Title	**Structure-function relationships in proteins**
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Research Group	Biomolecular structures – DiSC
Curriculum	Scienze Chimiche
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Project description

My research focusses on the study of the relationship between the structure and function of proteins, in particular those involved in diseases. As main structural techniques we use X-ray crystallography, Cryo-EM (cryo-electron microscopy) and SAXS (Small-Angle X-ray Scattering). Experimental data are collected in international facilities, for instance at the European Synchrotron Radiation Facility ESRF (Grenoble, F). We usually produce our targets in house using recombinant methods and purify them using chromatographic techniques. Structural studies are integrated by the biophysical characterization of the samples, for instance, by DLS (Dynamic Light Scattering), ITC (Isothermal Titration Calorimetry), CD (circular dichroism), enzymatic essays, and others, with instrumentation available at DiSC.

Currently we are interested in two enzymes, the main protease of SARS-CoV-2 M^{pro} and a human Aspartate dehydrogenase AspDH (in collaboration with prof. Riccardo Percudani and prof. Giulia Mori from the University of Parma).

M^{pro} works as a homodimer with two distant catalytic sites, but the reason for this choice, in contrast to function in a monomeric form, is not clear. We are currently investigating how the two distant active sites can functionally communicate through allosteric effects and how this can influence the catalytic cycle of the enzyme. We are also applying the novel approach of the "serial synchrotron crystallography" to obtain time-dependent data on the catalytic cycle.

AspDH is a new enzyme recently discovered by colleagues of the University of Parma with whom we are collaborating to investigate the structural features of this enzyme at the basis of its catalytic activity and physiological function.

Recent publications

- Malatesta, M. et al. One substrate-many enzymes virtual screening uncovers missing genes of carnitine biosynthesis in human and mouse. Nature Communications, accepted for publication.
- Fornasier, E. et al. A New Inactive Conformation of SARS-CoV-2 Main Protease. Acta Crystallogr D Struct Biol 2022, 78 (Pt 3), 363–378. https://doi.org/10.1107/S2059798322000948.
- Fabbian, S. et al. Mechanism of CK2 Inhibition by a Ruthenium-Based Polyoxometalate. Front Mol Biosci 2022, 9, 906390. https://doi.org/10.3389/fmolb.2022.906390.

Main collaborations

Prof. Alice Sosis and prof. Barbara Gatto, DSF, University of Padova.
Prof. Riccardo Percudani and prof. Giulia Mori, University of Parma.
Dr. Daniele De Sanctis, European Synchrotron Radiation Facility ESRF (Grenoble, F).