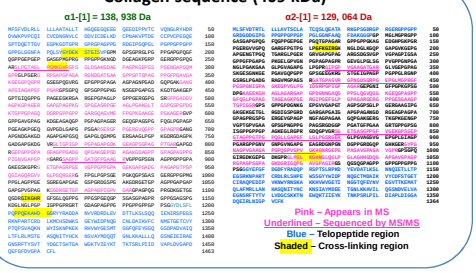
One Shot Proteomics

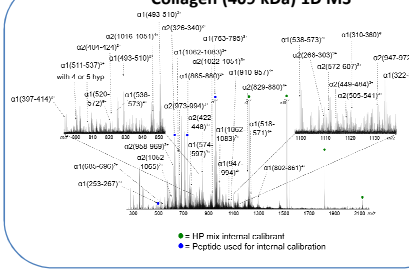
Prof. Peter B. O'Connor, Dr. Maria van Agthoven, Dr. Mark Barrow, Federico Floris, Haley Simon
Department of Chemistry, University of Warwick, Coventry CV4 7AL, UK

Proteomics often runs into two problems: 1) precursor ions selection windows can admit more than one precursor ion for fragmentation, resulting in confusion of which fragment comes from which precursor and 2) ion selection and MS/MS are serial processes requiring a decision about which ions are important to fragment. A new tandem mass spectrometry method, which addresses these problems, called 2-dimensional (2D) mass spectrometry, is now possible as shown below. Here we present the first proteomics data using 2DMS methods.

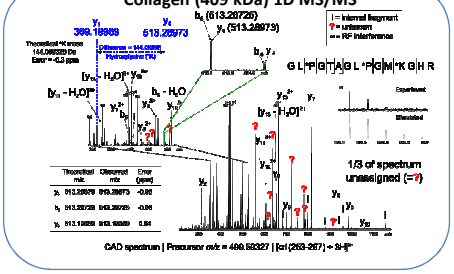
Collagen sequence (409 kDa)



Collagen (409 kDa) 1D MS



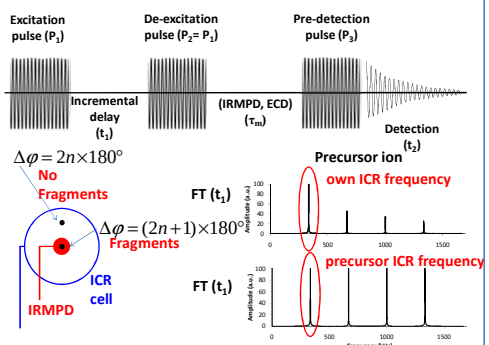
Collagen (409 kDa) 1D MS/MS



The principle of 2DMS

Ion cyclotron radius modulation by introducing a delay between two identical pulses:

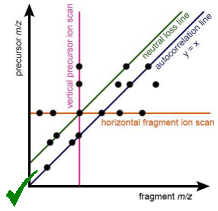
$$\Delta\varphi = \omega_{ion} \times t_1 + \varphi_0 \longrightarrow r_A = r_0\sqrt{2(1+\cos(\omega_{ion} t_1))}$$



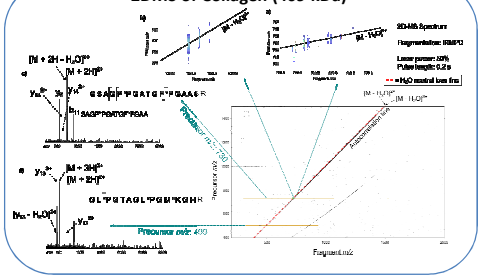
Fourier transform according to t_1 (delay between P1 and P2) and t_2 (measurement date):
MS/MS precursor and fragment ion spectra of all ion species

2DMS Scan Lines

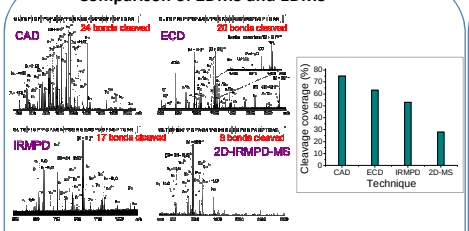
- All ions in a complex sample fragmented a visualised on one spectrum
- NO isolation
- YES fragmentation



2DMS of Collagen (409 kDa)

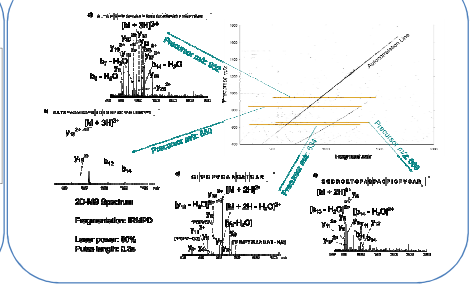


Comparison of 2DMS and 1DMS

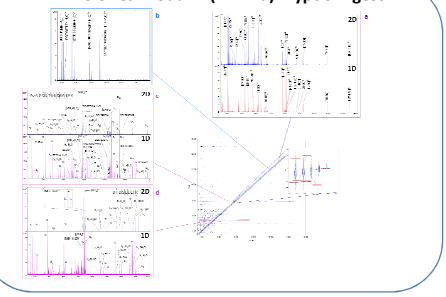


Precursor *m/z* 951.8092 | [α1 (763-795) + 3H] $^{3+}$ | 33 A.A. length

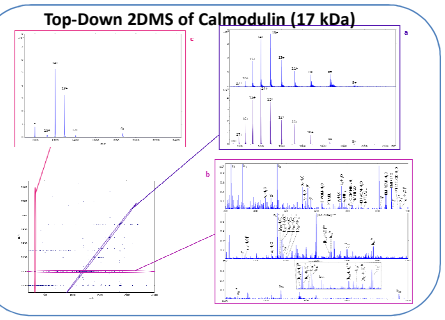
2DMS of Collagen (409 kDa)



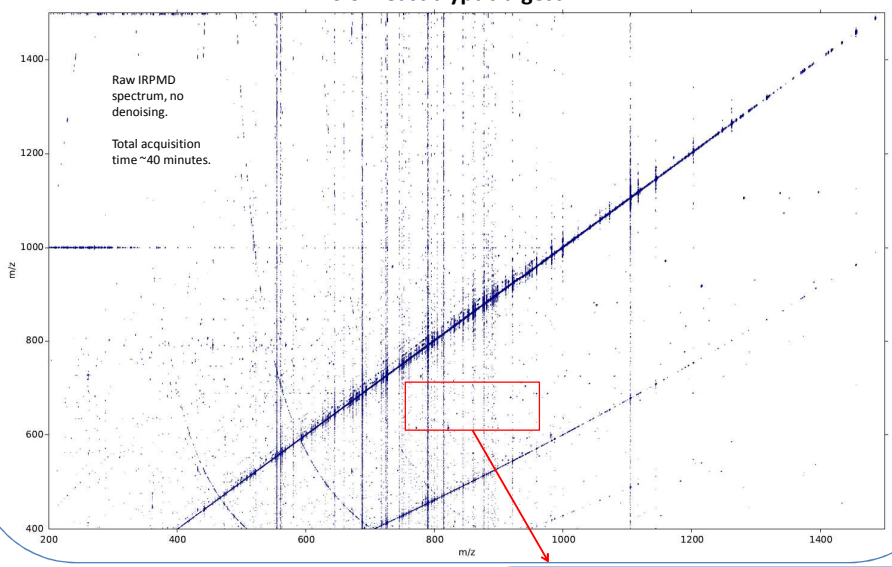
2DMS of Calmodulin (17 kDa) Tryptic Digest



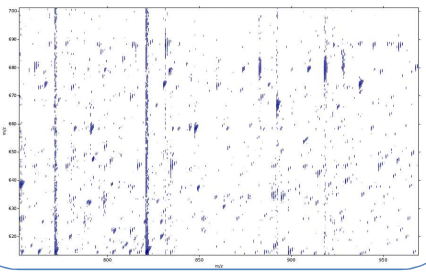
Top-Down 2DMS of Calmodulin (17 kDa)



2DMS of Yeast tryptic digest.



2DMS of Yeast tryptic digest, expansion of the ~600-700 Da (precursor ion) and ~750-950 Da (product ion) region.



Conclusions

- 2-Dimensional mass spectrometry of proteomic samples is possible. The 2DMS method generates fragment ions for all ions at the same time, so it avoids the ion preselection bias and multiple ion selection problems of traditional MS/MS methods.
- There are a lot of issues to solve, including stabilizing the method, calibrating the spectra, picking peaks and interpreting spectra, but the method works.
- Thus, we can now get an entire proteome in 'one shot' with a 2DMS experiment.
- 'One Shot' proteomics is possible.

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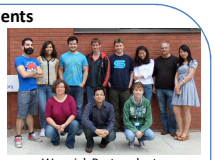

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