

# Optimized data analysis pipeline for MALDI MSI based tumor typing from FFPE tissue samples evaluated on six benchmark classification tasks

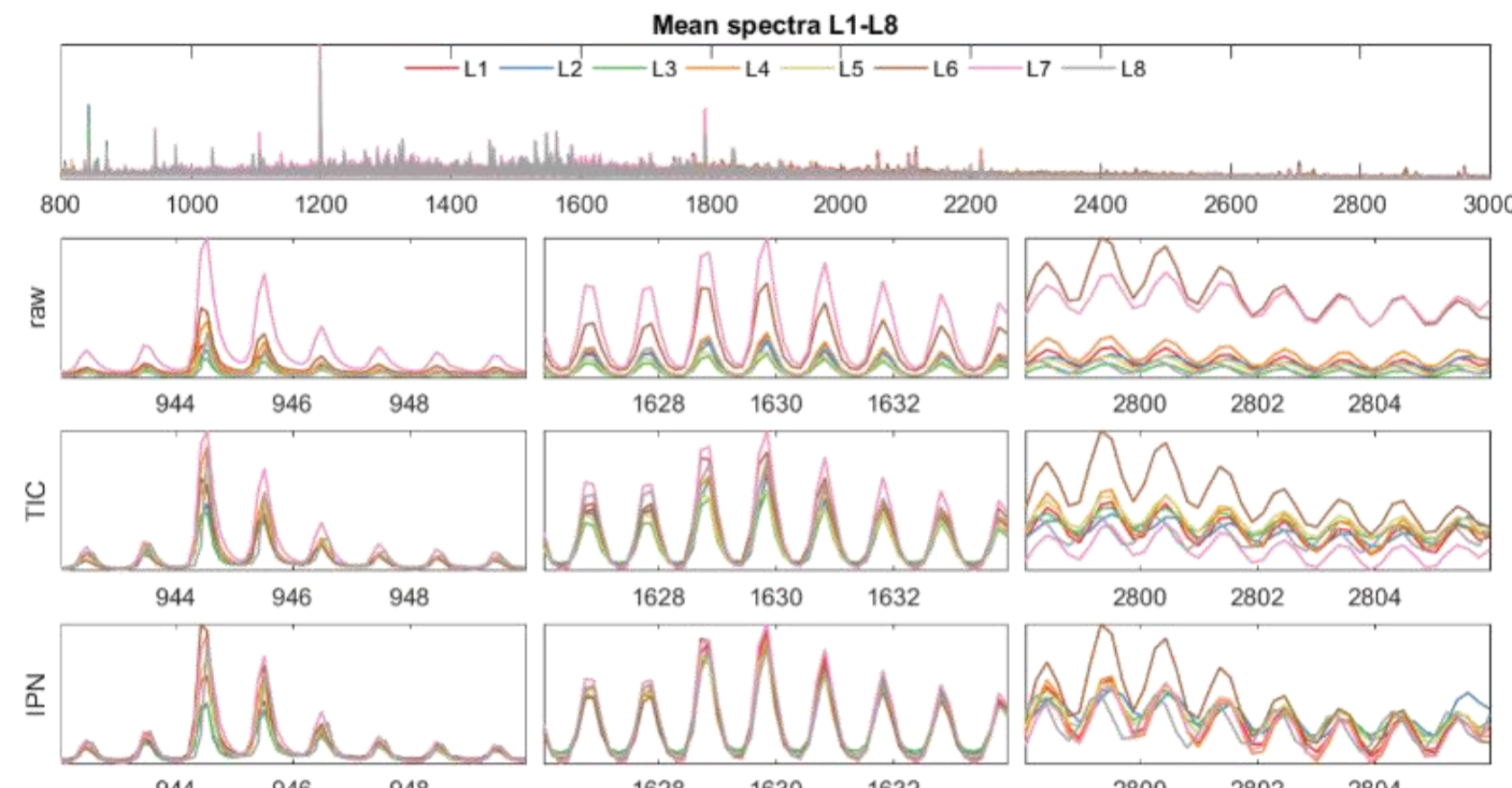
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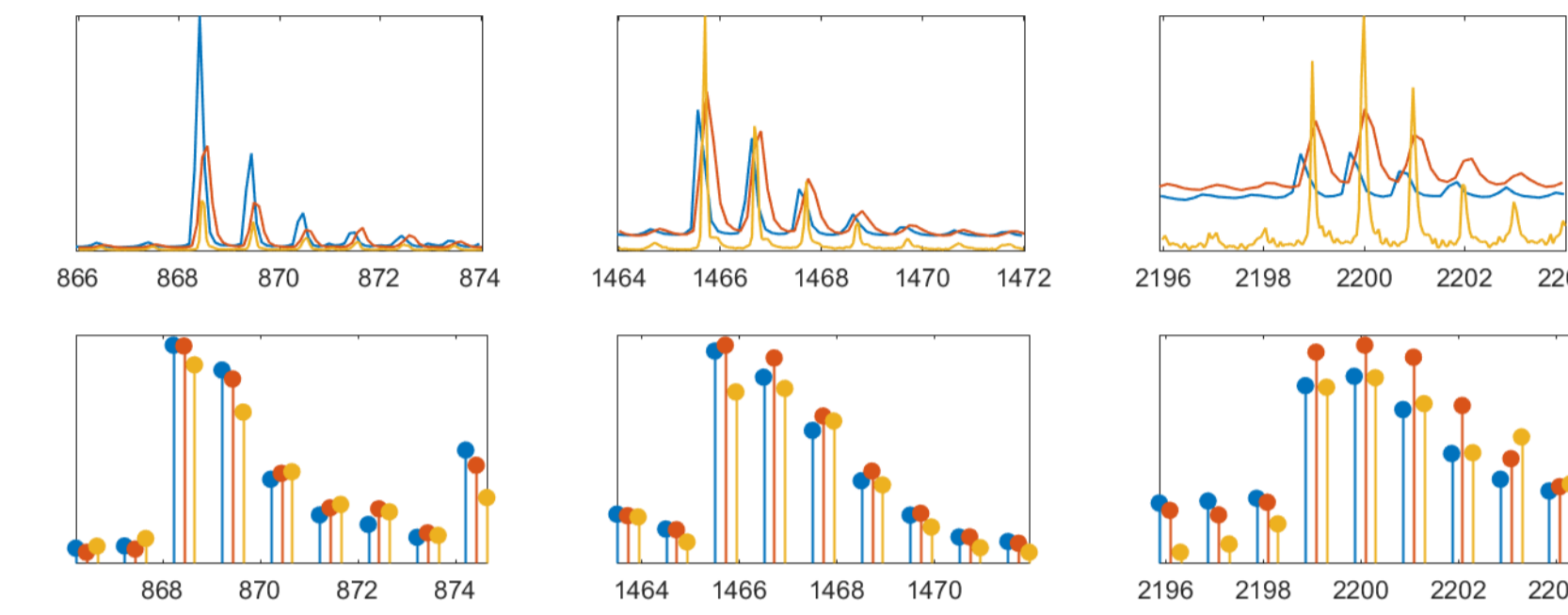
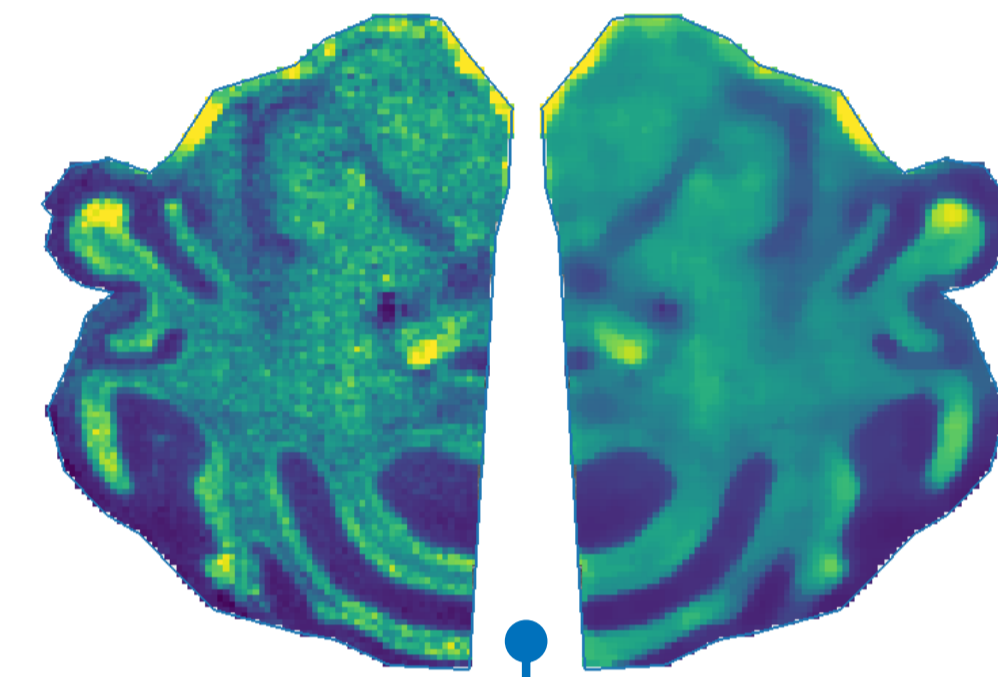
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## Goals

- Develop optimized pre-processing pipeline for MALDI MSI based tumor typing
- Consider different clinical tumor typing and subtyping tasks
- Consider intra- and inter-lab scenarios and different instrument types

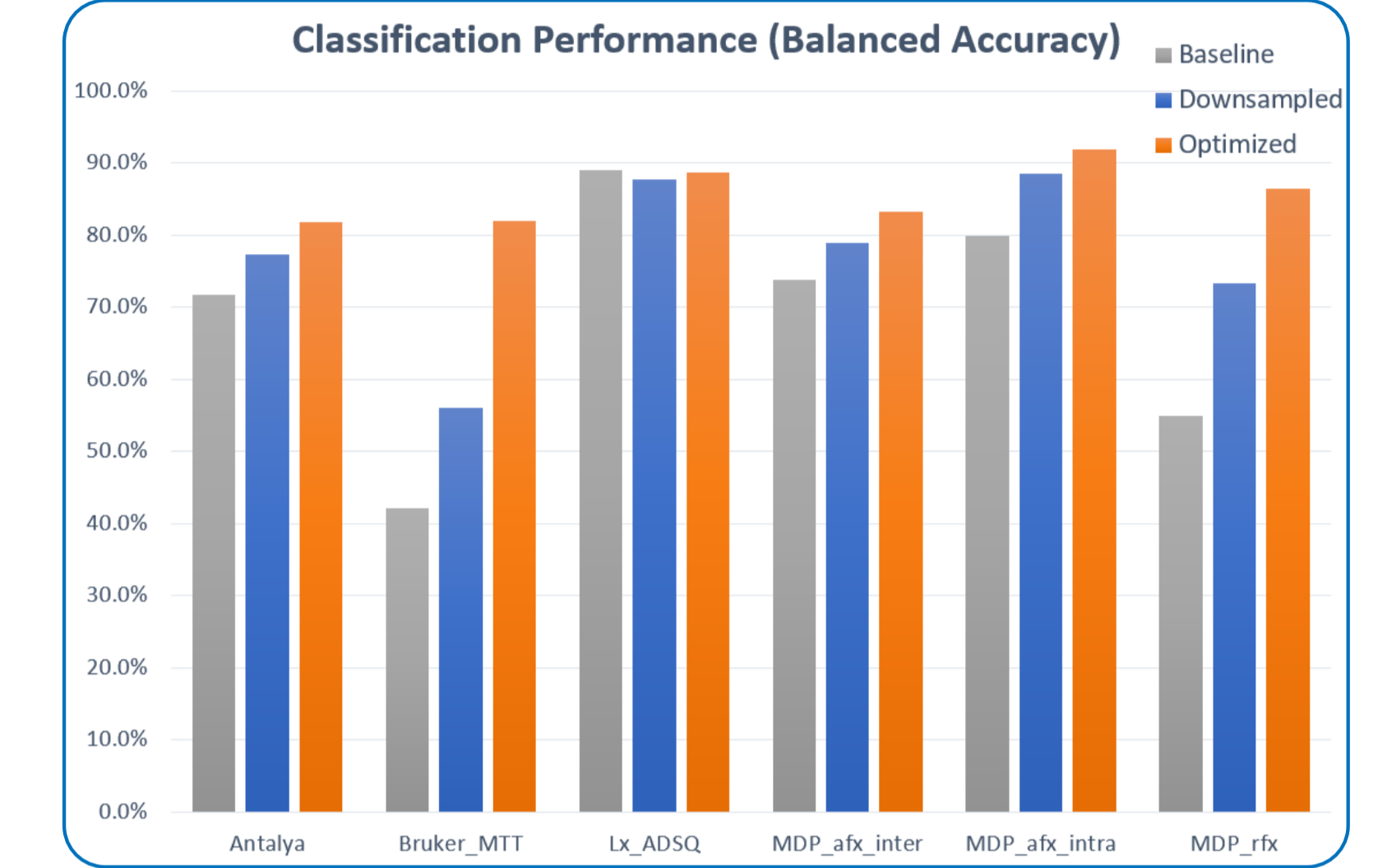


Mild Gaussian kernel **spatial denoising** (right) increases signal-to-noise ratio as compared to original data (left)



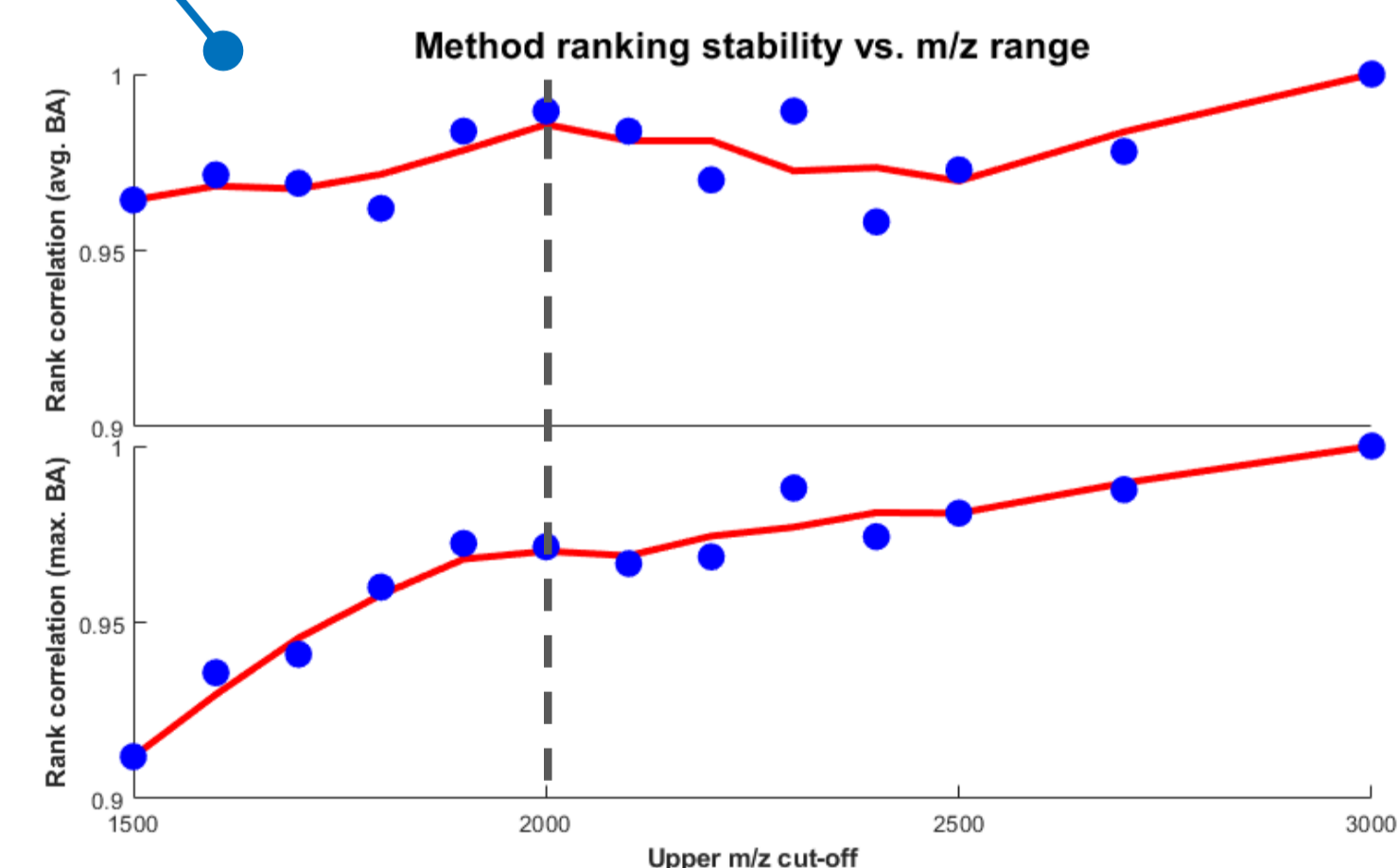
**Dimensionality reduction** by downsampling to peak areas over 0.4 Da intervals (Boskamp et al, ASMS 2018)

Non-linear **intensity profile normalization** (IPN, bottom row) improves comparability across different acquisitions (Boskamp et al, ASMS 2018)



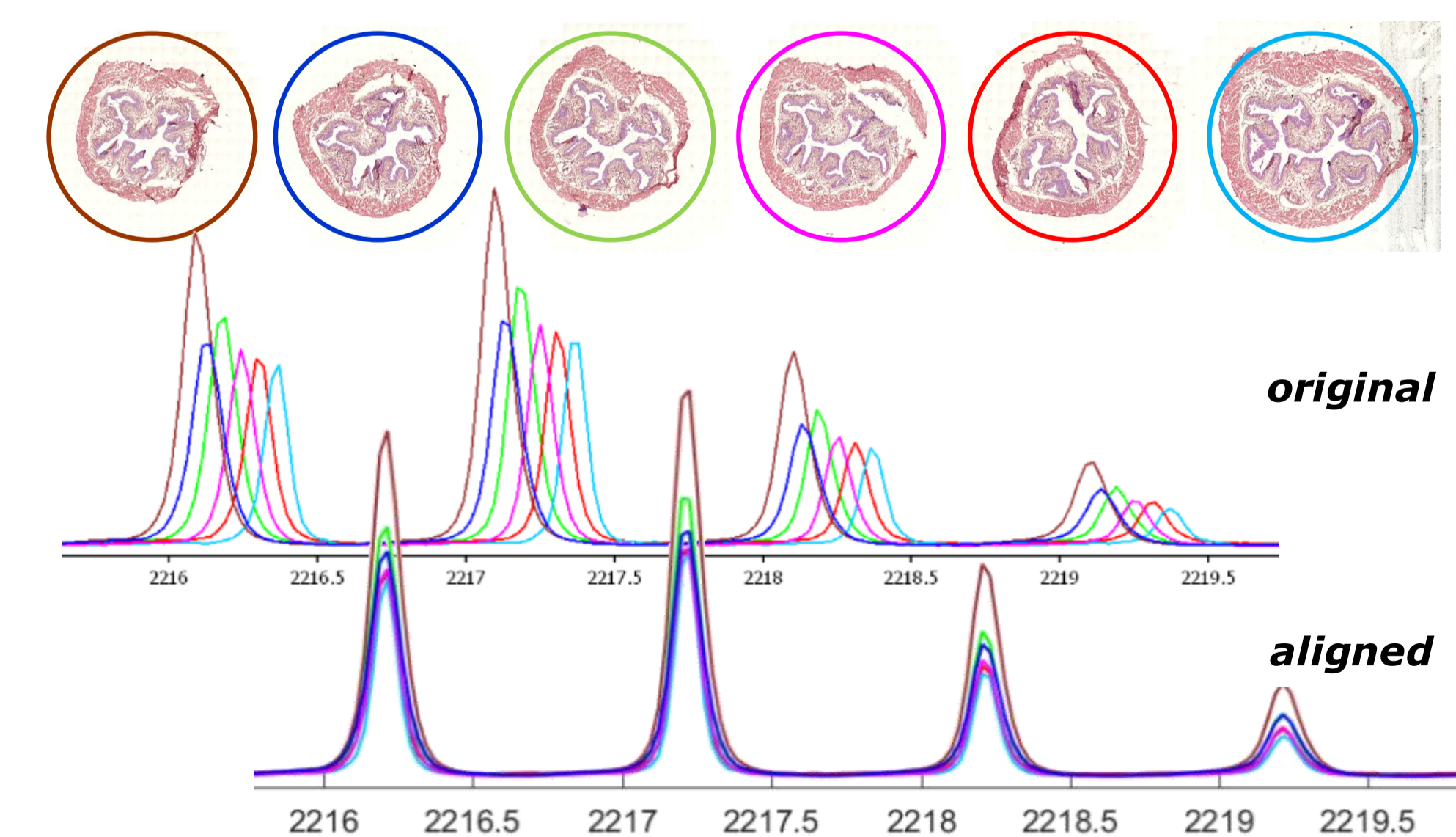
Benchmark panel acquired from **25 TMAs**, **2031 cores** and **1410 patients** total

Task	Instrument	Description
Antalya	autoflex	• Four tumor entities, 8 TMAs • Lung, pancreas, colon, breast
Bruker MTT	rapiflex	• Six tumor entities on one TMA • Five measurements in four labs • Training and test data from different SOP's
Lx ADSQ	autoflex	• Eight TMAs with mix of adenocarcinoma and squamous cell carcinoma, afx
MDP afx inter	autoflex	• Breast, ovary tumors, 5 TMAs • Measured in two labs • Inter-lab cross-validation
MDP afx intra	autoflex	• Same as above, but intra-lab cross-validation
MDP rfx	rapiflex	• Breast, ovary tumors, 5 TMAs • Single lab

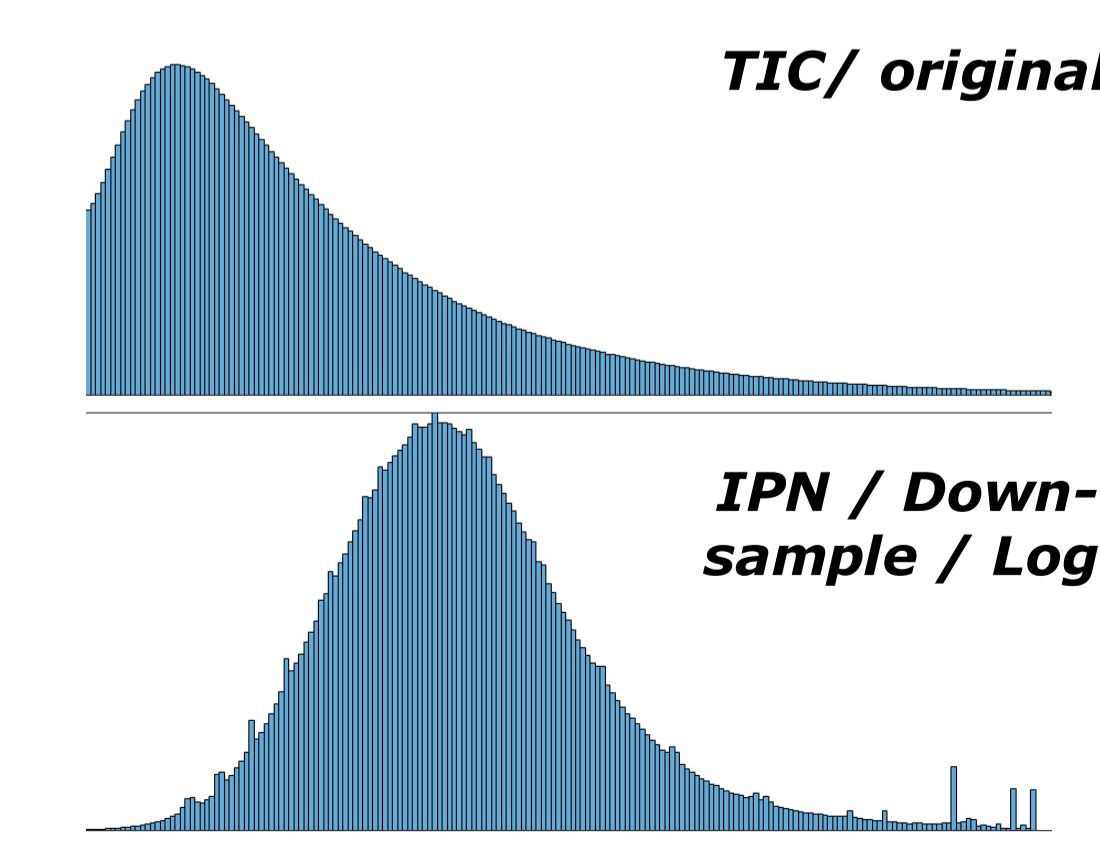


**Reducing mass range** for feature selection down to 700 ... 2000 m/z increases robustness and speed without affecting accuracy

**Mass calibration** based on statistical peptide mass model reduces misalignment (Boskamp et al, ASMS 2018)



**Logarithmic transform** with appropriate scaling results in more symmetric intensity distributions – beneficial for subsequent LDA classification



- Balanced accuracy 82% and 92%
- **Performance gain** over baseline (TIC only) **9.5 ... 39.8% pts.** for five of six tasks
- Mass alignment / downsampling alone yields 5 ... 18.5% pts. for five of six tasks

**Conclusion**

- Systematic investigation of six benchmark problems yields an **optimized pre-processing pipeline** for MALDI MSI tumor typing applications
- **Significant performance gains** achieved in intra- and inter-lab scenarios
- **Improved robustness** towards SOP variations and technical variability

Imaging MS