Laidlaw Scholars
Undergraduate Research and Leadership Programme

Multiple Ionisation of Pyrimidine

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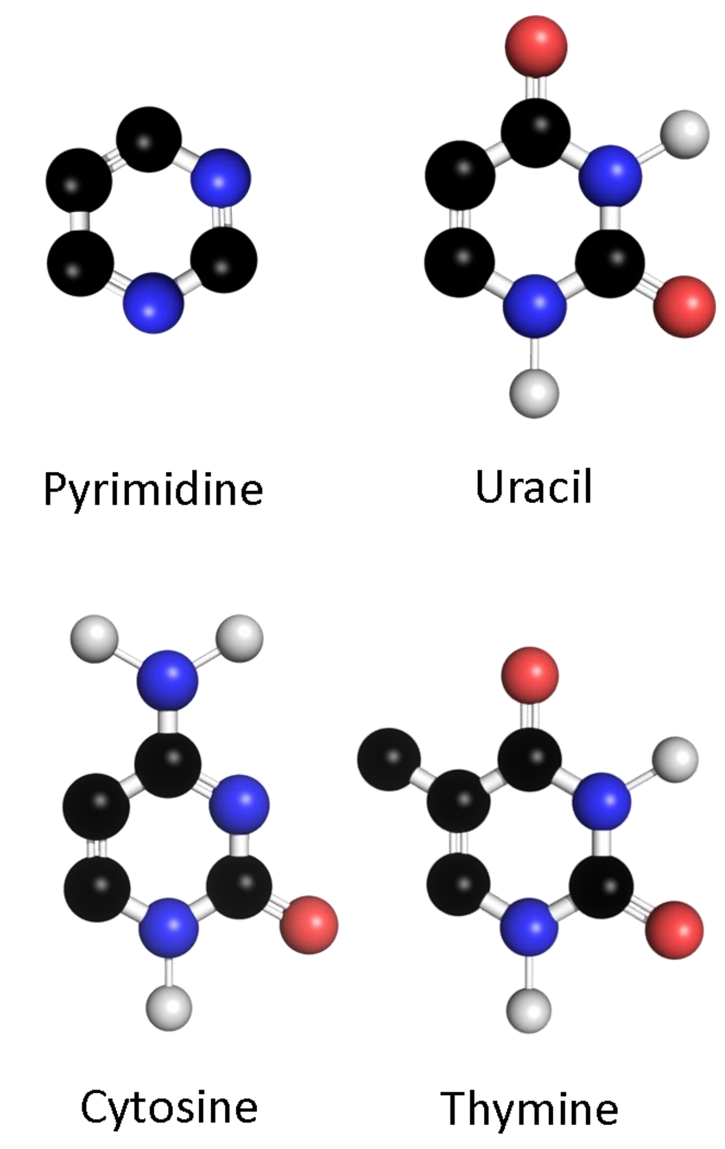
Abstract

Radiotherapy is an effective treatment for cancer but it can damage healthy tissue. Specifically, when ionising radiation interacts with healthy DNA, necrosis (cell death) and other complications can occur. To improve treatment a better understanding of DNA damage is required.

Pyrimidine is a model for DNA and RNA bases Thymine, Cytosine and Uracil. Data collected using Electron Impact Time of Flight Mass Spectroscopy (EI TOFMS) can be used to understand how ionizing radiation affects pyrimidine, and by extrapolation DNA bases, on the molecular level.

The future results of this work may be used to produce models that allow doctors to design better treatment for patients.



Why Pyrimidine?

Pyrimidine is the core of these bases (Fig. 1.). Pyrimidine related bases share properties with their parent molecule such as charge distribution and order of core ionisation energies.[1] Therefore, they can be studied instead of the individual bases, reducing costs and time.

Compared to molecules previously investigated by the Price Group, mostly three and four atom species, it is large. Consequently, the spectra were expected to be complex.

Figure-1. Diagrams of pyrimidine and the related bases. Colour code: black is carbon, blue is nitrogen, white is hydrogen and red is oxygen.

Radiotherapy and Pyrimidine

During radiotherapy, ionising radiation ionises cancerous DNA. Once ionised, it breaks, preventing the cell from duplicating. This process kills the cancer cells and shrinks the tumour. However, DNA in healthy tissue surrounding the tumour is often also ionised.

By using pyrimidine as a model, the mechanism of the ionisation of the DNA bases can be studied and the data used to produce ionisation cross sections of pyrimidine. An ionization cross section is a measure of the probability that a certain ion forms upon the collision of an electron with a molecule. [2]

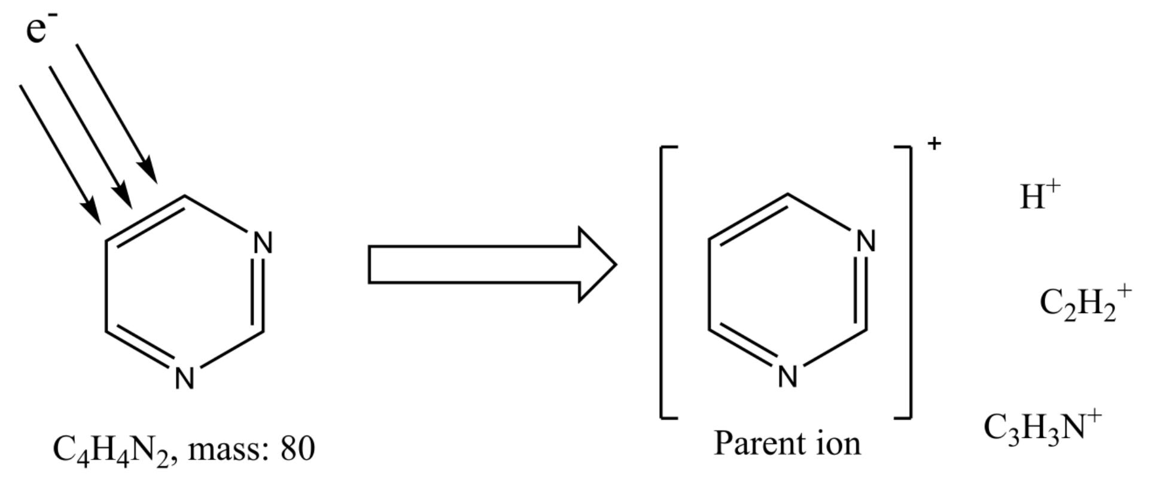


Figure-2. The possible results of electron impact ionisation of pyrimidine[3]

Experimental Apparatus

A hypodermic needle feeds the gaseous sample into the chamber perpendicular to the electron beam.[4] The pulse generator controls the experiment and can be adjusted to produce electrons of different energies(Fig. 3.). In this experiment the highest energy used is 200ev and the lowest is 40eV. The apparatus is kept under vacuum.

After each pulse, a start signal is sent to the time to digital converter (TDC) to begin timing. The repeller plate is pulsed from 0 to +400V, propelling all cations from the source region into the accelerator where a second electric field produced by a grid at negative potential accelerates the ions further into the field free drift region; here the cations separate by mass.

The cations collide with a microchannel plate detector (MCP) and a constant fraction discriminator (CFD) amplifies and discriminates the signals, sending a stop pulse to the TDC. The TDC can record multiple stop signals. The time of flight (TOF) of the cation is the time between the electron pulse and the collision with the MCP.

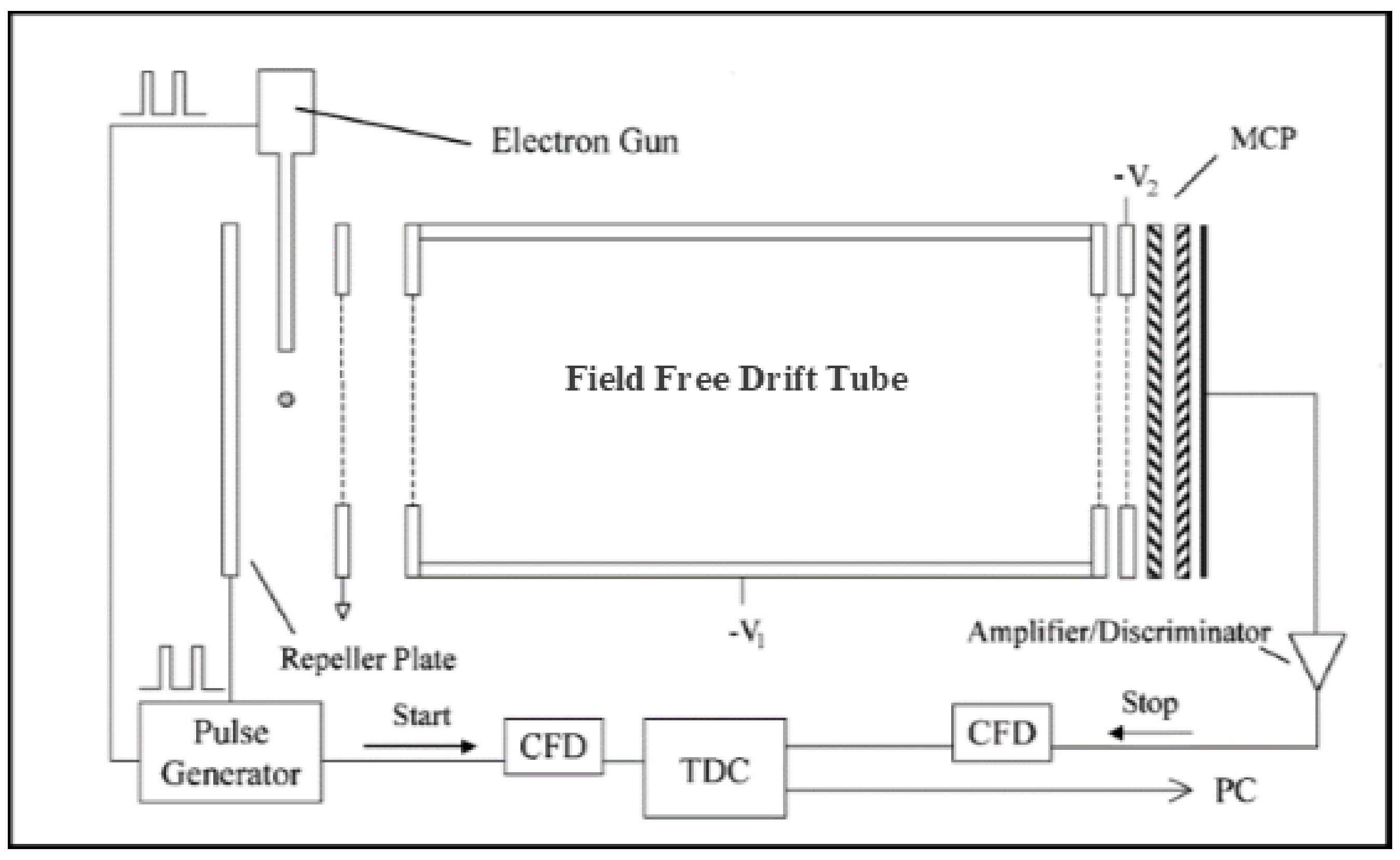


Figure-3. Schematic of EI TOFMS equipment[4]

Singles

A single is the arrival of one ion at the detector following a repeller plate pulse. [4]

To analyse the spectrum the intensity of each peak is found. For sharp individual peaks, it is calculated using measurements from the analysis program.

A peak fitting procedure is required to analyse peak clusters[2] (Fig. 4.). The final intensity of each ion peak is the sum of the intensities of the constituent fitted peaks.

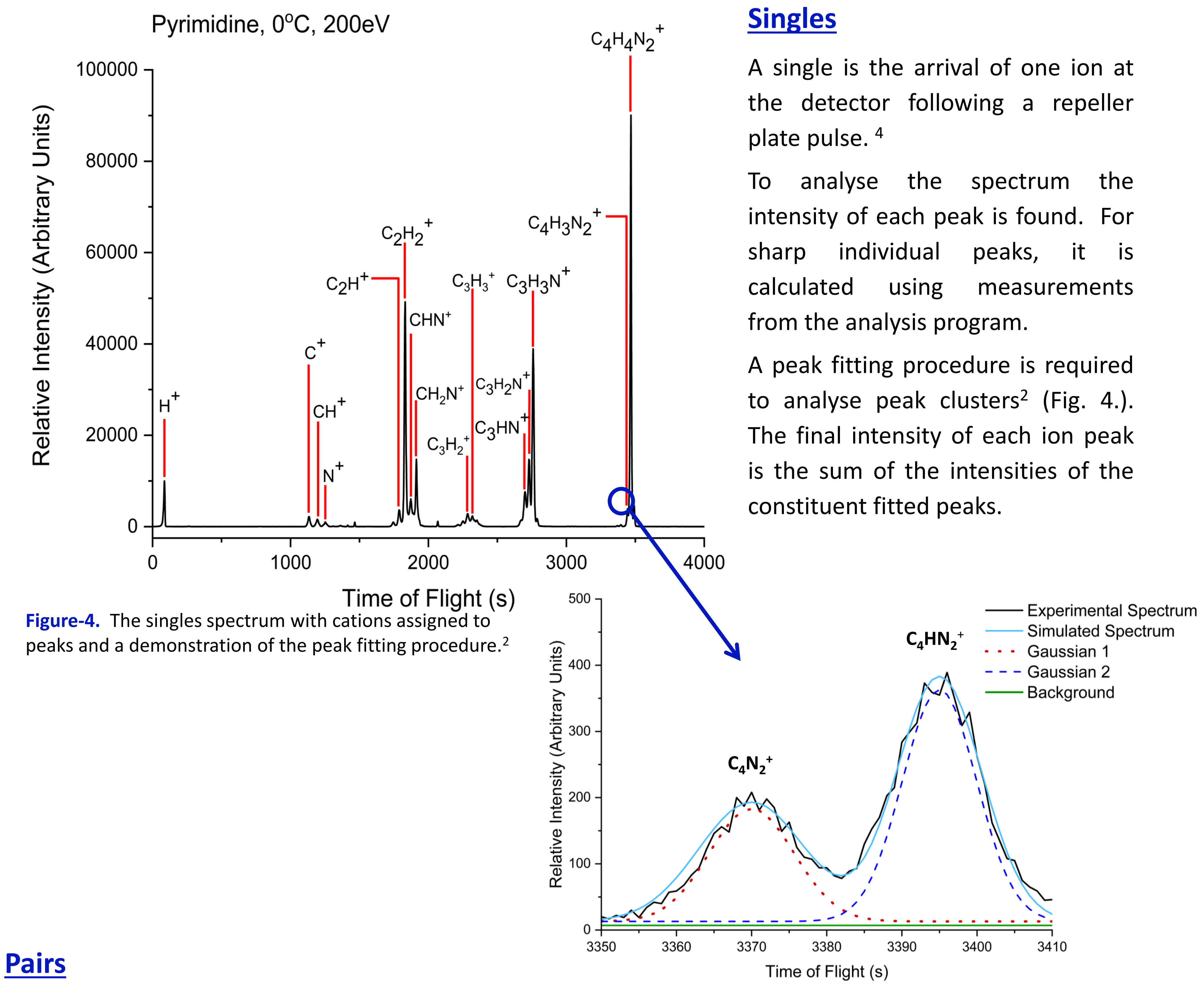


Figure-4. The singles spectrum with cations assigned to peaks and a demonstration of the peak fitting procedure.[2]

Pairs

Pairs refer to two ions arriving in coincidence after one ionizing pulse.[4]

Pairs spectra are analysed by totalling the counts in each peak.[2] Dead time is a 32ns period after the arrival of the first ion (Fig. 5.). If the second ion arrives within that time, the pair is not recorded, losing some counts. t_1 is the TOF of the first ion to arrive at the detector and t_2 is the TOF of the second ion after a single ionising pulse.

False peaks occur when ions from separate ionisation events are detected in coincidence after one ionising pulse. To reduce false coincidences, pyrimidine was kept at 0°C to lower the vapour pressure and ensure a low pressure of the target molecule in the source region.

Due to the size of the molecule lots of peaks in the pairs spectrum overlapped (merged peaks, Fig. 5.), so a method was developed to extract the individual intensity for each pair in the merged peak.

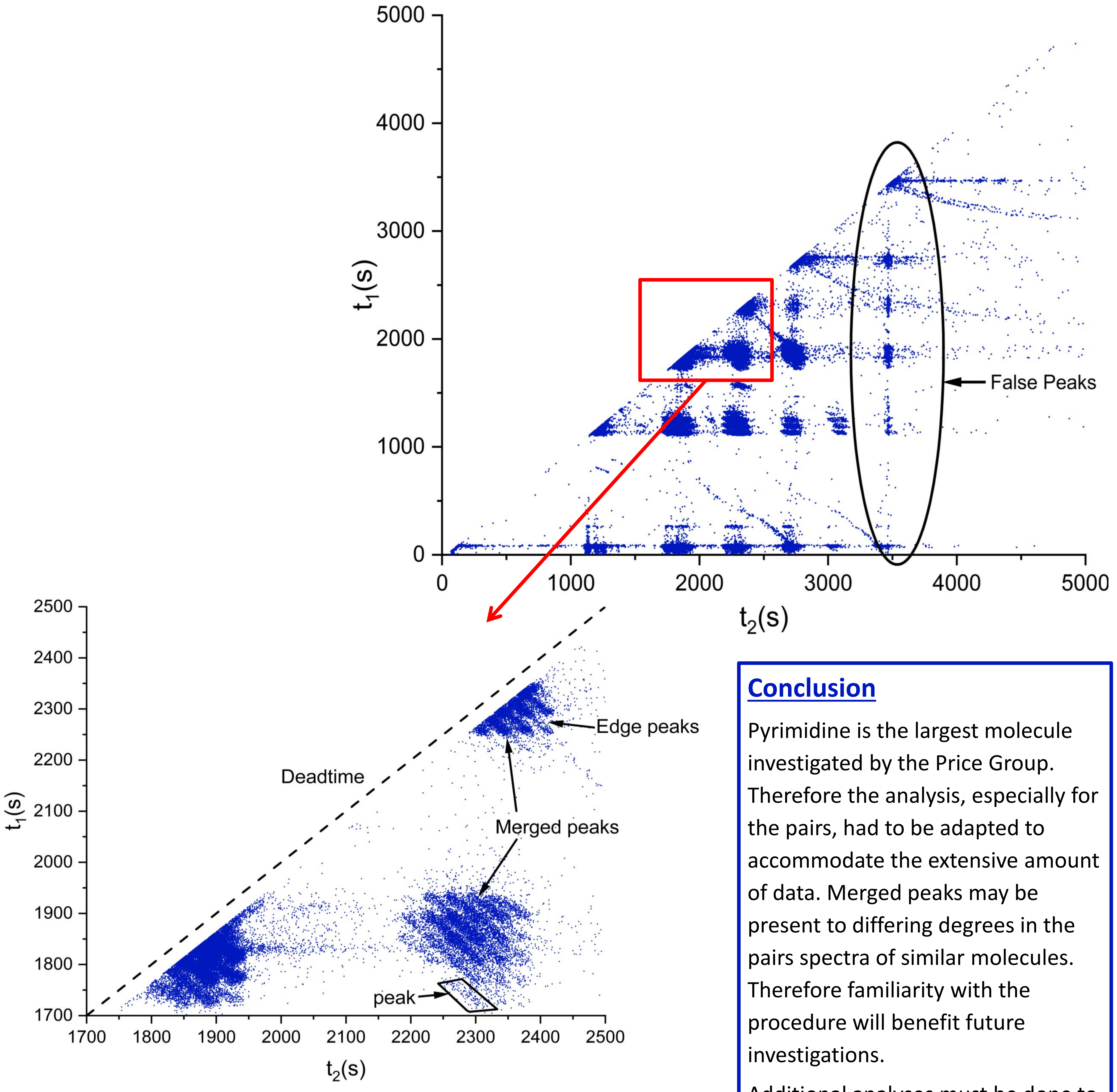


Figure-5. The pairs spectrum of pyrimidine at 0°C and electron energy 200eV

Conclusion

Pyrimidine is the largest molecule investigated by the Price Group. Therefore the analysis, especially for the pairs, had to be adapted to accommodate the extensive amount of data. Merged peaks may be present to differing degrees in the pairs spectra of similar molecules. Therefore familiarity with the procedure will benefit future investigations.

Additional analyses must be done to produce ionisation cross sections. The Price Group continues to study the ionisation of pyrimidine with the goal to produce a series of ionisation cross sections to aid the planning of radiotherapy treatment.

1. Linert et al., *Eur. Phys. J. D,* 2012, **60**, 20
2. S.J. King, PhD thesis, University College London, 2008
3. T.D. Märk, *Electron-Molecule Interactions and Their Applications,* ed. L.G. Christophorou, Academic Press Inc., Florida, 1st edn, 1984, vol. 1, ch. 3, pp 251- 315
4. S.J. King, S.D. Price, *J. Chem. Phys.*, 2007, **127**, 174307