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Bridging the gap: From hypothesis-independent tests to understanding of biological mechanisms

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A hypothesis-independent approach to building clinically relevant tests allows the creation of multivariate classifiers that reflect the complexity of biological interactions without any bias from expectations about their mechanisms. However, once the classifier is created, it is of interest to understand the biological underpinnings of its performance. Biodesix has developed a new data analytic platform, the Diagnostic Cortex™ that utilizes mass spectral data collected from patient serum samples to create clinically relevant tests without a prior hypotheses or molecular understanding of the underlying biology. It was successfully used to discover and validate a test predicting outcomes for patients with metastatic melanoma treated with the immune checkpoint inhibitor, Nivolumab. To broaden our biological understanding, we applied ideas similar to GSEA (Gene Set Enrichment Analysis) to mass spectral data (PSEA). This approach allowed us to find correlations between classification and sets of proteins associated with known biological functions, such as acute response, wound healing, and complement system. Through the association of mass-spectral features with functional sets of proteins, we constructed a biological score, calculated for each individual sample and serving as a measure of importance of a particular biological process. These scores, as well as their changes, were found to be associated with clinical outcomes of patients, at the same time providing some insights into related biological mechanisms.

Biography

Heinrich Roder is an author of more than 100 publications and talks spanning the fields of theoretical physics, computational sciences, and molecular diagnostics. A Rhodes Scholar, he earned his DPhil in Theoretical Physics from Oxford University and has held positions at the Universities of Hanover and Bayreuth and Los Alamos National Laboratory. He is a Founder of Biodesix. Serving as CTO, he leads the work of the Research and Development team on sensitive, high-throughput MALDI mass-spectrometry profiling of blood-based samples and the development of molecular diagnostic tests using a machine learning platform incorporating elements of deep learning.

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