Ph.D. in Information Technology
Thesis Defense

February 20th, 2026
at 14:30 pm
“Alessandra Alario” Seminar Room – building 21

Letizia MESSA – XXXVII Cycle

Leveraging Computer-Based Methods for Biomarker Discovery and Drug Repurposing in Neurodegenerative Diseases

Supervisor: Prof. Pietro Pinoli

Abstract:

Neurodegenerative diseases are among the most urgent health challenges of our time. Parkinson’s Disease (PD), in particular, remains without disease-modifying therapies, and current treatments address symptoms without altering the underlying biology. Identifying early molecular changes and new therapeutic strategies is therefore a critical unmet need. This PhD project tackles these challenges through an integrated computational framework built on three pillars: transcriptomics, interpretable machine learning, and drug repurposing. First, large-scale RNA-seq analyses across six brain regions revealed strong spatial heterogeneity, highlighting that PD affects different brain circuits in distinct ways. In parallel, longitudinal blood analyses from the PPMI cohort identified dynamic molecular changes during the prodromal phase, with a “critical window” emerging one to two years before clinical diagnosis. Integration of brain and blood data uncovered a shared cross-tissue molecular signature, laying the groundwork for blood-based biomarkers. Second, interpretable machine-learning models were developed to quantify a “PD-likeness” score, positioning individuals along a continuum from health to disease. This approach enabled molecular stratification of prodromal subjects and linked disease similarity to biologically relevant pathways, including oxidative stress and neuroinflammation.

Third, a novel network-based computational framework for drug repurposing was introduced. The proposed method achieved high predictive performance and identified promising therapeutic candidates supported by independent evidence. Finally, the work contributes to the Horizon Europe BETTER project, advancing GDPR-compliant, federated infrastructures for secure and large-scale biomedical data analysis. Together, these results demonstrate how computational methods can bridge molecular biology, patient stratification, and therapeutic innovation—paving the way toward earlier diagnosis and more effective interventions in Parkinson’s Disease.

PhD Committee

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