A supervised learning approach to select the collision energy maximizing peptide fragmentation in ion mobility-mass spectrometry

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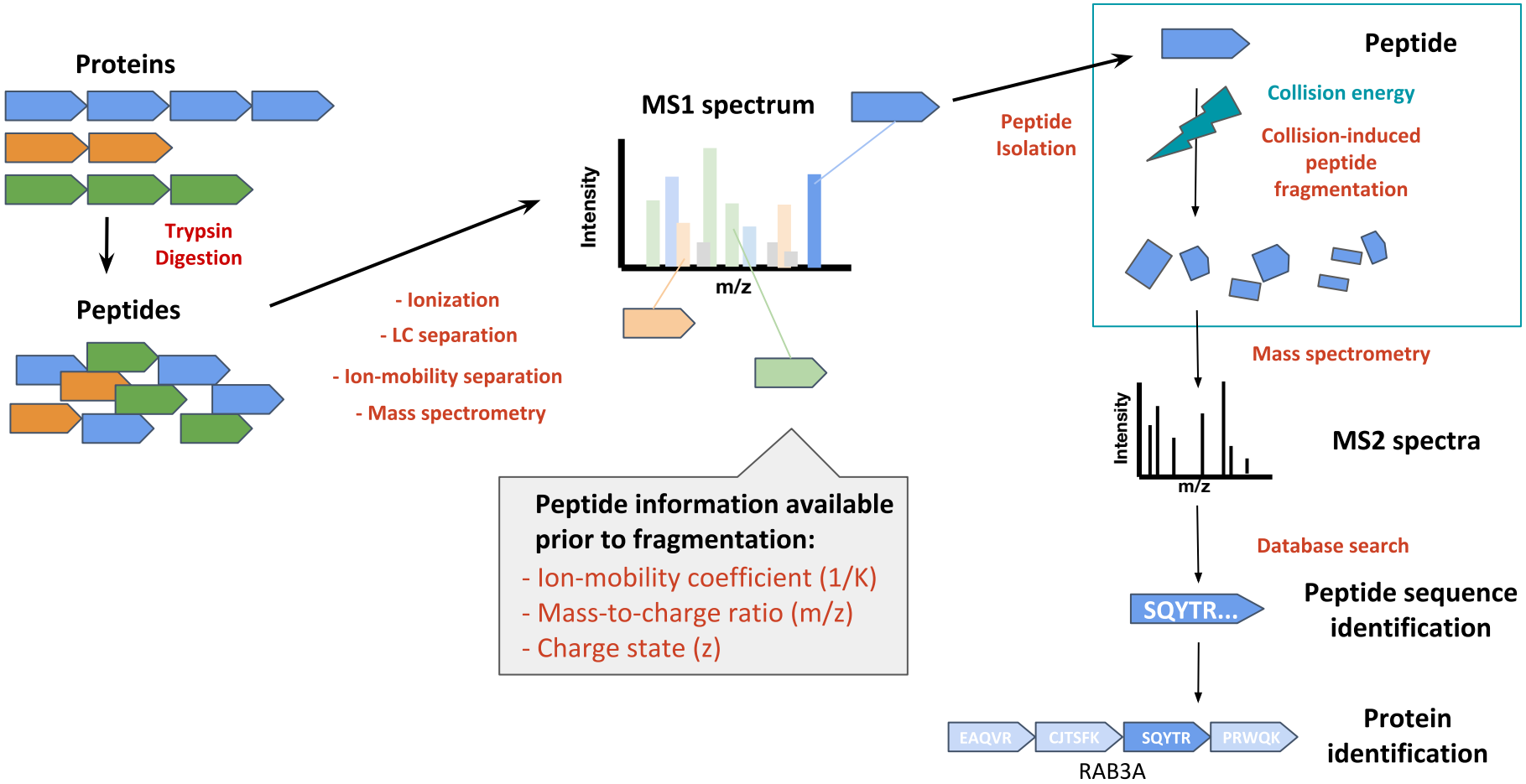
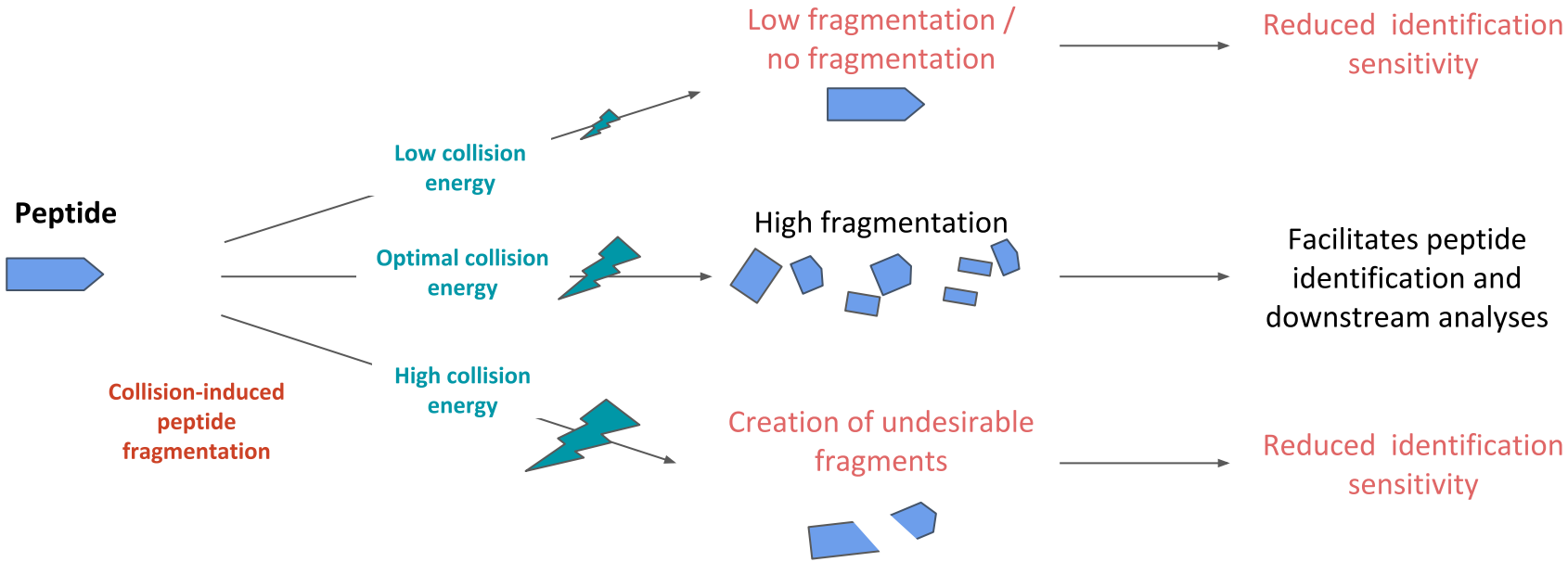
Workflow of an ion-mobility–mass spectrometry proteomics experiment

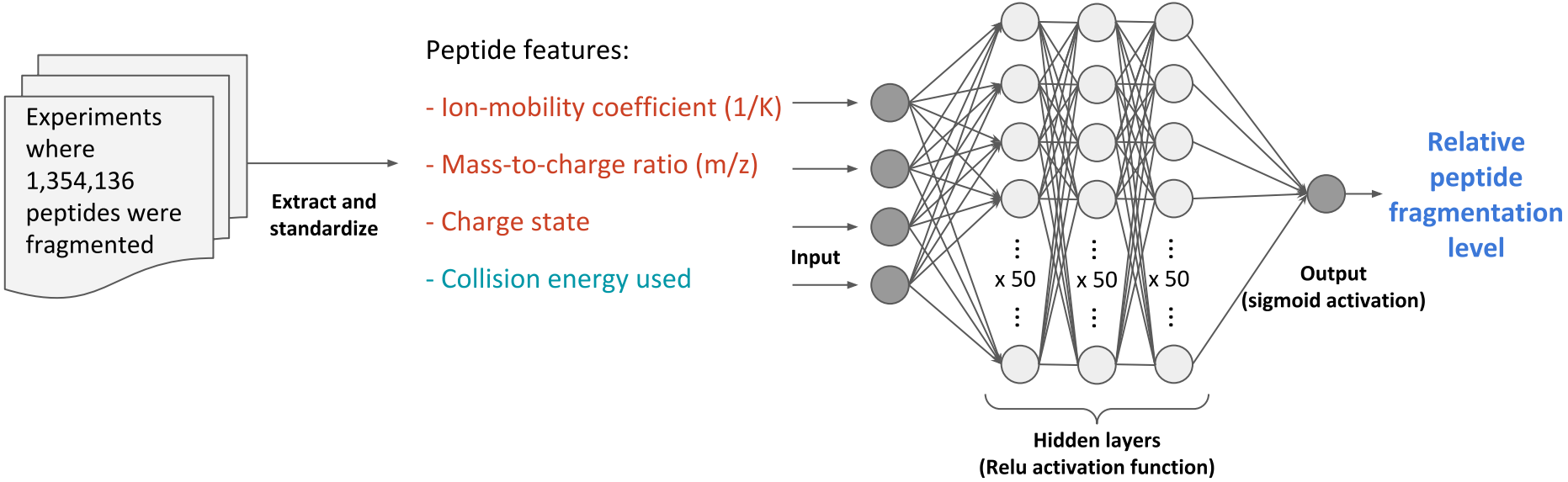


Challenges with peptide fragmentation and collision energy selection



- Mass spectrometers often fail to select the optimal collision energy.
- A significant portion of peptides fail to reach maximum fragmentation, reducing identification sensitivity.
- Collision energy selection is most commonly based on the peptide mass-to-charge ratio, but most mass spectrometers do not consider other peptide properties that are thought to affect to optimal collision energy required.

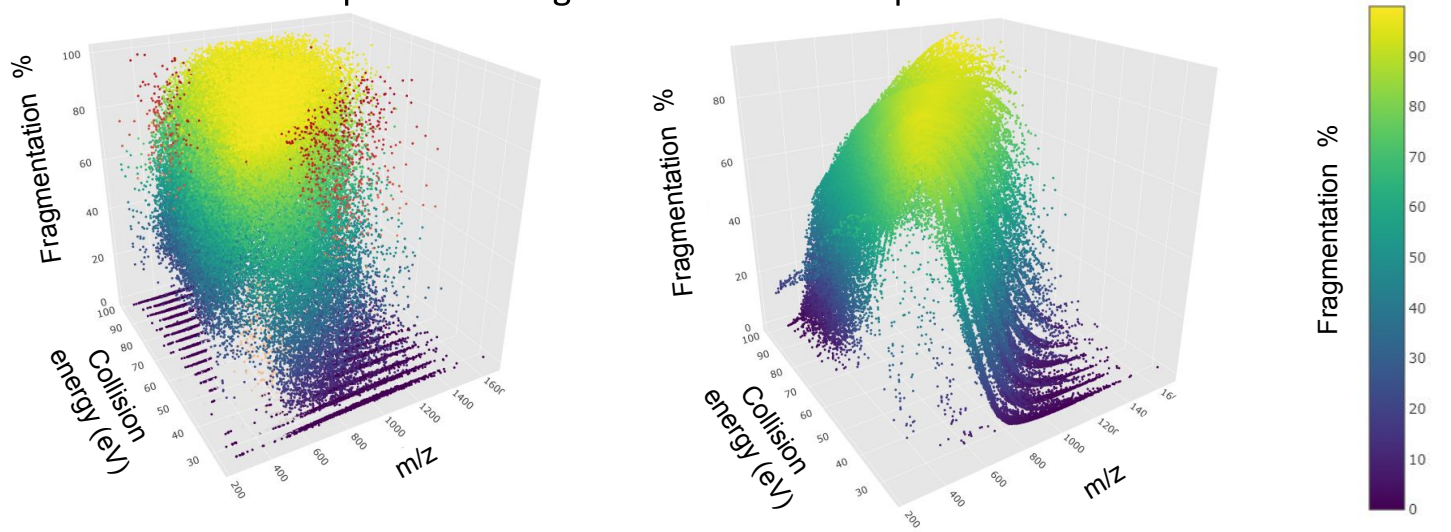
Objective 1: Create an artificial neural network to predict peptide fragmentation level from collision energy and other peptide features.



- A sequential neural network with 3 hidden layers of 50 nodes was constructed.
- Experimental proteomics data gathered with a Bruker timsTOF Pro from 35 HEK293 cell lysates were used as a training set. The amount of collision energy applied was limited to a narrow range in each experiment, giving an uniformly distributed collision energy values spanning from 20~100 eV over the training data.

Neural network performance

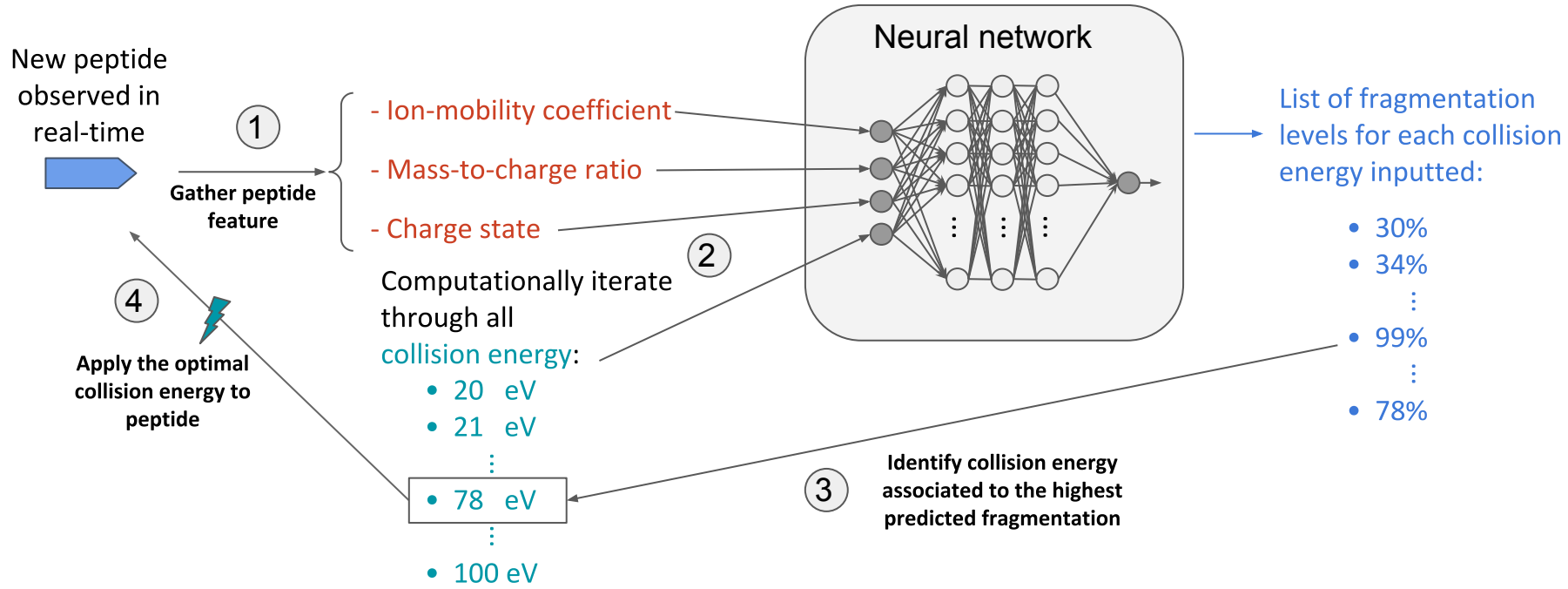
Observed vs predicted fragmentation - scatter plot illustration



Observed Values **Model prediction**

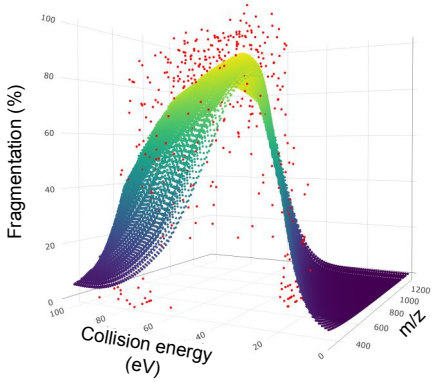
- Modeled capture the general trend that confirms and exemplifies the positive correlation between m/z and collision energy required for optimal fragmentation.
- Note only 2 of the 4 features are displayed here as the independent variables.
- Red-colored points show peptides with fragmentation prediction error > 50% (2.4% of total peptides on the testing set).
- The predicted and observed fragmentation levels have a Pearson's correlation coefficient of 0.80, and a mean-squared-error of 0.0388 (on a output scale of 0~1) on the testing set.

Objective 2: Using the trained neural network, determine the optimal level of collision energy that will result in the highest fragmentation for a given peptide in real-time.

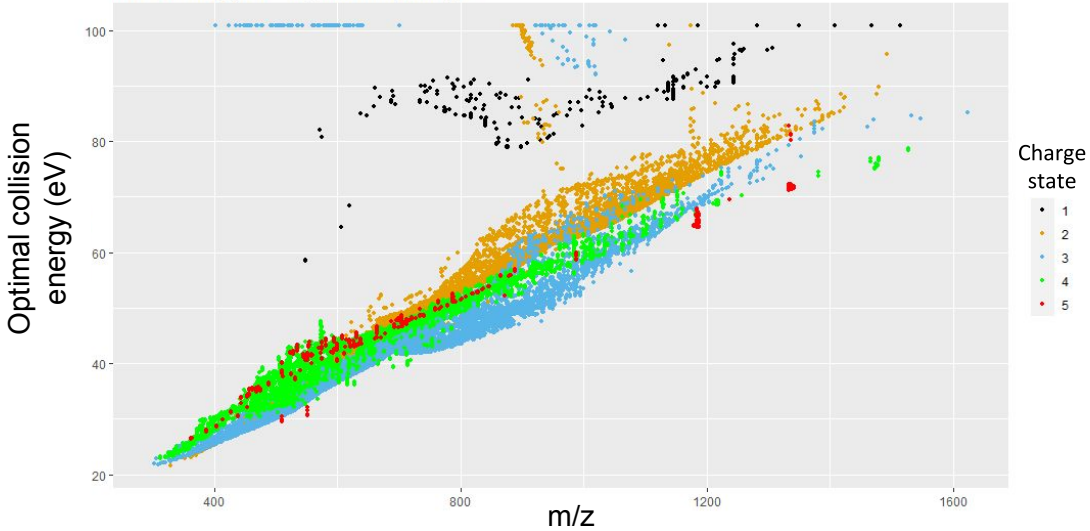


➢ The optimal collision energy selection process could be executed under 5 ms on average, demonstrating capacity to be run in real-time during mass spectrometry.

Predicted optimal collision energy



The collision energy used and fragmentation achieved in the testing set is shown in red, while the neural network prediction for varying collision energy levels of 0~100 eV are plotted in the Viridis color scale. The majority of the red dots fall close to the predicted model.



Predicted optimal collision energy v.s. m/z of a peptide, color-coded by charge

Conclusion

- The artificial neural network we have constructed is able to predict relative peptide fragmentation level from the collision energy applied and other peptide features.

- Prediction accuracy of peptide ion fragmentation reaches a Pearson's correlation coefficient of 0.80

- Selection of optimal collision energy using the model can be executed under 5 ms, demonstrating capacity for real-time application on instruments in future developments.

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