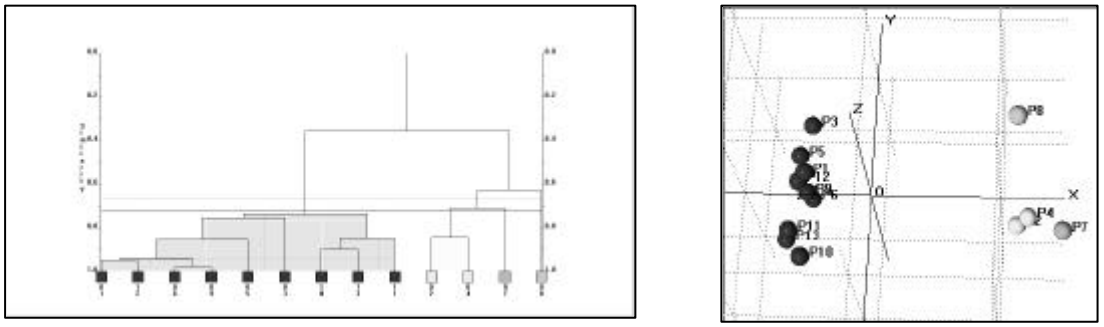
THE SEARCH FOR POLYMORPHS AND SALTS USING HIGH THROUGHPUT POWDER DIFFRACTION, SPECTROSCOPY AND OTHER TECHNIQUES.

Chris Gilmore, Gordon Barr and Wei Dong. Department of Chemistry, University of Glasgow, Glasgow G12 8QQ, Scotland.

With modern robotics and a suitable powder diffraction system (*e.g.* the Bruker GADDS system) it is possible to explore a wide variety of crystallisation conditions in a routine manner, and thus to search systematically for polymorphs or salts. However, the experiments produce 100s or even 1000s of diffraction patterns, and these can be supplemented by the corresponding Raman spectroscopy data and other measurements. Analysing this morass of information and extracting the important features, especially identifying new or unusual solid forms, is a formidable task. We present here the mSNAP software, which is a development of PolySNAP [1-3]. The latter uses full peak profile pattern matching methods to correlate PXRD patterns, and then applies the concepts of cluster analysis and multivariate statistics to group and classify the patterns. The method employs dendrograms with variable cut levels to define the data partitions as well as metric multidimensional scaling (MMDS) or principal components analysis as a visualization aid. Typical output is shown in the figures below:



The left hand figure shows a dendrogram in which 13 aspirin powder samples are partitioned into four clusters and these are displayed on the right using an MMDS plot in which each sphere represents a single sample. It is expected that unusual samples will be clearly identified as new distinct clusters in both plots, and this has been our experience.

In mSNAP the same principles are applied except that up to four different data types are permitted. In particular, data from PXRD, Raman spectroscopy, DSC and IR on the same samples are readily imported and processed. The analysis is carried out for each single data type individually as well as all the possible combinations. To date, our experience with PXRD and Raman indicates that the analysis of the combined data sets is more powerful than any individual technique.

References:

[1] Gilmore, C.J., Barr, G. & Paisley, J. (2004). *J. Appl. Cryst.* **37**, 231-242.
[2] Barr, G., Dong, W., & Gilmore, C. J. (2004). *J. Appl. Cryst.* **37**, 243-252.
[3] Barr, G., Dong, W., & Gilmore, C. J. (2004). *J. Appl. Cryst.* **37**, 658-664.