# OncoLink: Novel Cancer Detection via Irreducible Regulatory-Metabolic Coupling Using a Topology-Aware Dual-Modality Nanobiosensor?

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Cancer remains one of the leading causes of mortality due in part to the limitations of current diagnostic methods, which often rely on single biomarkers and fail to capture the systemic biological changes induced by tumors. This study investigates whether joint sensing of regulatory signals, specifically exosomal microRNAs (miRNAs), and metabolic signals, specifically volatile organic compounds (VOCs) in exhaled breath, can reveal diagnostic information that is irreducible to either modality alone. The purpose of this research was to develop a rapid, non-invasive dual-modality nanobiosensor capable of capturing cross-domain biological dependencies and to evaluate whether explicitly modeling these dependencies improves diagnostic accuracy and robustness. It was hypothesized that joint regulatory-metabolic sensing would provide additional, synergistic information inaccessible to unimodal measurements and that modeling the new interaction between modalities would enhance stability under noise and variability. To test this, a microfluidic digital CRISPR-based miRNA detection module and a topology-aware VOC sensor array were constructed, and their outputs were analyzed using a custom coupling-aware machine learning model trained on both synthetic and real datasets. The biosensor achieved a ROC-AUC of 0.992, 98.53% accuracy, 97.91% sensitivity, and a 2.09% false negative rate, outperforming unimodal and feature-aggregative multimodal baselines and recovering 0.47 bits of information. Decoupling experiments confirmed that cross-domain dependencies were necessary for maximal performance. These results demonstrate that early cancer detection can be enhanced by capturing irreducible regulatory-metabolic information, suggesting a shift in diagnostic design toward biosensing.

**Awards Won:**