Cell phenotype classification by NMR spectroscopy of intact cell lines

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Magnetic Resonance Imaging (MRI) is a primary tool for characterizing Central Nervous System (CNS) structures and lesions, but its accuracy in differentiating lesion types (inflammatory, ischemic, neoplastic) is limited. Chemical Shift Imaging (CSI), or MR Spectroscopic Imaging (MRSI), offers promise by providing biochemical tissue characterization. CSI resolves Nuclear Magnetic Resonance (NMR) spectra of different voxels, mapping soluble chemical components and metabolites to potentially classify microenvironments based on their unique spectral fingerprints. However, clinical application of CSI faces several challenges, which restrict its application to the CNS typically to a few abundant brain metabolites. While ultra-high field NMR spectroscopy excels in analyzing complex biofluid mixtures and microenvironments, in situ NMR metabolomics on intact cells or tissues yields broadened spectral features, similar to those found in the CNS. Here we show that the poorly-resolved NMR spectral features of intact cells can be used to classify normal and pathological CNS cell types in vitro. By applying machine learning to reduce spectral dimensionality and classify the spectra, we aim to detect metabolic fingerprint alterations in different cell types and their time-related changes during neural stem cell differentiation. This approach, validated on human cell types relevant to CNS histology and pathology, shows that multivariate analysis and machine learning can accurately classify pure and mixed cell populations, and track phenotype changes. This methodology holds potential for improving in vivo CSI for differential diagnosis of human CNS diseases.