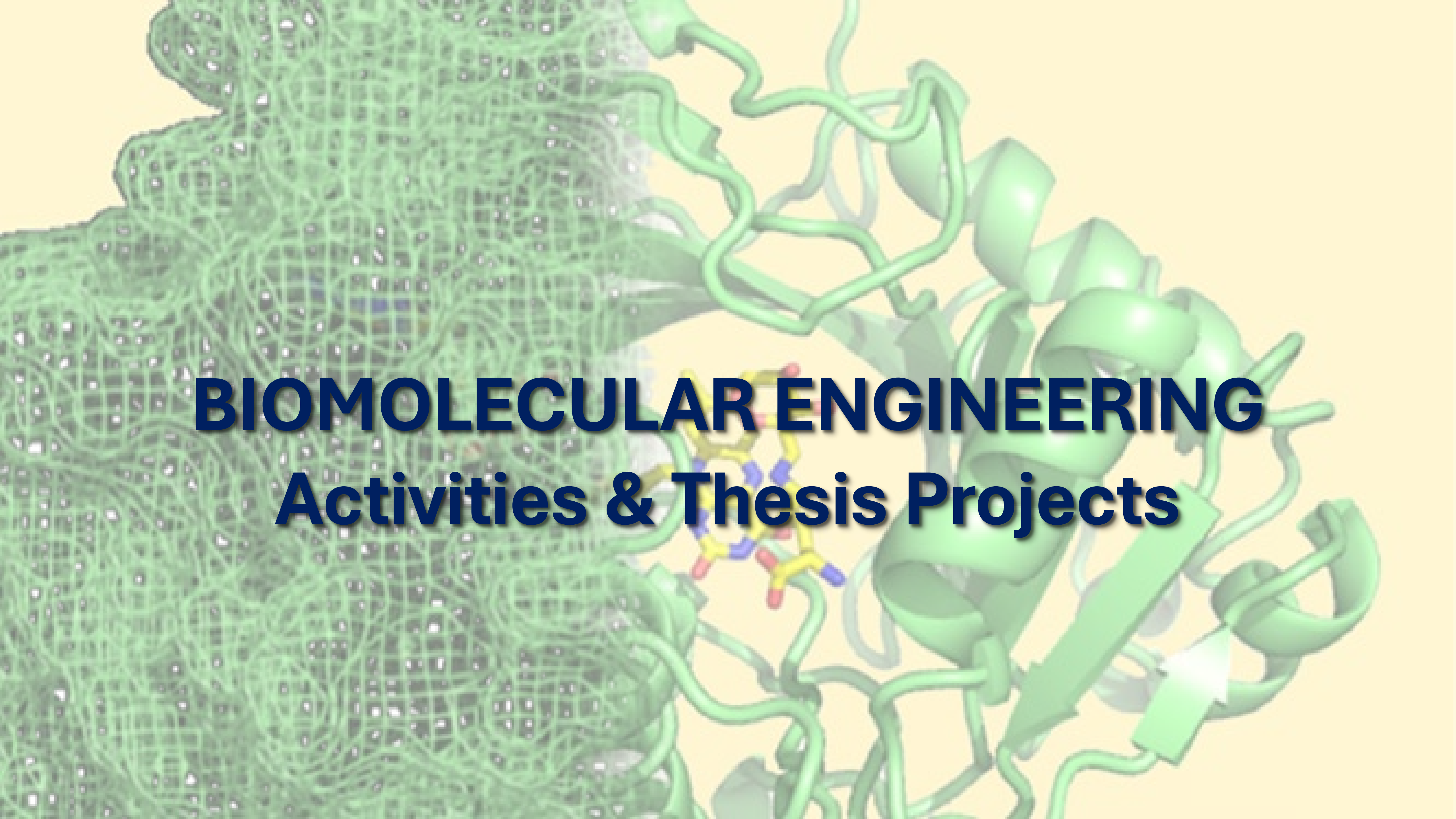
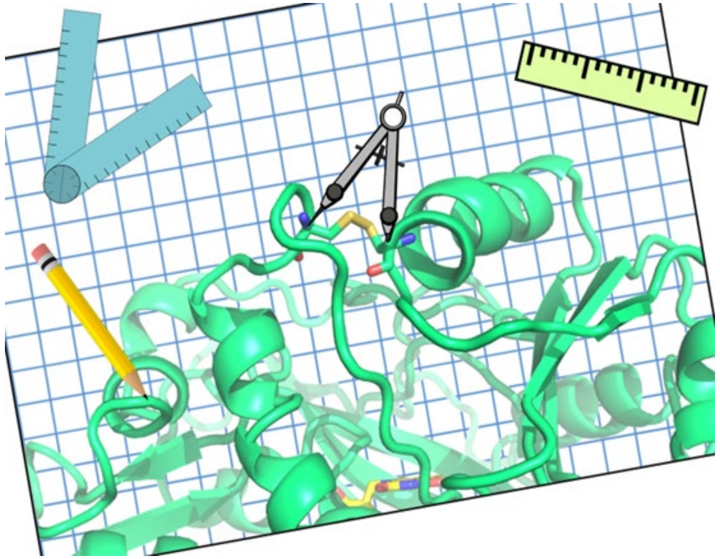
BIOMOLECULAR ENGINEERING
Activities & Thesis Projects

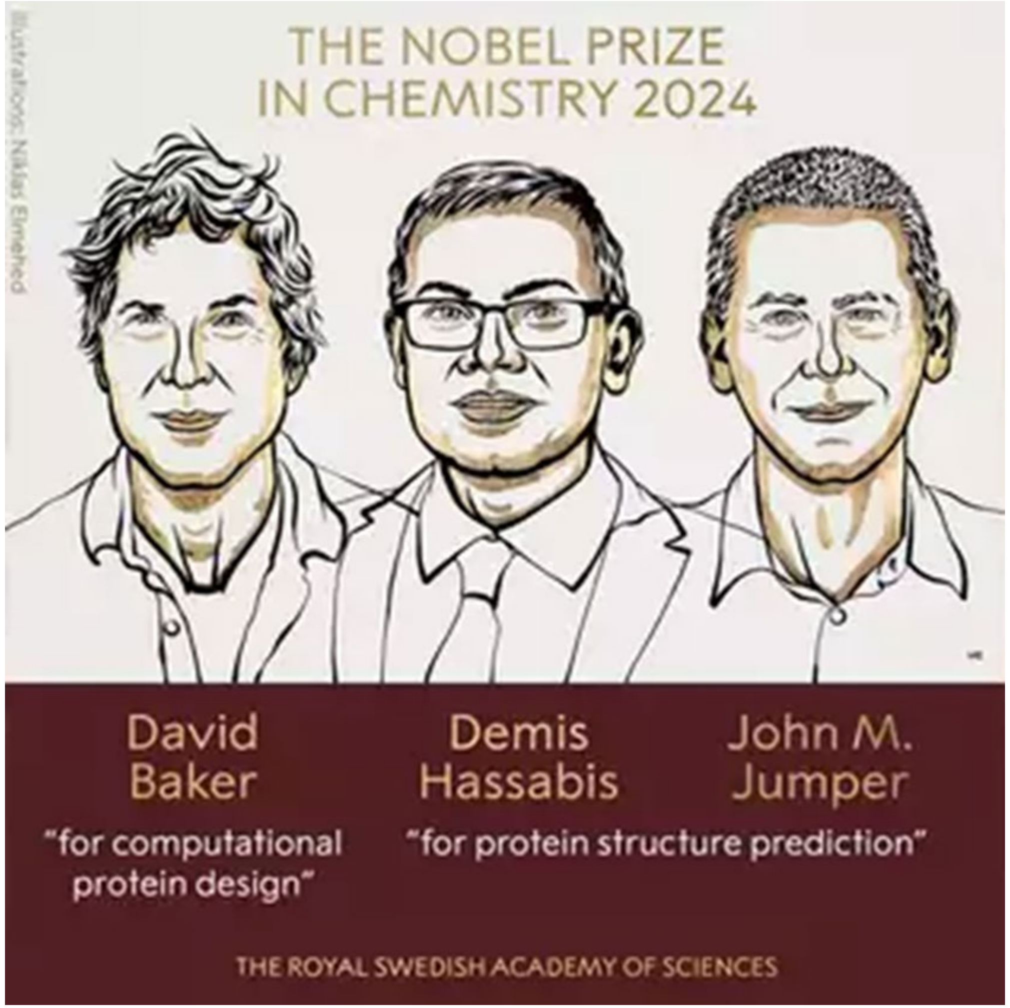


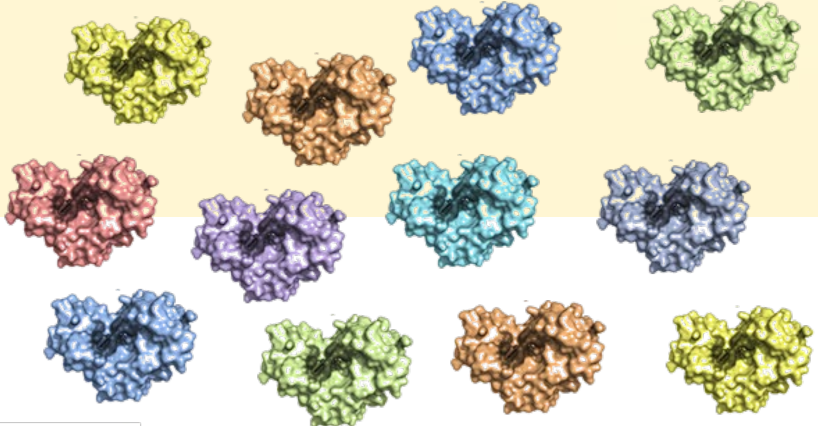
Research Activity

The **Nobel Prize in Chemistry of 2024** was awarded for the development of **computational tool for protein prediction and design**.

At the **BioMolecular Engineering Lab** we "stand on the shoulders of giants" and apply **computational engineering methods** to study and design **biomolecules and biomaterials.**







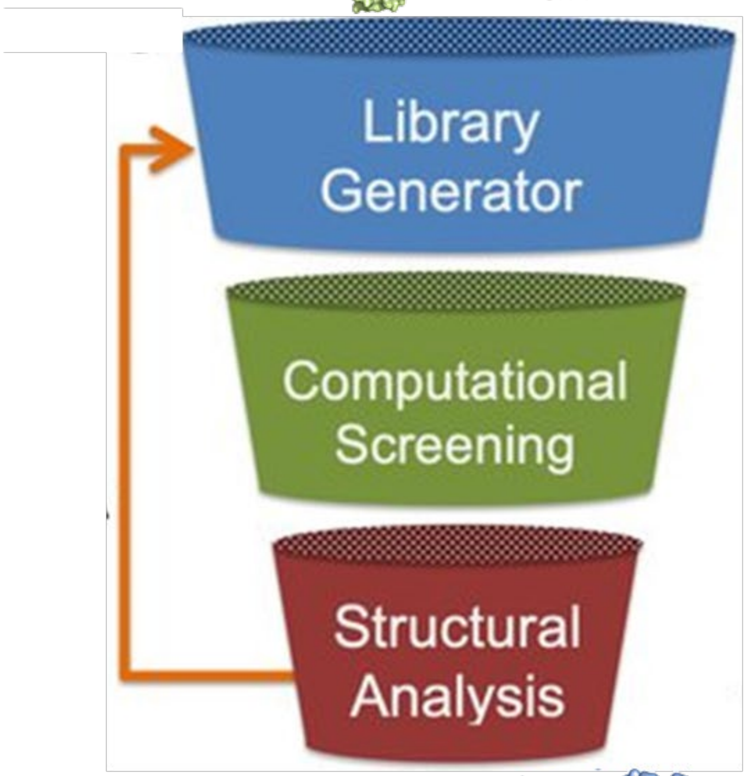
Enzyme engineering - Can we engineer better enzymes?

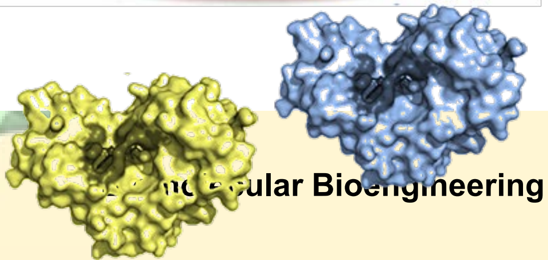
Enzymes are **biological catalysis** with great potentials for many applications.

Naturally occurring enzymes need often to be **improved to be of practical use** (tuning activity, increase stability, ...).

At the Biomolecular Engineering Laboratory we develop strategies to
•Generate libraries of enzyme variants
•Screen and rank enzyme variants

The most promising are subject to **experimental characterization in partner laboratories**.

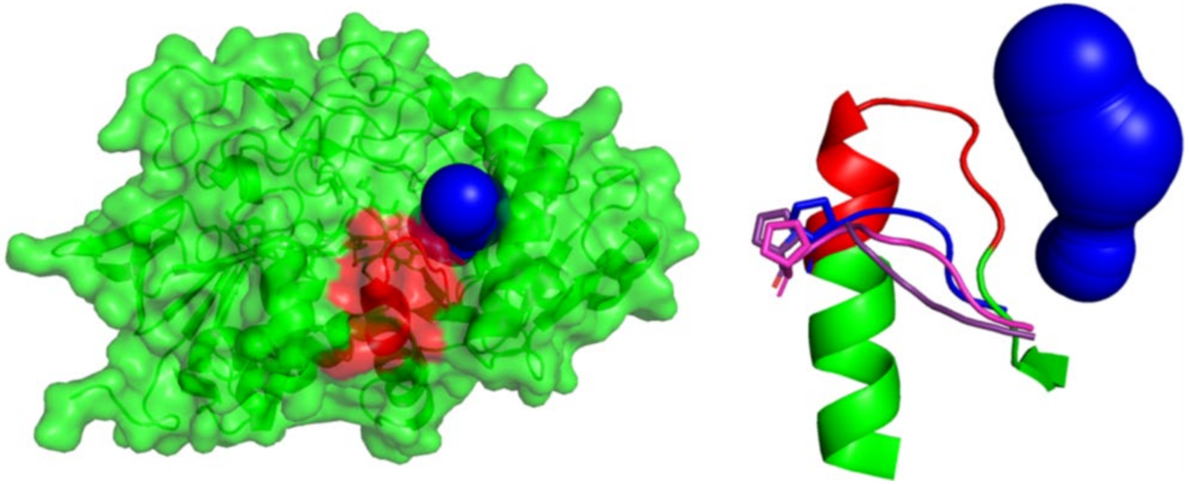




Enzyme engineering – Amadoriase

- The level of glycated haemoglobin (HbA1c) is a marker of diabetes
- Current methods for measuring HbA1c require complex equipment
- Enzymatic tests are fast and cheap, but require optimized enzyme

We engineered an enzyme to widen access to catalytic site.
Further optimization is required to allow direct detection of HbA1c



(1) H. Estiri, S. Bhattacharya, J. Alexander, R. Buitrago, R. Castagna, L. Legzdiņa, G. Casucci, A. Ricci, E. Parisini, A. Gautieri. 2023. Tailoring FPOX enzymes for enhanced stability and expanded substrate recognition. Scientific Reports 13, 18610.
(2) F. Rigoldi, S. Donini, A. Torretta, A. Carbone, A. Redaelli, T. Bandiera, E. Parisini, A. Gautieri. 2020. Rational backbone redesign of a Fructosyl Peptide Oxidase to widen its active site access tunnel. Biotechnology and Bioengineering 117, 3688–3698 (cover paper).

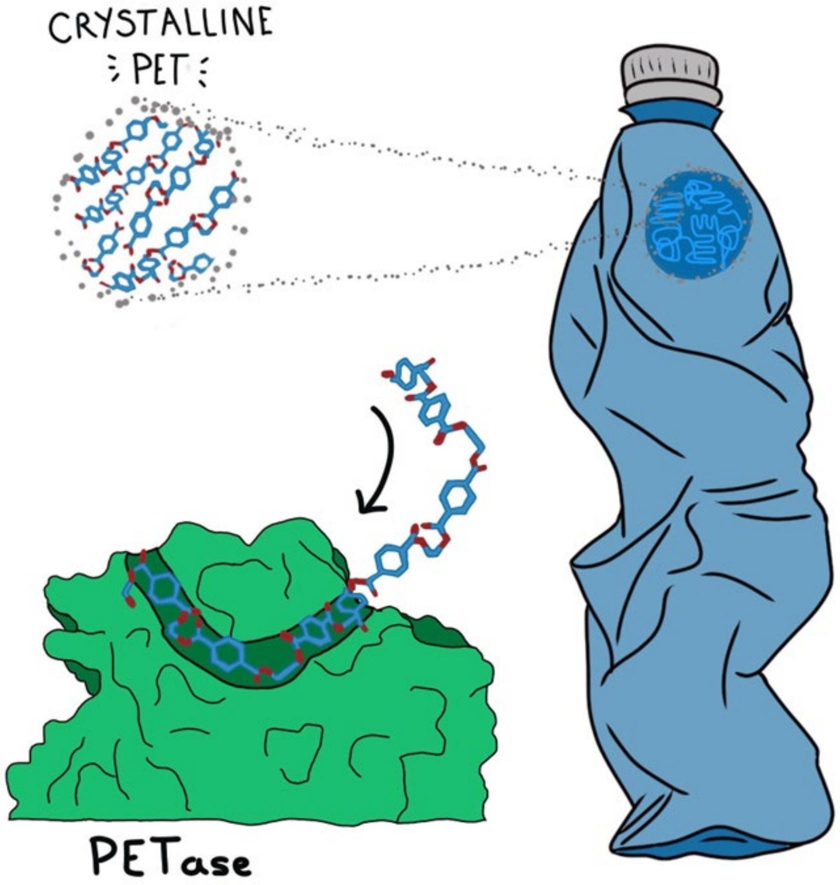
Enzyme engineering – PETase

PET is one of the most abundant plastic in use. The recycling process of PET results in a loss of mechanical properties.

Consequently, de novo synthesis is preferred and **PET waste continues to accumulate**, being non-biodegradable, with large **effects on the environment and ultimately of human health**.

Several P**ET hydrolase (PETase) enzymes** have been recently reported, but they show limited activity to be of practical use.

The project aim at the engineering of optimized PETase enzymes with improved thermal and catalytic activities.



S. Bhattacharya, R. Castagna, H. Estiri, T. Upmanis, A. Ricci, A. Gautieri, E. Parisini. 2024. Development of a highly active engineered PETase enzyme for polyester degradation. BiorXiv, doi: https://doi.org/10.1101/2024.07.04.602061

Research Activity

Nanoplastics - What are their effects on health?

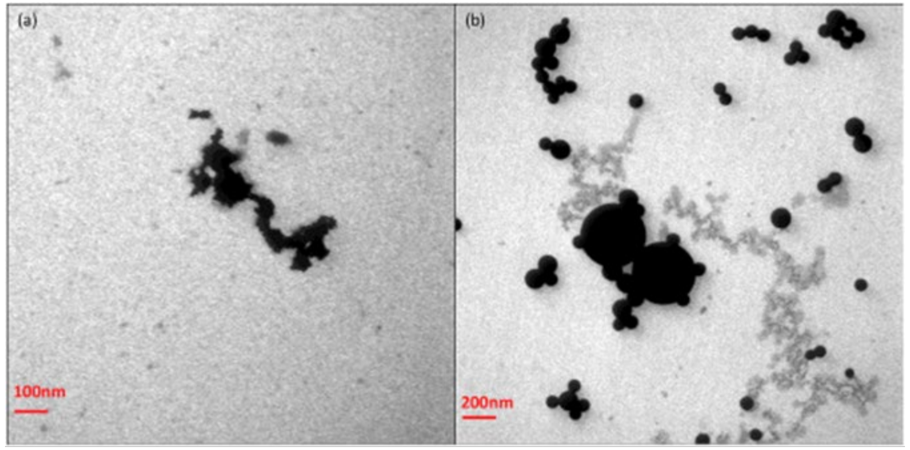
Nanoplastics (Ø < 100 nm) are formed by the degradation of polimeric materials and due to their size **easily penetrate in biological systems**.

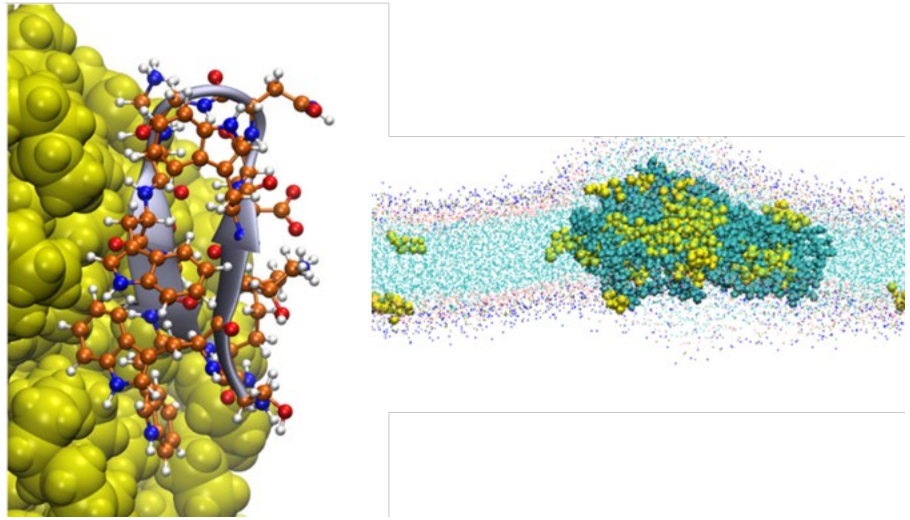
Plastic nanoparticles may have an **impact on health** by interfering with biomolecular function and celluar stuctures, but the extent is still unknown.

The project aims at **understanding the effect of nanoplastics at the molecular level**:

- Influence of protein structure and funtion
- Ability to cross biological barries (e.g., cell membrane)
- Engineer molecular baits to remove nanoplastics

A. Vismara, A. Gautieri. 2024. Molecular insights into nanoplastics-peptides binding and their interactions with the lipid membrane. Biophysical Chemistry 308, 107213





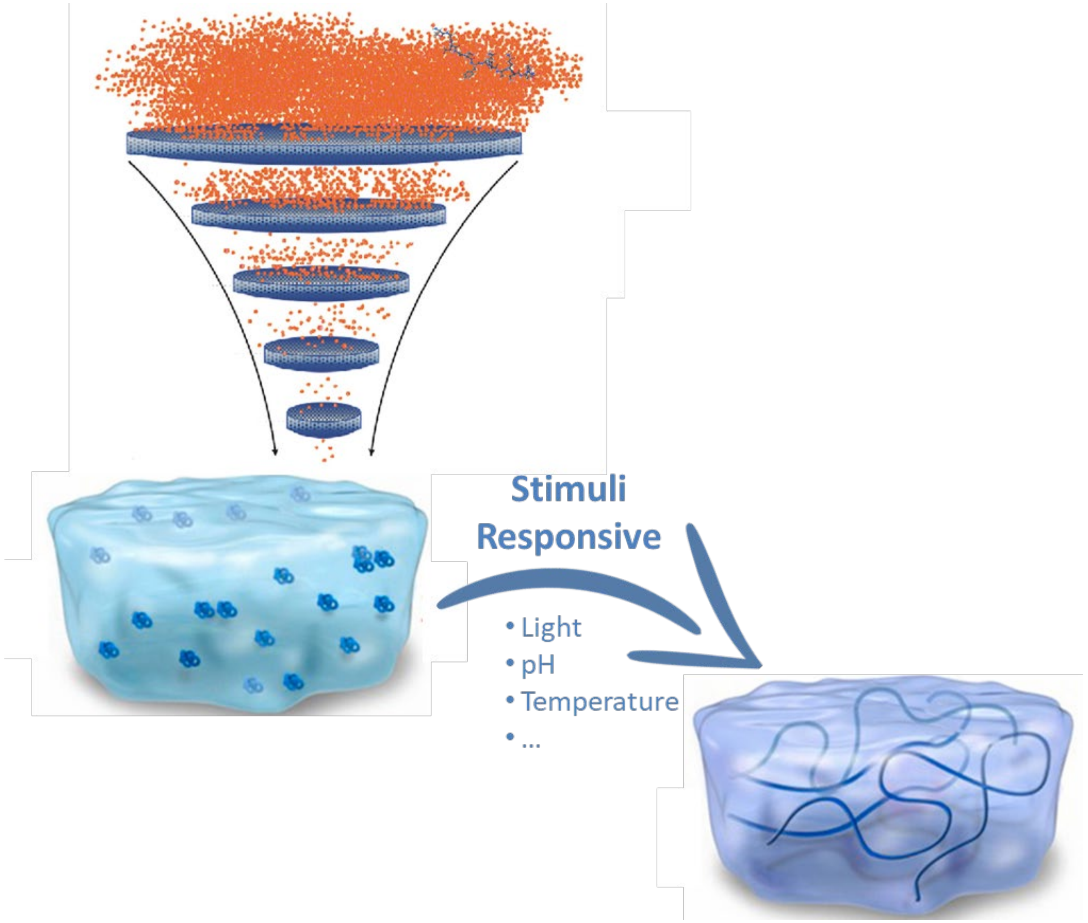
Self-Assembling Peptides - Can we design tunable peptides?

Self-assembling peptides are a category of peptides which undergo spontaneous assembling into **ordered nanostructures.**

These designer peptides have attracted interest in the field of nanotechnology for their potential for **application in areas such as biomaterials and cell culturing**.

The frontier in the field is to design **stimuli-responsive self-aggregating peptides**

Sequence space of a pentapeptide: $20^5 \approx 3M$ sequences -> we need a computational filter



Y. Hu, F. Rigoldi, H. Sun, A. Gautieri, B. Marelli. 2023. Unbiased in-silico design of pH-sensitive tetrapeptides. ChemComm 59, 10157.

Biomolecular Modelling Laboratory (Fall Semester)

The objective is to introduce atomistic modeling techniques and motivate its potential for solving problems in molecular biology and biomolecular engineering.

BioArtificial Systems at the Micro and Nano Scale (Spring Semester)

The course is focused on methods, technologies and operating principles that enable the manipulation and control of biological entities at the microscale (lab-on-chips, bioMEMS, organs-on-chips) and nano-scale (carbon nanotubes, dendrimers, liposomes, and biological nanostructures obtained from peptides and proteins)

Team

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Monica Soncini

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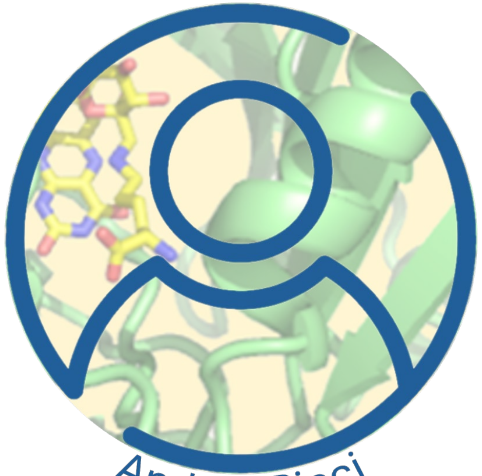

Andrea Ricci