Title	**Stochastic Approaches to LargE Molecules (SALEM)**
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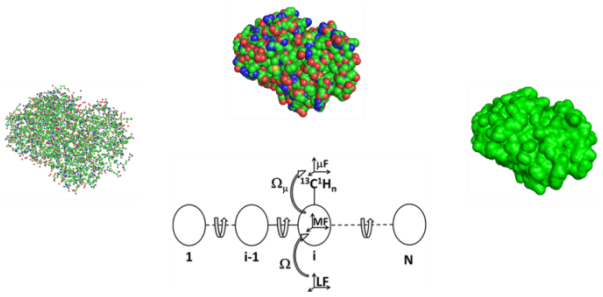
Project description:

Objectives - Biochemical patterns in living systems are based in several instances on mechanical events, resulting from proteins undergoing large amplitude motions (LAMs) triggered by chemical signals. This projects aims at 1) interpreting and simulating LAMs and their related spectroscopic signatures using advanced computational chemistry approaches, 2) describing at molecular level behaviors induced by localized structural changes due to chemical modifications, 3) extend this methodology to supramolecular systems



Background - Chemical and spectroscopic properties are affected by the rotational and internal dynamics in macromolecules and supramolecular constructs. In particular, spectroscopic observables can be used for monitoring of relaxation processes in macromolecules, including LAMs. Integration with advanced theoretical/computational methods proves to be particularly effective to acquire direct information on long-range relaxation processes, based on molecular dynamics, multiscale approaches and coarse-graining treatments. Together, the analysis of spectroscopic signatures and the integrated computational approach can provide a fundamental tool to understand the effect of biochemical changes on specific proteins, and contribute to the rational design of dedicated drugs. As such, a bottom-up approach based on the joint efforts of biochemists, spectroscopists and theoretical chemists is pursued in several advanced laboratories worldwide.

Project description - The roadmap will be as follows: 1) set up of computational interpretation of spectroscopic evidences based on in-silico evaluation of structural properties at atomistic level (obtained via mechanics/molecular mechanics), 2) short time scale dynamics (ps-ns scale, via molecular dynamics) 3) long time-scale dynamics (above ns scale, stochastic and coarse grained approaches); 4) classification, rationalization and prediction/simulation of the effects that chemical changes cause as perturbations of the molecular movements, 5) investigation of dynamic properties of supramolecular systems

Expected results - Basic science outcomes are expected: 1) the development of advanced *in-silico* tools (novel software packages) capable to reach predictive level relatively to the relation between structural changes and dynamics for triggered mechanics of macromolecules; 2) refined characterization tools bridging the gap between indirect spectroscopic observation of large amplitude motions and chemical properties of macromolecules; 3) rationalization of the effect of inter and intramolecular motility on the construction of self-assembling systems.

Publications:

- Flexibility at a glycosidic linkage revealed by molecular dynamics, stochastic modeling, and C-13 NMR spin relaxation: conformational preferences of alpha-L-Rhap-alpha-(1 -> 2)-alpha-L-Rhap-OMe in water and dimethyl sulfoxide solutions R. :Pendrill, R O. Engstrom, O A Volpato, M Zerbetto, M A Polimeno, G Widmalm, G Phys Chem Chem Phys , 18 (4) 3086-3096 DOI: 10.1039/c5cp06288h (2016)
- Decomposition of Proteins into Dynamic Units from Atomic Cross-Correlation Functions P. Calligari, Gerolin, D Abergel, A Polimeno J. Chem Theory and Computation, 13, 309-319 DOI: 10.1021/acs.jctc.6b00702 (2017)

Collaborations/Network:

Collaborations with French (École Normale Supérieure, Paris), American (Cornell University, Case Western Reserve University), Swedish (Stockholm University) groups will be carried on during this project, with the possibility of short (one months) or medium (up to twelve months) term secondments abroad for the students involved.

Research funding:

Fondi di ateneo (P-DISC) and European (COST) limited funds will be accessible.