Contribution ID: **33** Type: **not specified**

Molecular dynamics insights into the stabilization of nucleic acid quadruplexes

Wednesday, 18 March 2026 11:00 (30 minutes)

Guanine-rich nucleic acid sequences can fold into G-quadruplexes (GQs), noncanonical DNA structures stabilized by stacked G-tetrads and monovalent cations, which play important roles in genome regulation and are widely investigated as drug targets. Despite extensive experimental and computational work, predicting G-quadruplex stability and ligand-induced stabilization remains difficult. Molecular dynamics simulations have shown that even for well-characterized telomeric GQs, apparent structural stability depends sensitively on the choice of ion parameters and water models, with different parameterizations leading to distinct ion residence times, channel occupancies, and loop dynamics. This sensitivity underlies a key limitation of docking approaches: while docking can identify plausible ligand binding poses, it cannot predict whether ligand binding will stabilize or destabilize the GQ, as it neglects the dynamic coupling between ligands, ions, hydration, and flexible loop regions, and docking energies do not reflect GQ stability. Atomistic molecular dynamics simulations provide a way to address this limitation by explicitly capturing ligand-induced reorganization of the ionic environment and local structure. To overcome the gap between accessible simulation times and experimental denaturation times, simulations performed at variable temperature can be used to accelerate destabilization events. I will present studies combining docking and variable-temperature molecular dynamics simulations to clarify ligand effects on G-quadruplex stability.

Primary author: Prof. MOCCI, Francesca (University of Cagliari)

Presenter: Prof. MOCCI, Francesca (University of Cagliari)