Rethinking Natural Product Discovery Workflows Using Ambient Mass Spectrometry

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Natural products (NP) remain one of the richest sources of new bioactive molecules, yet workflows traditionally used them are slow, resource-intensive and often unsustainable at scale. This PhD seminar will present a streamlined approach that combines ambient mass spectrometry with machine learning to accelerate early stage decision making in natural product discovery. Specifically, I integrated the Liquid Microjunction Surface Sampling Probe (LMJ-SSP) with Partial Least Squares Discriminant Analysis (PLS-DA) as a triaging tool, in conjuction with the Global Natural Products Social Molecular Networking (GNPS) platform.

Using this workflow, we analyzed three strains of *Penicillium spp.* grown under seven different carbon conditions *in situ*, without sample preparation. PLS-DA enabled us to highlight growth conditions that generated distinct chemical profiles and prioritize features (specific m/z values) most responsible for driving metabolic diversity. These prioritized metabolites were then placed in context through GNPS molecular networking, where connected chemical communities provided insight into novel or underexplored compounds.

Overall, this integrated approach reduces time, cost, and solvent use while providing chemically informed guidance before more resource-intensive isolation and characterization steps. This workflow demonstrates how the LMJ-SSP and machine learning can reshape the efficiency and sustainability of natural product discovery.