ASMS Short Course

Top-down Mass Spectrometry Data Analysis and Visualization

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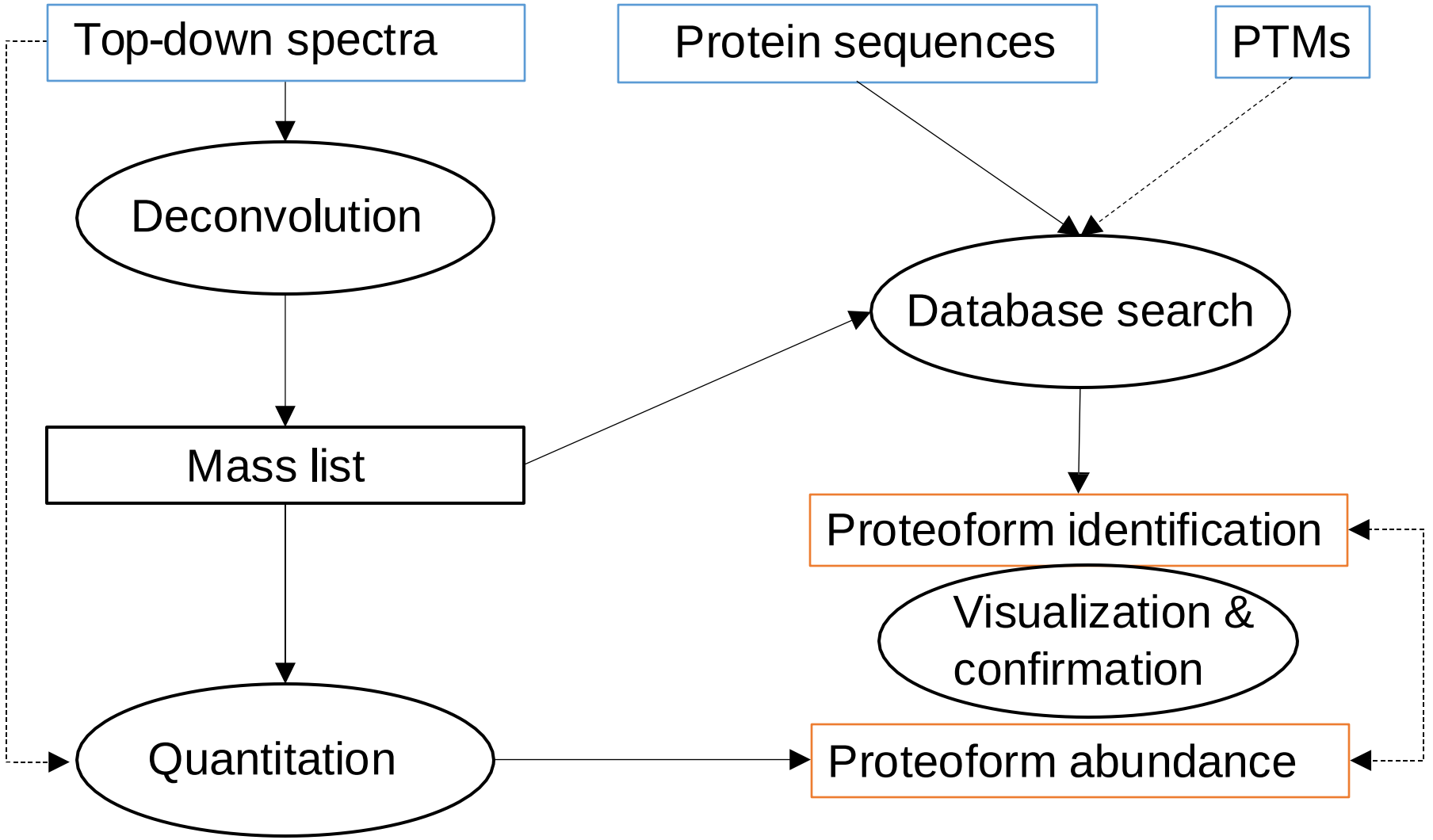
Top-Down MS Data Analysis workflow



Top-down MS software

Spectral Deconvolution

- **Thrash** [Horn *et al*., JASMS 2000]
- **Thrash/Xtract** [Horn *et al*. JASMS 2000,Zabrouskov et al., JASMS 2005]
- **RAPID** [Park *et al*., Anal. Chem. 2008]
- **Decon2LS** [Jaitly *et al*., BMC Bioinformatics, 2009]
- **Hardklör** [Hoopmann *et al*., Anal. Chem. 2007]
- **MS-Deconv** [Liu *et al*. MCP, 2010]
- **MS-Deconv+/TopFD** [Kou et al., BMC Bioinformatics 2014]
- **UniDec** [Marty et al, AC, 2015]
- **pParseTD** [Sun et al, AC, 2016]
- **ProMex** [Park et al., Nature Methods 2017]
- **Intact** [ProteinMetrics, 2018]
- **ProteinDeconvolution** [Thermo]
- **FLASHDeconv** [Jeong et al., Cell Systems 2020]

Database Search

- **ProSightPC** [Zamdborg et al., Nucleic Acids Res., 2007]
- **PIITA** [Tsai et al., JASMS., 2009]
- **USTag** [Shen et al., Anal. Chem., 2008]
- **MS-TopDown** [Frank et al., Anal. Chem., 2008]
- **MS-Align+** [Liu et al., MCP 2011]
- **MS-Align-E** [Liu et al., JPR 2013]
- **pTop** [Sun et al., AC, 2016]
- **TopPIC** [Kou et al. Bioinformatics 2016]
- **ProteinGoggle** [Xiao et al. Scientific Reports, 2016]
- **Proteoform Suite** [Shortreed et al., JPR, 2016]
- **TopMG** [Kou et al. Bioinformatics 2017]
- **MSPathFinder** [Park et al., Nature Methods 2017]
- **TDPortal** [Northwestern, ~2017]
- **PERCEPTRON** [Khalid et al., Nucleic Acid Res 2021]

Several packages with complete solutions for top-down proteomics applications

- TDPortal

  http://nrtdp.northwestern.edu/tdportal-request/
- ProSightPC™

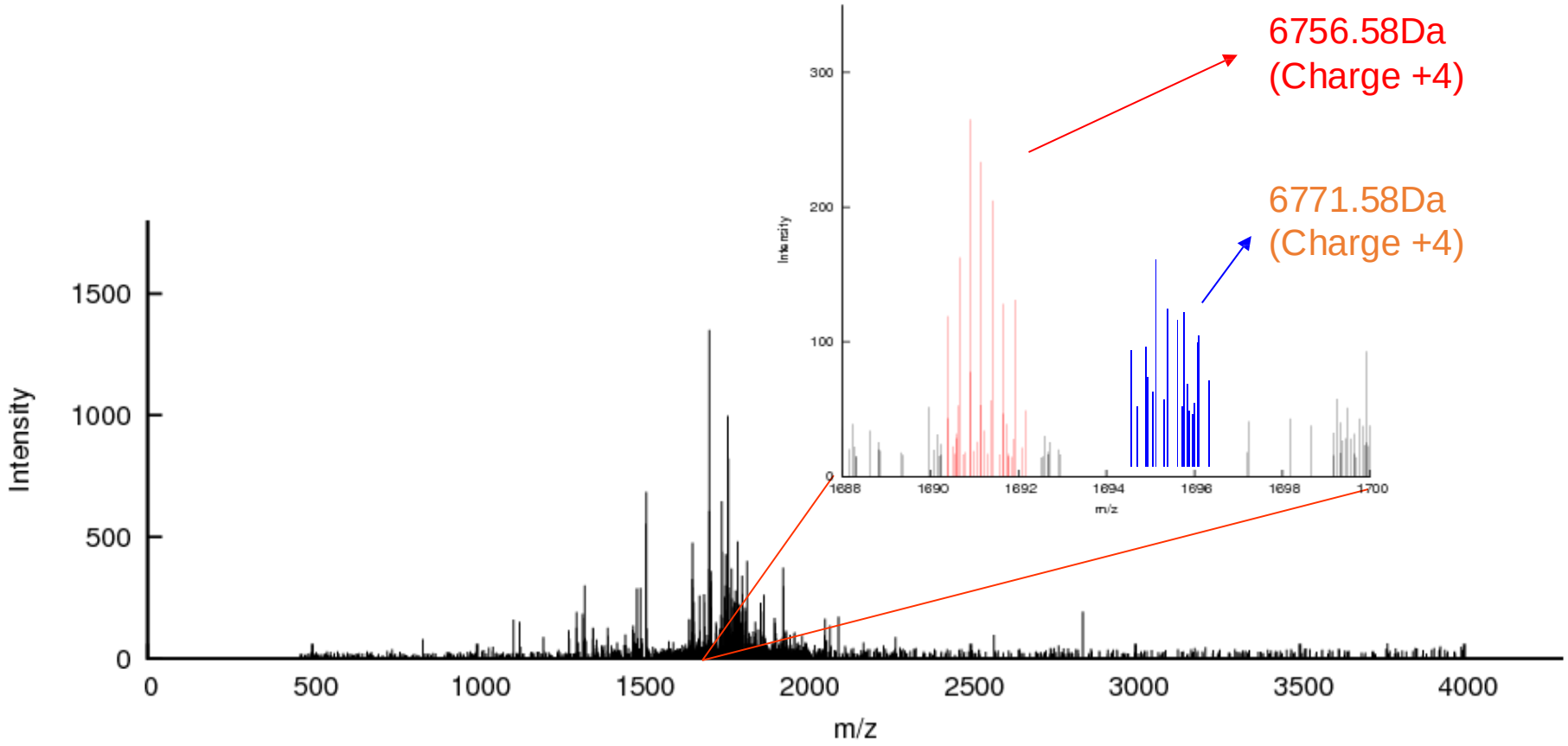
  https://www.thermofisher.com/order/catalog/product/PROSIGHTPC10
- Mash Explorer

  https://labs.wisc.edu/gelab/MASH_Explorer/index.php
- FlashDeconv

  https://openms.de/FLASHDeconv
- TopPIC

  http://www.toppic.org/

Deconvolution of top-down mass spectra

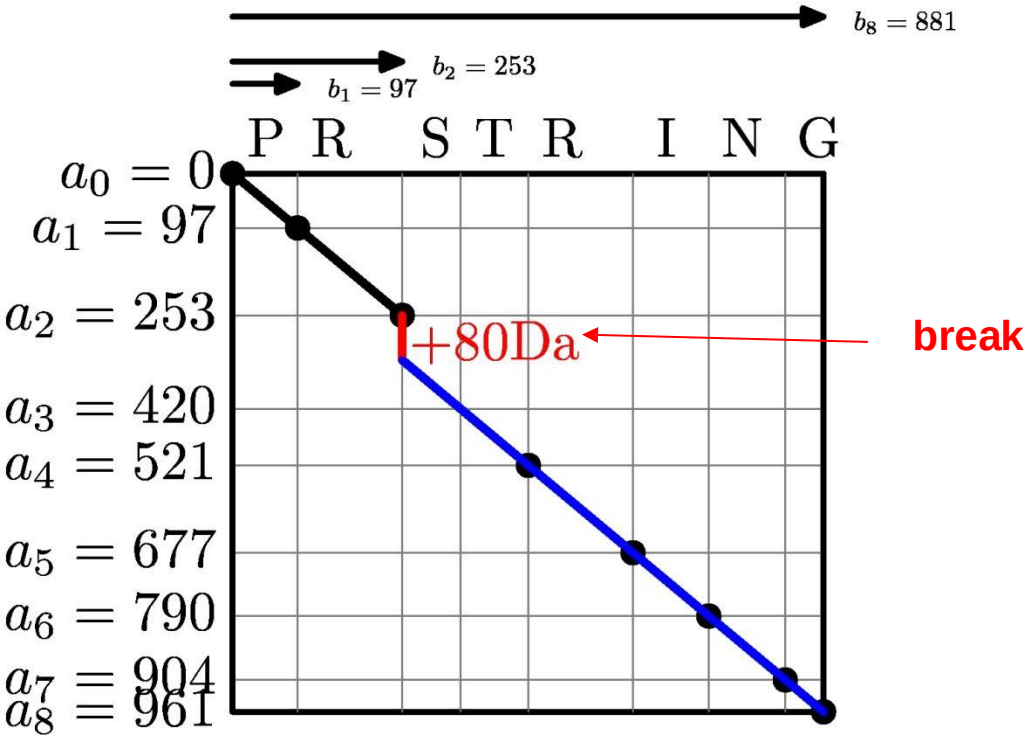


Top-down mass spectra usually have many peaks and complex patterns of **isotopic envelopes.** This spectrum has about 19,000 peaks.

Spectral alignment for blind PTM search

Spectrum of prefix ions for **PRS^{+80}TRING**
{0, 97, 253, 420, 521, 677, 790, 904, 961}

Database protein: **PRSTRING**



Spectral alignment

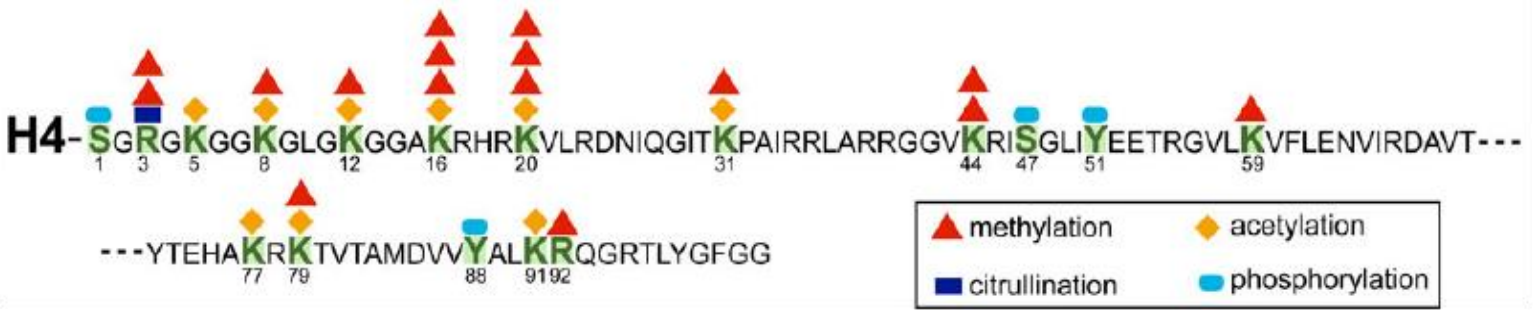
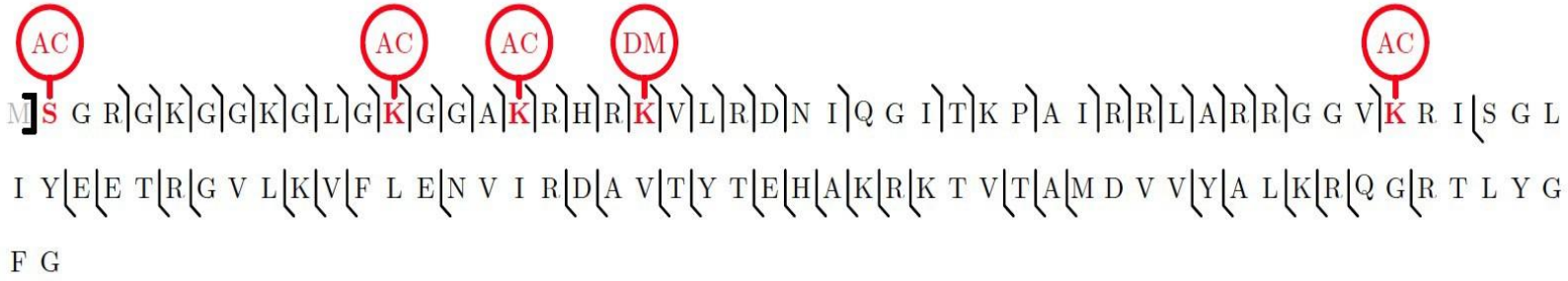
Spectral alignment with *F* modifications is a diagonal path from the top left node to the bottom right node with at most *F* **breaks**.

Spectral alignment score

Number of 2-D points (a_i, b_j) that the path passes through.

Ultramodified proteoforms

- Histone H4 has billions of possible proteoforms



- Histone H4 proteoform identified by top-down MS