Dottorato di Ricerca in Fisica

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All-atom computer simulations empower a new paradigm in drug discovery

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Physics-based computer simulations can provide microscopic insight into fundamental biomolecular processes, but are limited by their huge computational load. Our team has developed algorithms that exploit some mathematical methods of theoretical physics to overcome some of these issues, making it possible for the first time to microscopically reconstruct the folding mechanisms of biologically relevant proteins with an atomic level of resolution. This technology led us to develop a new paradigm for drug discovery named Pharmacological Protein Inactivation by Folding Intermediate Targeting (PPI-FIT), which is based on finding small molecules that trigger protein degradation by hindering the folding process. For example, using PPI-FIT we found small molecules that can selectively modulate the cellular expression of the human prion protein, which is involved in neurodegenerative diseases for which conventional methods have been largely ineffective. We then planned an experiment in the International Space Station executed in August 2023 that aims at developing the technology to exploit microgravity conditions to obtain crystals partially folded proteins in complex with one of the small molecules we discovered using PPI-FIT.

In the last part of this talk, how integrating emerging computational technologies (AI and quantum computers) may help us enlarge the range of applicability of molecular simulations will be discussed, and this could potentially suggest new therapeutic strategies.

The seminar is in presence up to the maximum occupancy of the lecture hall.