniite.

[1] F.C. Hawthorne *Am. Mineral.* **1985**, *70*, 455.
[2] M. Schindler, F.C. Hawthorne *Can. Mineral.* **2001**, *39*, 1225.
[3] W.H. Casey, M.M. Olmstead, B.L. Phillips *Inorg. Chem.*, **2005**, *44*, 4888.
[4] A.R. Kampf, M.A. Cooper, J.M. Hughes, B.P. Nash, F.C. Hawthorne, J. Marty *Am. Mineral.* **2020**, *105*, 123.
[5] A.R. Kampf, M.A. Cooper, J.M. Hughes, C. Ma, W.H. Casey, F.C. Hawthorne, J. Mary, *Am. Mineral.* **2022**, *107*, 1181.

Toward the understanding of inclusions trapped in a diamond from Rio Soriso, Juina (Brazil): a multi-technique approach

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Inclusions in diamonds, comprising minerals entrapped within the diamond host, have long been regarded as pristine samples of regions of the Earth that we cannot access directly. Being encapsulated at depth and protected during their ascent to the surface by the diamond, inclusions can provide valuable information on the environment in which the host-inclusion pair grew, in terms of temperature, pressure and redox conditions. Crystallographic methods can play a major role in the study of this kind of samples, since they allow to identify the minerals entrapped in the diamond and to explore growth relationships between the host and the inclusions and their stress state [1]. Thanks to the recent progress in laboratory X-ray source, large scale facilities and detector technology, this approach can also be applied *in situ*, in a non-destructive way [1]. Coupled with other techniques, this methodology can provide a thorough and detailed characterization of mineral inclusions unveiling possible mechanisms of formation. A diamond from Rio Soriso, Juina (Brazil) was selected for this study. It contains ten mineral inclusions, both colourless and greenish, ranging from 20 to 200 μm in size. The inclusions were identified *in situ* by means of synchrotron X-ray tomography and single-crystal diffraction at the 13BM-D (GSECARS) beamline at the Advanced Photon Source (Argonne, US) [2]. The identification was confirmed by infrared and Raman spectroscopy. Mössbauer spectroscopy, carried out at the ID18 beamline of the European Synchrotron Radiation Facility (Grenoble, France), was employed to determine the Fe oxidation state of the selected inclusions. One exposed inclusion was also analysed by scanning electron microscopy, electron microprobe and laser ablation-inductively coupled plasma-mass spectrometry to determine its texture and chemical composition in terms of major and trace elements. Our preliminary results highlight the wherlitic mineral assemblage typical of metasomatized environments. The measured $Fe^{3+}/\Sigma Fe$ ratio can provide important information on the possible mantle redox state at the time of entrapment of syngenetic inclusions.

[1] R.J. Angel, M. Alvaro, F. Nestola *Rev. Mineral. Geochem.* **2022**, *88*, 257.
[2] M.D. Wenz, S.D. Jacobsen, D. Zhang, M. Regier, H.J. Bausch, P.K. Dera, M. Rivers, P. Eng, S.B. Shirey, D.G. Pearson. *J. Synchrotron Radiat.* **2019** *26*, 1763.

Novel sustainable MOFs: mechanochemical synthesis, structural characterization, and applications

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The research field on Metal-Organic Frameworks (MOFs) has seen an increasing interest in last decades due to the great variety of applications of such porous materials. In addition to classical monometallic MOFs, a mention of interest should be given to bimetallic frameworks. The presence of different metal nodes has the bivalent benefit to improve the application fields and create new structures. MOFs are commonly synthetized through solvothermal processes that involve a great energy consumption and the use of toxic reagents or solvents. Nowadays, a more sustainable method could be represented by mechanochemistry (MC). Fast, low-cost, and potentially green, this technique allows to prepare a huge variety of materials through solid-state reactions. The resulting powders can possess a sub-micrometer particle size, well below the limits of common Single Crystal X-ray Diffraction (SCXRD) techniques. The only alternative remains in the use of 3D Electron Diffraction (3DED) [1]. Furthermore, the selection of biocompatible ligands and metals could bring benefits from the point of view of more sustainable applications [2].

In this work, we present a study focused on the MC synthesis of monometallic or bimetallic frameworks using biocompatible reagents and solvents. Each substance chosen (e.g., ligands and solvents) is listed on FDA databases as contact substance or food additive. Alternatively, they possess a very low toxicity (e.g., pyromellitic acid). Some molecules can even be extracted by plants i.e., protocatechuic or caffeic acid. The metallic sources (Cu and Zn in particular), on the other hand, belong to the class of carbonates and acetates hydrated.

Our best result so far is represented by the very first 2D-MOF obtained with protocatechuic acid and copper acetate dihydrate (3:4 ratio). This material can be prepared both in co-precipitation and MC in water. The second process is preferable while the yield is 45% larger and the water used is 30 times less than first. Powder X-Ray Diffraction was used as screening process and, through 3DED, it was possible to determine the structure and even to detect water contained in channels. This material has shown a great stability in different organic solvents as well as a relevant activity in the absorption and subsequent release of histologic dyes like methylene blue. Current studies are underway to establish if this behavior can be applied to drug delivery or water purification applications.

[1] M. Gemmi, A. E. Lanza *Acta Cryst.* **2019**, *B75*, 495-504.

[2] E. S. Grape, J. G. Flores, T. Hidalgo, E. Martínez-Ahumada, A. Gutiérrez-Alejandre, A. Hautier, D. R. Williams, M. O'Keeffe, L. Öhrström, T. Willhammar, P. Horcajada, I. A. Ibarra, A. K. Inge *J. Am. Chem. Soc.* **2020**, *142*, 39, 16795–16804

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Crystal Structures of Metal-Porphyrin-Calixarene Complexes: Microporous Materials with Diverse Architectures

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Microporous frameworks with voids and channels of varying sizes and shapes are crucial for numerous technological applications, including selective guest storage, molecular sieving, and nanoreactors. A new class of microporous materials has emerged in the form of crystalline open frameworks based on supramolecular host-guest complexes. These self-assembled materials have garnered interest due to their ability to combine specific catalytic and stereochemical properties with plasticity. Porphyrins are particularly advantageous as molecular building blocks for supramolecular solids, offering intriguing applications such as artificial antennas for light-harvesting, mimicking natural systems. Additionally, the incorporation of metal ion coordination has expanded the range of metallo-porphyrin-based frameworks. Cavitand molecules, with their preorganized cavity, serve as another essential building block for the supramolecular assembly of porous solids, particularly in molecular sensing applications.

In previous works [1-4], we have observed the self-assembly of the polyanionic 5,11,17,23-tetrasulfonato-25,26,27,28-tetrakis(hydroxylcarbonylmethoxy)calix[4]arene around the tetracationic porphyrin meso-tetrakis(4-N-methylpyridyl)porphyrin resulting in the formation of star-shaped supramolecular complexes (Fig. 1). These complexes are stabilized by noncovalent forces, such as electrostatic interactions, π stacking, and multiple host-guest CH$\cdots\pi$ interactions. The highly symmetric star-branched complexes offer the potential for designing new bicomponent materials that possess the chemical properties of both building blocks.

In this study, we present the crystal structures of various metal-porphyrin-calixarene systems synthesized in an aqueous environment through self-assembly. These systems exhibit diversification in terms of components and synthesis conditions, including the type of metal center (Co(II), Zn(II), Cd(II), and Au(III)) in the porphyrins, the charge of the cationic porphyrins, and the pH value of the buffer solution used for obtaining the crystals for solid-phase analysis. These factors significantly influence the formation of solid-state lattice structures characterized by distinct crystallographic symmetry, host-guest stoichiometry, different coordination geometry and stacking of porphyrins, as well as the presence of large channels.

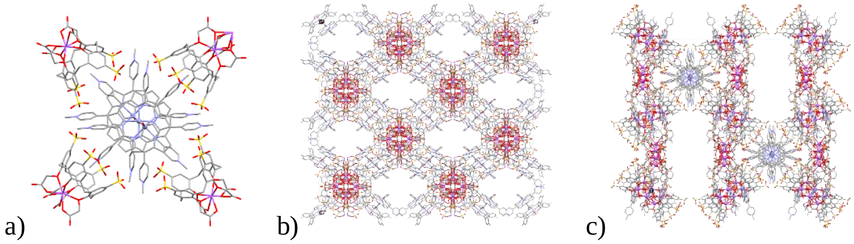

Figure 1. a) Star-shaped host-guest complex; Packing of Zn(II)-porphyrin at pH 7.0 (b) and pH 9.5 (c).

[1] L. Di Costanzo, S. Geremia, L. Randaccio, R. Purrello, R. Lauceri, D. Sciotto, F. Gulino, V. Pavone *Angew. Chem.-Int. Ed.* **2001**, *40*, 4245.

[2] R. De Zorzi, N. Guidolin, L. Randaccio, R. Purrello, S. Geremia *JACS* **2009**, *131*, 2487.

[3] R. De Zorzi, N. Guidolin, L. Randaccio, S. Geremia *Crystengcomm* **2010**, *12*, 4056.

[4] G. Brancatelli, R. De Zorzi, N. Hickey, P. Siega, G. Zingone, S. Geremia *Crystal Growth & Design* **2012**, *12*, 5111.

Structure-Property Investigation of Lanthanum-based Perovskites Oxides for Thermocatalytic Green Hydrogen Production

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High **E**ntropy **P**erovskites **O**xides (HEPOs) have gained significant attention in recent years as potential catalysts for the thermochemical synthesis of green hydrogen. This is because they exhibit several unique properties that make them well-suited for this application such as high stability, good activity, and the ability to operate under a wide range of conditions.[1] In addition, high entropy perovskites have shown good activity and selectivity for these types of reactions thus suggesting their possible use to produce green hydrogen.[2] The simplest configuration of a thermochemical cycle makes use of a metal oxide undergoing a reduction and re-oxidation in two consecutive steps.[3]

The twofold object of the present work is therefore to develop novel materials with the aim of: i) increasing the presence of oxygen vacancies and thus the 'active sites' of the catalyst; and ii) decreasing the temperature at which they are formed (e.g., T<800K). To achieve these objectives, we started to investigate perovkites oxides of general formula ABO_3 by adopting a chemometric approach to map the compositional space of the perovskite oxide. In particular, we focused on the following compositions: on the site A we chose to keep lanthanum due to its stability, while, on the B site, we explored different cation mixtures based on Cr, Mn, Fe, Co, Ni and Zn, to determine an experimental domain by including various experimental data, *i.e.* crystal structure, oxygen vacancies extent and temperature-dependance, and composition.[4] The synthesized samples were subjected to x-ray diffraction (XRD) analysis followed by Rietveld refinement to determine crystallographic parameters. Through multivariate analysis, elemental concentrations were correlated to phase stability and cell parameters. The structural study aims at highlight possible correlations between the crystal symmetry and the catalytic characteristics of the material at high temperature. Finally, through thermogravimetric analysis, it is possible to study non-stoichiometry, phase transitions, and redox ability to be integrated within the previously designated experimental domains. The overall experimental results will allow to define the best compositions to be used for the thermochemical synthesis of hydrogen.

[1] Bayon, A.; de la Calle, A.; Stechel, E. B.; Muhich, C. *Energy Technol.* **2022**, *10*, 2100222.
[2] Nguyen, T. X.; Liao, Y. C.; Lin, C. C.; Su, Y. H.; Ting, J. M. *Adv. Funct. Mater.* **2021**, *31*, 2101632.
[3] Bayon, A.; de la Calle, A.; Ghose, K. K.; Page, A. J.; McNaughton, R. *Int. J. Hydrogen Energy* **2020**, *45*, 12653.
[4] Okazaki, Y.; Fujita, Y.; Murata, H.; Masuyama, N.; Nojima, Y.; Ikeno, H.; Yagi, S.; Yamada I. *Chem. Mater.* **2022**, 34, 10973-10981.

Water stable Cu(II)-based porous Metal-Organic materials for CO_2 capture and environmentally application

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Metal-Organic porous materials have received great attention thanks to their numerous applications. Among them, the storage and release of different molecules in a controlled manner could be considered one of the most important applications, given the current urgency to deal with climate change.[1], [2] In our attempt to obtain new Cu(II)-based porous metal-organic materials, we exploited the use of β-diketone ligands featuring functional groups with N- and O-donor atoms. In particular, reacting the asymmetric β-diketone/carboxylic ligand H_2L (1- (4'-carboxyacetophenyl), 3-phenyl-1,3-propanedione)[3] with copper acetate we obtained three isostructural Metal-Organic Cages (MOCs) of general formula $[Cu_{16}(L)_{16}(A)_n(B)_8](S)_x$ [A= THF (tetrahydrofuran), n=8, B=H_2O (**1**); A=diox (dioxane), n=4, B=H_2O (**2**); A = B = dme (dimethoxyethane), n=8 (**3**) (Figure 1a). Interestingly, the cages resulted to be very stable in water and preliminary host-guest investigation indicates that the coordinated THF molecules in **1** can be quantitatively exchanged with organic ether molecules. This interesting behavior is under investigation for organic pollutants removal in water.

Besides, we report here on the water and CO_2 adsorption ability of the water stable MOF $[Cu(L^2)(H_2O)_2]_2 \cdot (SO_4)$ (**4**) (HL^2 = 1,3-Bis(4-pyridyl)-1,3-propanedione), whose structure is characterized by 70% of free void and third-generation nanoporous behavior (Figure 1b). Interestingly, it has been found that the desolvated-amorphous phase of **4** can reversibly adsorb large amounts of water (at least five cycles). Moreover, CO_2 adsorption measurements revealed that, although only a negligible amount of the gas is adsorbed in dry condition, the CO_2 uptake largely increase under humid conditions.

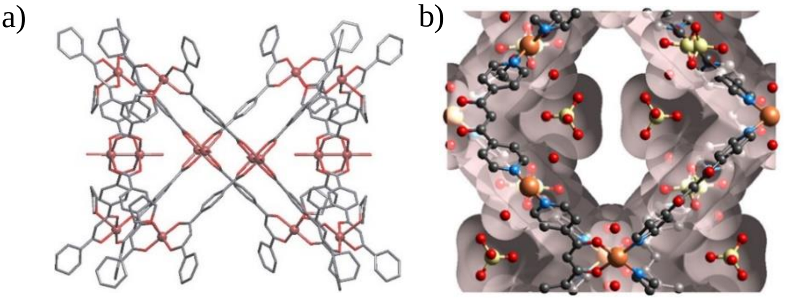

Figure 1: (a) Structure of the molecular cage **1**; (b) View of the porous structure of **4**.

[1] J. Yu, L. H. Xie, J. R. Li, Y. Ma, J. M. Seminario, and P. B. Balbuena, *Chem Rev*, **2017**, *117*, 9674.
[2] S. Rojas and P. Horcajada, *Chem Rev*, **2020**, *120*, 8378.
[3] J. Zawadiak, J. Zawadiak, M. Mrzyczek, and T. Piotrowski, *Eur. J. Chem*. **2011**, 3, 289

Development of Lead-Free Chiral Perovskites

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Hybrid metal halide perovskites have received significant attention as suitable materials for various electronic applications in photovoltaic cells, photodetectors, light emitting diodes, and sensors, owing to their outstanding and unique properties such as high-power conversion efficiency, tunable bandgap, and high absorption coefficient [2]. Starting from the hybrid organic-inorganic perovskites (HOIPs) and due to the introduction of a chiral molecule as organic cation, such as Methylbenzylamine (MBA) or (4-Chlorophenyl)ethylenimine (Cl-MBA), the structure presents the breaking of the spatial inversion symmetry and this design new possibilities, by combining polarity and chirality [1,3]. To extend the actual knowledge of these novel chiral systems, here we report the synthesis, by single crystal and powder and the characterization of new lead-free chiral perovskites, namely, (R/S/rac-ClMBA)$_2$SnI$_4$, (R/S/rac-ClMBA)$_2$GeI$_4$ and (R/S/-ClMBA)$_3$GeI$_5$ with different kind of organic spacer incorporated and we provide an overview of future studies about chirality transfer, between the organic cation and the inorganic framework, spin-selectivity, ferroelectricity, and piezoelectricity.

[1] Liu, Y.; Han, S.; Wang, J.; Ma, Y.; Guo, W.; Huang, X.; Luo, J.; Hong, M.; Sun, Z. *J. Am. Chem. Soc.* **2021**, *143,* 2130-2137
[2] Park, H.; Ha, C.; Lee, *J. J. Mater. Chem. A.* **2020**, *8,* 24353
[3] Li, H.; Li, F.; Shen, Z.; Han, S.; Chen, J.; Dong, C.; Chen, C.; Zhou, Y.; Wang, M. *Nano Today,* **2021**, *101062.*

Low dimensional systems of chiral perovskites: unveiling the role of composition and crystal structure in the photophysical properties

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In the recent years, hybrid organic inorganic perovskites (HOIPs) have appeared as promising materials for applications including solar cells, light emitting diodes and photodetectors, thanks to the outstanding luminescence quantum yield and easy emission tunability [1]. In this research area, employment of chiral organic cations capable of transferring the chiroptical properties to the emissive HOIPs is gaining more and more interest for the intriguing potential applications in spin transport, chiroptoelectronics, piezoelectricity, and spintronics. The resulting materials combine the advantages of chiral molecules, as the second-order non-linear optical responses granted by the intrinsic noncentrosymmetry [2], and the good emissive properties typical of perovskites. Moreover, the fine chemical and structural tuning offered by HOIPs provides an encouraging playground for developing novel and more efficient materials, featuring higher spin selectivity, superior circular dichroism, improved stability, etc. In this growing field, several fundamental issues are still unsolved, such as the influence of chemical composition and structural parameters on the photophysical properties and the chirality transfer mechanism, which are a bottleneck to be overcome for breakthrough progresses in the research area.

To shed light on these aspects, we are designing, synthesizing and characterizing from the structural and photophysical viewpoint novel and rational series of chiral HOIPs, wisely selecting the constituents to investigate the variation of specific chemical properties. Regarding the role of the central atom, we are working with Ge^{II}, Sn^{II} and Pb^{II} to evaluate the effect of increasing the spin-orbit coupling (SOC) on the chiroptical features. To this aim, we have already obtained the 1D HOIP (S-3-APD)PbX_4 [S-3-APD = (S)-3-aminopiperidine, $X^- = Br^-, I^-$] [3,4], in form of single crystals, and are working for the attainment of the analogues novel phases with Sn^{II} and Ge^{II}. On the other hand, we are exploring other organic cations, either commercially available or *ad-hoc* synthesized, to investigate their influence in hydrogen bond network and octahedra disposition, and how these structural features impact on the photophysical properties. By adopting a multidisciplinary approach, involving synthesis, structural characterization, photophysical investigation and theoretical calculations we aim to correlate the emissive properties of chiral HOIPs to the structural features, providing new parameters useful in the design of novel materials.

[1] M. Yuan, L. N. Quan, R. Comin, G. Walters, R. Sabatini, O. Voznyy, S. Hoogland, Y. Zhao, E. M. Beauregard, P. Kanjanaboos, Z. Lu, D. H. Kim, E. H. Sargent *Nature Nanotechnology*. **2016**, *11*, 872.
[2] M. Kauranen, B. Busson, S. Van Elshocht, T. Verbiest, A. Persoons, C. Nuckolls, T. J. Kat *Optics & Photonics News*. **2000**, *11*, 24.
[3] Y. Peng, Y. Yao, L. Li, X. Liu, X. Zhang, Z. Wu, S. Wang, C. Ji, W. Zhang, J. Luo *Chem. Asian J.* **2019**, *14*, 2273.
[4] D Fu, J. Xin, Y. He, S. Wu, X. Zhang, X.-M. Zhang, J. Luo *Angew. Chem. Int. Ed.* **2021**, *60*, 20021.

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