A novel supervised learning algorithm for real-time collision energy selection to optimize peptide fragmentation in ion mobility-mass spectrometry

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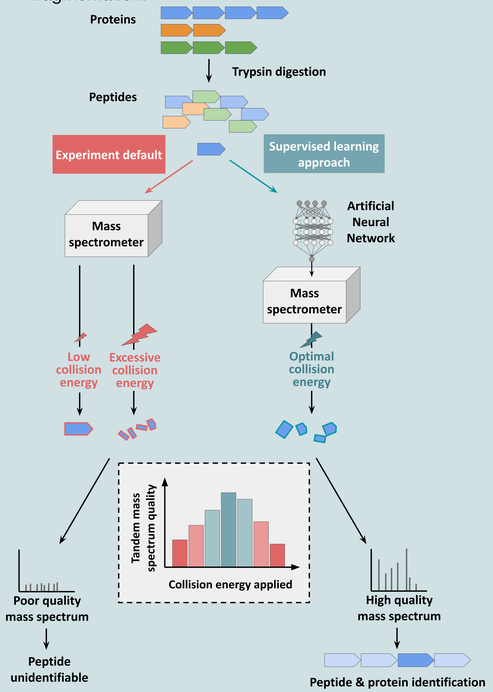
Introduction

- The ability to identify peptides, proteins, and their associated post-translational modifications using mass spectrometry is directly linked to the level of fragmentation of peptide precursor ions.
- Many precursor ion properties such as ion-mobility coefficient, mass-to-charge ratio and charge state affect the amount of collision energy required for optimal fragmentation.

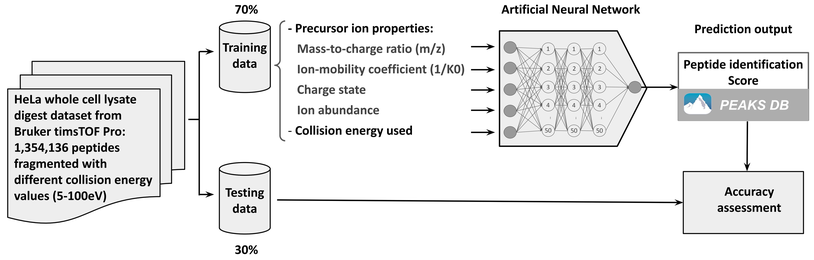


Objective

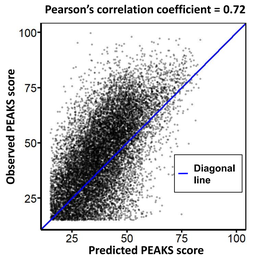
- To build an artificial neural network that selects collision energy that optimizes peptide fragmentation to improve peptide and protein identification sensitivity.

Methodology

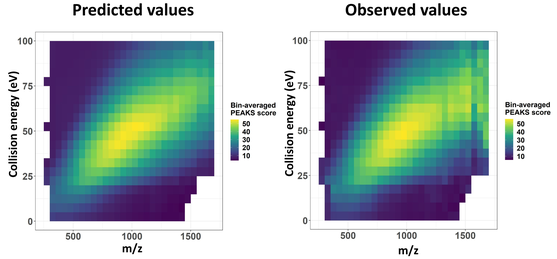
- **Train artificial neural network to predict peptide identification confidence score using precursor ion properties as input.**



Predicted peptide identification scores correlate with observed values

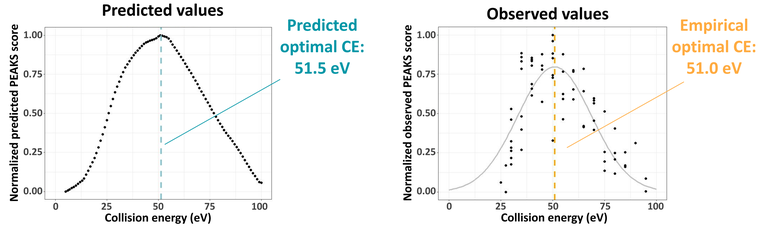


Artificial neural network captures the relationship between m/z and collision energy-dependence of peptide identification score.



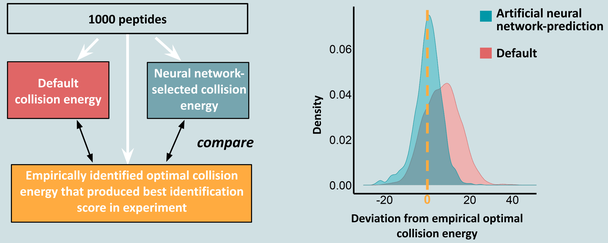
- **Use the trained artificial neural network to predict a peptide's identification score at different collision energy values.**
- **Select optimal collision energy that maximizes identification score.**

Artificial neural network-predicted v.s. observed identification scores at different collision energy values for peptide ion INEELESQYQQSMDSK (+2)



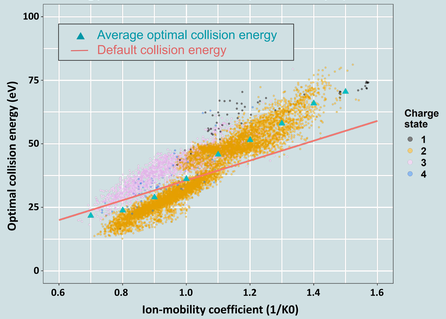
Results

Collision energy values from the artificial neural network reflect empirically-identified optimal collision energy values better than default instrument values.

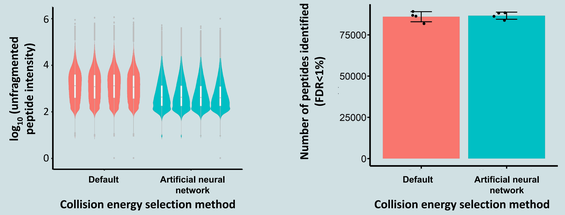


Artificial neural network-selected optimal collision energy shows distinct patterns according to charge state and varies from default collision energy used.

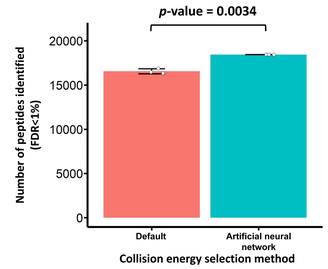
Artificial neural network-predicted optimal collision energy for 10,000 randomly selected peptides



Applying optimized collision energy in real-time improves fragmentation by reducing intensity of unfragmented precursor ion by 2.18-fold on average, without sacrificing peptide identification sensitivity.



Identified 9.7% more peptides with post translational modifications in phosphopeptide enriched samples when using collision energy values selected by the artificial neural network.



Conclusion and Future Directions

- The peptide identification score of a given precursor ion can be accurately predicted by an artificial neural network using only its ion properties and a collision energy value, without any peptide sequence information.
- The artificial neural network enables selection of the optimal collision energy for a given peptide, which improves fragmentation and increases the number of phosphopeptides identified.
- We will assess how our approach improves characterization of samples that are challenging to characterize, such as post-translational modifications of different types (eg. acetylation) or cross-linked peptides.

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