Quality assessment of MALDI TOF and ion mobility MSI data based on mass defect and CCS filtering

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Motivation

- MALDI imaging and ion mobility MSI (IMS-MSI) are valuable tools for peptide, lipid, or glycan imaging from biological tissue samples
- Variation of matrix effects relative to analyte signals limits robustness and reproducibility
- We use mass defect filtering to analyze matrix contribution and quantify spectral data quality, as well as an adaptation to collisional cross-section (CCS) aware IMS-MSI

Methods and Results

- Kendrick mass defect filtering with a peptide specific scaling factor allows separation between peptide and matrix signal (**Fig. 1**)
- A signal quality score (SQS) is computed representing the relative total ion current attributable to peptides (**Fig. 2**). A similar approach is feasible for glycan imaging (**Fig. 3**).
- In developing tissue typing classifiers, normalization to SQS improves classification accuracy. Moreover, classifier performance is directly correlated to spectral data quality (**Fig. 4**).
- In IMS-MSI, signal quality scoring is achieved similarly by defining a signal corridor in the mass-mobility-plane, allowing to automatically recognize spatial regions with low spectral data quality (**Fig. 5**)

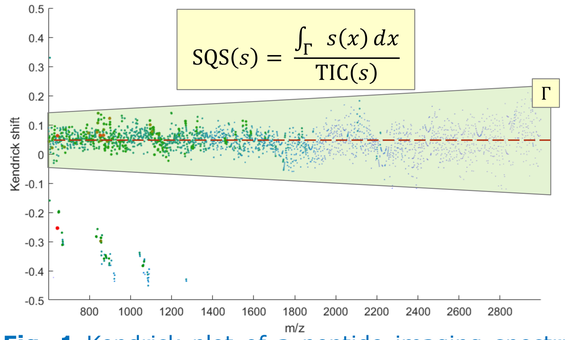


Fig. 1 Kendrick plot of a peptide imaging spectrum using an appropriate Kendrick scale. Signal quality score (SQS) is computed as the relative total ion count (TIC) in the horizontal peptide corridor Γ. Location and shape of Γ is adapted to the data [1].

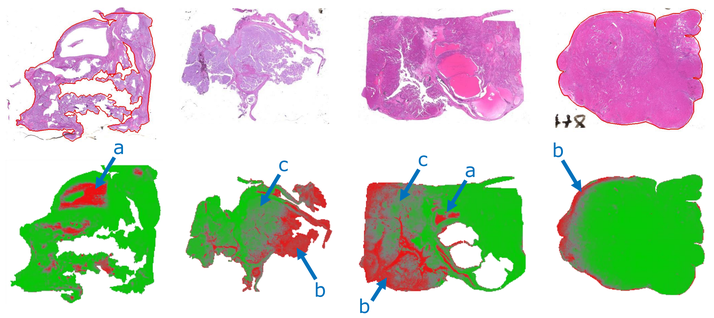


Fig. 2 SQS maps reveal areas affected by low signal quality (red), such as off-tissue regions (a), as well as effects of inhomogeneous sample preparation (b) or increased tissue vascularization (c) [2]. *MALDI axial TOF, tryptic digestion*

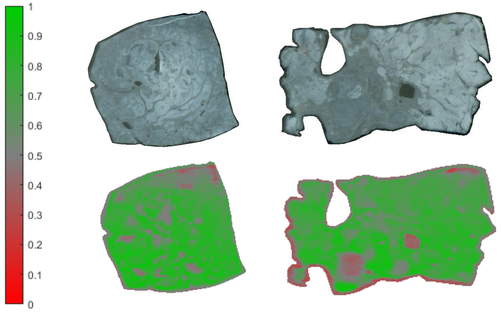
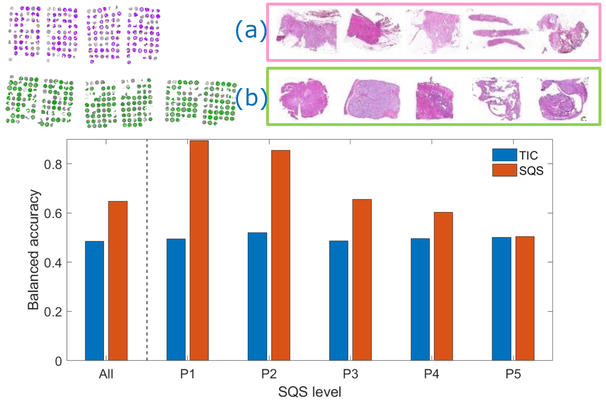


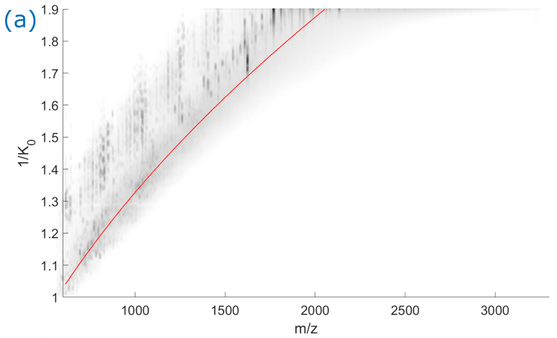
Fig. 3 The method is also applicable to imaging of N-linked glycans when using a Kendrick scale appropriate for this class of molecules [2]. *MALDI axial TOF, PNGase digestion*

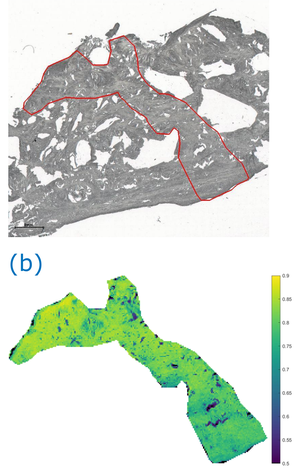
Fig. 4 Tissue typing of breast (a) vs. ovarian (b) cancer tissue [3]. Classifier was trained on TMAs (left), tested on whole sections (right). *MALDI axial TOF, tryptic digestion*



Accuracy increases when normalizing on SQS (red) instead of standard TIC (blue). Accuracy on high quality spectra subsets (P1, P2) is significantly higher than on low quality spectra subsets (P3-P5).

Fig. 5 Adaptation to IMS-MSI. (a) Dominant N-glycan signal corridor is localized automatically in mean mobilogram by logarithmic regression. (b) SQS is computed per spot by comparing signal in corridor to overall TIC. Low SQS regions correspond to tissue gaps within measurement region. *MALDI TIMS Q-TOF, PNGase digestion*





Conclusions

- Automated quantify-cation of matrix and analyte components in MALDI MSI and IMS-MSI data allows assessing spectral data quality and acquisition artifacts
- Signal quality score based on Kendrick mass defect filtering improves tissue classification
- In CCS imaging, auto-mated signal quality scoring reveals sample regions with low analyte abundance

References

[1] Boskamp et al.; Anal. Chem. 2020, 92, 1, 1301-1308. DOI: 10.1021/acs.analchem.9b04473 [2] Boskamp et al.; Ourcon VII, 2019, Saint-Malo (FR) [3] Cordero et al.; Prot. Clin. Appl. 2019, 13, 1700168. DOI: 10.1002/prca.201700168