



ALMA MATER STUDIORUM  
UNIVERSITÀ DI BOLOGNA

DIPARTIMENTO  
DI FARMACIA  
E BIOTECNOLOGIE

## AVVISO DI SEMINARIO

Il giorno **19 Aprile 2024**  
alle ore **14.00**

# Prof. Matteo Dal Peraro

Institute of Bioengineering, School of Life Sciences, Ecole Polytechnique  
Fédérale de Lausanne (EPFL), Lausanne, Switzerland  
(ospite di Prof. Matteo Masetti)

terrà un seminario dal titolo:

## **Single-molecule sensing with aerolysin pore-forming toxins**

Keywords: biological nanopores, membrane proteins, molecular simulation,  
nanopore sensing, post-translational modifications, biomarkers, informational polymers,  
data storage

*in presenza:*

**Aula A, Farmacologia, via Irnerio 48, Bologna BO**

Collegli e studenti sono cordialmente invitati

## ABSTRACT

Evolution has found countless ways to transport material across cells and cellular compartments separated by membranes. Protein assemblies are the cornerstone for the formation of channels and pores that enable this regulated passage of molecules in and out of cells, contributing to maintaining most of the fundamental processes that sustain living organisms. As in several other occasions, we have borrowed from the natural properties of these biological systems to push technology forward and have been able to hijack these nano-scale proteinaceous pores to learn about the physical and chemical features of molecules passing through them [1].

Using integrative structural biology, i.e. combining molecular modeling and simulations along with biochemical and cryo-EM analysis, we have revealed the structure and assembly mechanism of one of the most studied bacterial pore-forming toxins [2], namely aerolysin from *A. hydrophila* [3,4], recently obtaining its highest resolution structure at 2 Å by cryo-EM in nanodiscs (unpublished). Leveraging this structural and functional understanding, we have been able to characterize its properties as a molecular sensing device that can accurately discriminate nucleic acids and peptides [5], as well as detect post-translational modifications associated with validated biomarkers of neurodegenerative diseases (e.g.  $\alpha$ -synuclein phosphorylation in Parkinson's disease)[6]. Moreover, we have explored the ability of aerolysin pores to decode the information stored in hybrid polymers with the aim of finding new, alternative solutions for the emerging problem of data storage [7]. We are further leveraging and engineering the exquisite sensitivity of aerolysin pores as well other biological pores from the same superfamily to develop the next generation of sensor devices for single-molecule proteomics and analytical chemistry.

### References:

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4. Iacovache et al., Cryo-EM structure of aerolysin variants reveals a novel protein fold and the pore-formation process, *Nature Communications*, 7(1):1, 2016
5. Cao, Cirauqui, Marcaida, Buglakova, Duperrex, Radenovic, Dal Peraro, Single-molecule sensing of peptides and nucleic acids by engineered aerolysin nanopores, *Nature Communications*, 10:1, 2019
6. Cao, Magalhães, ..., Lashuel, Dal Peraro, Deep learning-assisted single-molecule detection of protein post-translational modifications with a biological nanopore, *ACS Nano*, 18(2):1504, 2024
7. Cao, Krapp, Al Ouahabi, König, Cirauqui, Radenovic, Lutz, Dal Peraro, Aerolysin nanopores decode digital information stored in tailored macromolecular analytes, *Science Advances*, 6(50), eabc2661, 2020.

## BIOGRAPHICAL SKETCHES

Matteo Dal Peraro graduated in Physics at the University of Padua in 2000. He obtained his Ph.D. in Biophysics at the International School for Advanced Studies (SISSA, Trieste) in 2004. He then received postdoctoral training at the University of Pennsylvania (Philadelphia) under the guidance of Prof. M. L. Klein. He was nominated Tenure Track Assistant Professor at the EPFL School of Life Sciences in late 2007. His research at the Laboratory for Biomolecular Modeling (LBM), within the Interfaculty Institute of Bioengineering (IBI), focuses on the multiscale modeling of large macromolecular systems.