Predicting REIMS from MALDI: to prevent destruction of glioblastoma sections used for model improvement

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Introduction

Rapid evaporative ionization mass spectrometry (REIMS) is an analytical technique that determines the **metabolic composition** of evaporating tissue during electrosurgical resection in real-time. The destructive nature of this method, i.e., burning the tissue, complicates further analysis of a tissue sample [1].

The **matrix-assisted laser desorption ionization mass spectrometry imaging (MALDI-MSI)** technique is employed to gauge the **quantity and spatial distribution** of molecules within the tissue sample. **Both techniques measure mass spectra** at specific spatial locations, albeit with different spatial resolutions and different ionization sources, but identical Quadrupole Time-of-Flight detectors.

To circumvent the **destructive nature of REIMS**, a deep learning-based approach is developed to predict REIMS data based on the results obtained from a MALDI-MSI experiment on the tissue sample. The model can, at a later stage, be used to improve in surgery, real-time tissue-type prediction.

Challenges

This work focuses on the prediction of REIMS spectra from MALDI-MSI lipidomics data of human glioblastoma stage IV samples. A robust method is developed to overcome the challenges that arise due to the intermodal nature of the problem:

- Preprocessing REIMS: detecting and retrieving measurement from time signal, removing mass lock and its fragments, binning
- Preprocessing MALDI-MSI: intrasample peak alignment followed by alignment of average pixel to REIMS spectra, binning
- Detecting MALDI-MSI pixels from which the REIMS measurement was taken by intermodal peak alignment as REIMS burning point spans several MALDI-MSI pixels
- Matrix effects, not identical in a single MALDI-MSI sample and not identical between MALDI-MSI samples
- MALDI-MSI takes information from a slim tissue slice, whereas during a REIMS experiment, information aggregates from deeper within the tissue
- Fragmentation patterns can differ between modalities
- Scarse amount of output spectra
- Interpretability of the developed model (using Shapley values [2])

Method

Detection of pixels

Use similarity measure to detect most similar aggregated MALDI-MSI mass spectrum to the REIMS mass spectrum after alignment in the 600-900 Da m/z range

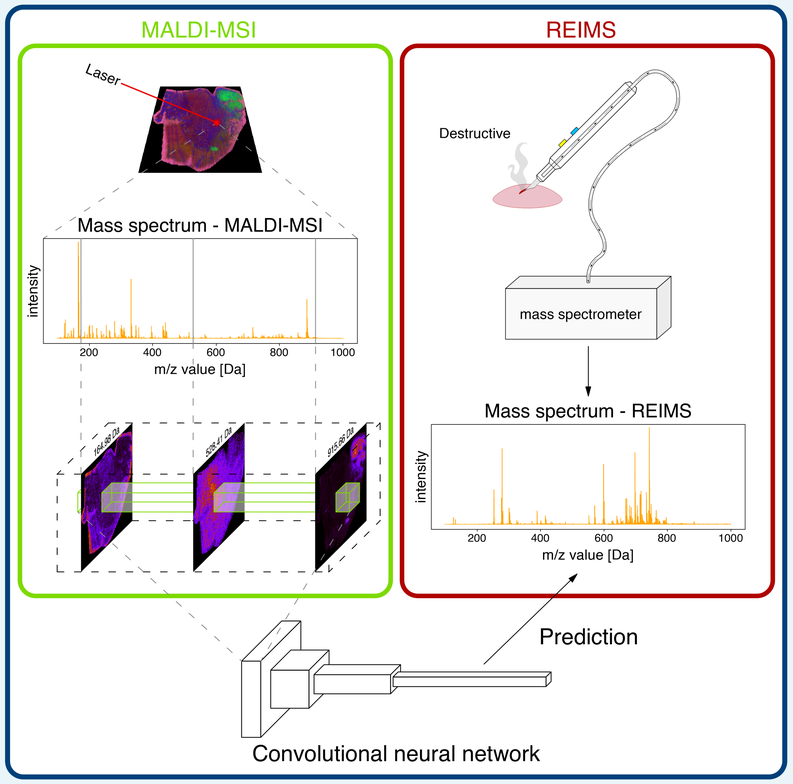


Figure 1: Overview of the prediction task.

Model

- Reduce computational cost by performing dimensionality reduction (1×1 convolution)
- Train a convolutional autoencoder on 48×48 patches (estimated size of surface of iKnife) of MALDI-MSI pixels to learn rich latent representation
- Predict REIMS mass spectrum using the detected MALDI-MSI pixels from learned latent space, as shown in Figure 1, to improve performance with scarce amount of data [3]
- Validate model on unseen data and interpret results

Results

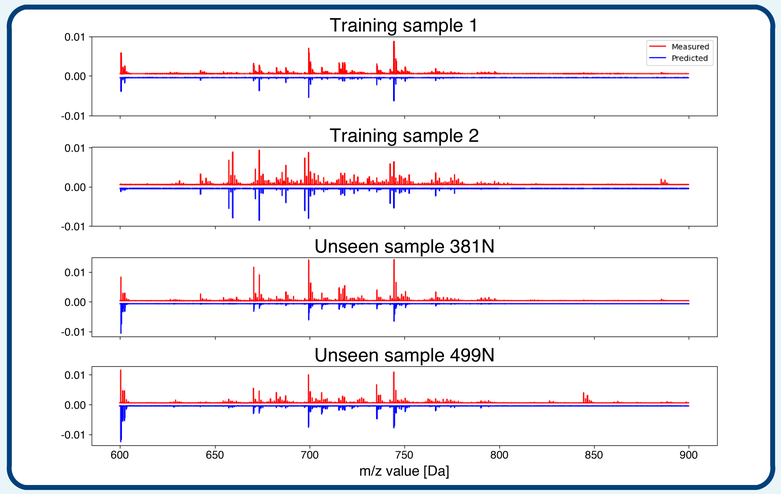


Figure 2: Predictions of the model on training and unseen samples.

The model learns the most relevant peaks and has difficulty predicting the m/z values which are underrepresented in the training data, or have a smaller amplitude, see Figure 2. For example, the model fails to predict m/z values around 850 Da, which were not present in any training sample. The targets are TIC normalized, but the predictions are not. As a consequence, absolute intensities are not always predicted correctly, whereas relative intensities are more accurate.

Conclusion

The proposed convolutional neural network is **able to capture** the majority of **important features** by leveraging the powerful abstract representations of the trained autoencoder to infer the REIMS measurement data from the MALDI-MSI results. However, the model fails to predict several m/z values and the results are not TIC normalized. The latter is possibly solved by incorporating the TIC normalisation in the cost function.

The model enables us to acquire REIMS measurement data without damaging the tissue, preserving them for further experimentation.

Once satisfactory results are obtained, they are fed to an existing REIMS model [4] to improve the model for in surgery, real-time tissue-type predictions during brain surgery.

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ACKNOWLEDGMENTS

This work was supported in part by the KU Leuven: Research Fund (iBOF/23/064, C3/20/117, C3I-21-00316), Industrial Research Fund and several Leuven Research and Development bilateral industrial projects; in part by Flemish Government agencies: FWO (S005319N, T001919N, 11K5623N), EWI and VLAIO (HBC.2019.2204, HBC.2021.0076); in part by the European Commission (ERC Adv. Grant under grant 885682); and in part by the NWO STEM (Project Number 19013 to E.C.) which is financed by the Netherlands Organization for Scientific Research. This research is part of the LINK program which is financially supported by the Dutch Province of Limburg. The authors are thankful to the Department of Neurosurgery of KU Leuven for providing the GBM samples. The resources and services used in this work were provided by the VSC (Flemish Supercomputer Center), funded by the Research Foundation - Flanders (FWO) and the Flemish Government. The authors declare no competing financial interest.