

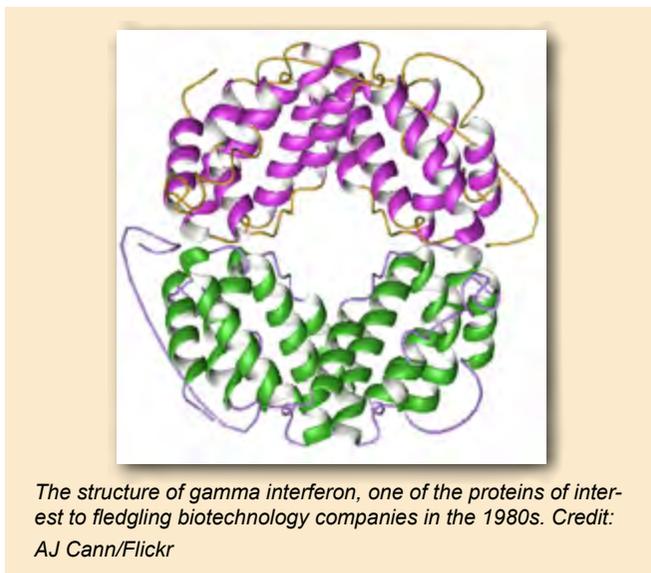
# M-SCAN: supporting the biopharmaceutical industry

Mass spectrometry mapping methods developed at Imperial College London since the 1970s have led to powerful new techniques for identifying and characterising the protein compounds produced by the biopharmaceutical industry. Much of the research that led to the new techniques received funding from BBSRC's predecessors.

The research was led by Professor Howard Morris<sup>1</sup>, who established spinout company M-SCAN<sup>2</sup> to commercialise advances in mass spectrometry, which allowed the company to characterise larger protein molecules, and provide a service to the fledgling 1980s UK biotechnology industry.

Since then M-SCAN has characterised new drug products for many hundreds of biotechnology and pharmaceutical companies worldwide, including the majority of the "top 50" biopharmaceutical products such as monoclonal antibodies, cytokines and blood glycoproteins.

In autumn 2010, M-SCAN merged with scientific testing company SGS to become SGS M-SCAN. At this point M-SCAN had a market capitalisation value of around \$45M, and had established GLP/GMP (Good Laboratory Practice and Good Manufacturing Practice) analytical laboratories in the UK, USA, Switzerland and Germany employing around 65 people, many of whom have PhDs.



The structure of gamma interferon, one of the proteins of interest to fledgling biotechnology companies in the 1980s. Credit: AJ Cann/Flickr

## Industry interest

Mass spectrometry is used to determine the composition and chemical structure of molecules. It allows biotechnology companies to confirm that the proteins they produce match the structure predicted for them based on the DNA sequence they were created from, and also identifies any differences, which the company must then explain and address. Many of these differences occur as the protein molecule is modified after it has been assembled – a process known as post-translational modification.

"Since the thalidomide tragedy many years ago, people

## Impact Summary

- Since the 1980s, spinout company M-SCAN has provided mass spectrometry services to many hundreds of pharmaceutical companies to help them characterise proteins and glycoproteins.

- The company was founded by Professor Howard Morris (Imperial College London) based on academic research funded by BBSRC's predecessors, amongst others.

- The company analyses thousands of industrial samples annually using Mass Spectrometric methods developed by Morris and colleagues.

- M-SCAN merged with the world's largest scientific testing organisation SGS in autumn 2010.

- Methods developed by M-SCAN have been incorporated into the International Committee on Harmonisation guidelines for Test Procedures and Acceptance Criteria for Biotechnology Products.

have realised that the more you know about your product at an early stage, the better,” says Morris. “In the old days people were happy with a bioassay, or a band on a gel, but now the regulators want to see a lot more than that, and that’s where mass spectrometric mapping can come in.”

Morris founded M-SCAN in the early 1980s, at a time when he was generating interest from emerging biotechnology companies in the mass spectrometry mapping methods he had developed for academic research<sup>3</sup>. These companies were specifically interested in proteins beyond the mass range accessible to the commercial mass spectrometry instruments available at the time, which were restricted to analysing molecules with a molecular weight of only 8-900 daltons.

“We developed a unique mass spectrometer at Imperial in the 1970s, which was purchased using funding from BBSRC’s predecessor, the Science Research Council,” says Morris<sup>4</sup>. “We began to get a lot of industrial interest because we could move to higher masses than were available on existing commercial instruments.”

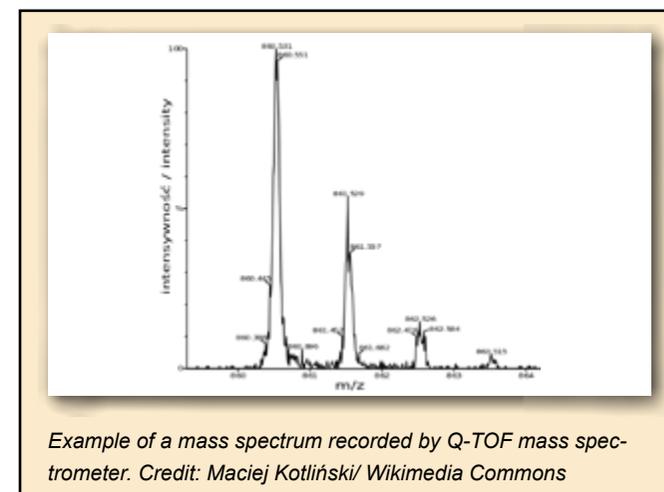
Morris realised that researchers could determine much of the protein’s structural information using specific enzyme digests to break up large protein molecules into a mixture of fragments with a molecular weight of less than 3,000 daltons - within range of his new mass spectrometry “mapping” techniques.

Unlike older techniques, mass spectrometry could also be used to describe post-translational modifications to the protein molecule, such as glycosylation and the presence of bonds called disulphide bridges. It was also faster, cheaper and gave more definitive results than cumbersome classical methods such as Edman degradation<sup>5</sup>.

### A regulatory requirement

Thanks to the requirement from regulators for reliable information, mass spectrometry is now one of the most common methods used by biotechnology companies for characterising protein molecules. The techniques developed at Imperial College, including MS peptide/glycopeptide fingerprinting and disulphide bridge analysis, are now included in international biotechnology testing guidelines issued by the International Conference on Harmonisation (ICH)<sup>6,7</sup>. The ICH brings together European, American and Japanese regulators and the pharmaceutical industry to discuss scientific and technical aspects of drug regulation.

According to Morris, “[regulators] recognise that every protein problem is different, so they issue guidelines to choices of method rather than instructions. Certainly mass spectrometry is now the method of choice for many of these types of analysis. That’s partly based on the mapping technologies and strategies we developed so many years ago.”



### Continuing growth

Since the 1980s, the size and complexity of the proteins of interest has increased, and M-SCAN has continued to develop its methods and expertise. “The first sort of molecules those folks were working on in the 1980s were things like gamma interferon; relatively small molecules with no particular difficulties structurally,” Morris explains. “Over the years that’s changed considerably, and now I would say the greatest emphasis among manufacturers is on monoclonal antibodies. That’s been the big development over the last twenty or thirty years with M-SCAN helping to pioneer the analytical side of those developments.”

Antibodies can have molecular weights in the order of 150,000 daltons, creating difficulties for both protein chemistry and the mass spectrometry instruments. Given their importance to industry, however, much of M-SCAN's expertise has been concentrated on solving problems most relevant to monoclonal antibodies and developing new techniques in this area. The advent of high resolution tandem mass spectrometry on advanced instruments (such as the Q-TOF<sup>8</sup>), which give good mass accuracy even on intact molecules, has also aided this high-mass work<sup>9</sup>.

M-SCAN has grown considerably since its creation. In 2010 the company had laboratories in the UK, USA, Switzerland and Germany, employed 65 people and had a market capitalisation value of around \$45M (£28M).

Between 2005 and 2010 M-SCAN was approached by several large contract research organisations interested in acquiring or merging with the company. M-SCAN chose to merge with a company called SGS, one of the world's largest scientific testing organisations, to become SGS M-SCAN<sup>10</sup>. Due to the high-tech products and know-how which M-SCAN had developed for biopolymer testing, it was able to fill a gap in the services SGS can offer to the biotechnology and pharmaceutical industries for the future.

## Notes and references

1. See <http://www3.imperial.ac.uk/people/h.morris>
2. See <http://www.m-scan.co.uk/>
3. Morris, H.R. and Greer, F.M. (1988) Mass Spectrometry of Natural and Recombinant Proteins and Glycoproteins Trends in Biotechnology. 6, p 140-147. Available online at: <http://www.sciencedirect.com/science/article/pii/0167779988900832>
4. The Science Research Council became the Science and Engineering Research Council in 1981. In 1994 it merged with the Agricultural and Food Research Council to become BBSRC.
5. Edman degradation can be used for determining the sequence of amino acids which make up a protein. It works by tagging and chemically removing one amino acid from the end (N-terminus) of the protein molecule. The technique can only be used on relatively small proteins or protein fragments, cannot be used if the N-terminus is hidden within the protein structure or has been chemically modified, and cannot determine the location of disulphide bridges.
6. See <http://www.ich.org/>
7. See [http://www.ich.org/fileadmin/Public\\_Web\\_Site/ICH\\_Products/Guidelines/Quality/Q6B/Step4/Q6B\\_Guideline.pdf](http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q6B/Step4/Q6B_Guideline.pdf)
8. Q-TOF: Quadrupole orthogonal acceleration Time Of Flight. It is a modern advanced tandem MS/MS mass spectrometer which Morris conceived as being the best potential ultra-high sensitivity instrument for biopolymer sequencing. He persuaded the manufacturers to build the instrument; many hundreds of which have since been sold. M-SCAN now possesses six such instruments (from a total complement of 20 mass spectrometers) to assist in its biopharmaceutical characterisation work.
9. Morris, H.R. et al. (1996) High sensitivity collisionally-activated decomposition tandem mass spectrometry on a novel quadrupole/orthogonal-acceleration time-of-flight mass spectrometer. Rapid Communications in Mass Spectrometry. 10, p 889-896.
10. See <http://www.pharma-mag.com/News/tabid/63/EntryId/142/SGS-Acquires-the-M-Scan-Group.aspx> also <http://www.m-scan.co.uk/> and <http://www.m-scan.co.uk/>