BRUKER BIOSPIN

The maXis system from Bruker Daltonics can use both UPLC and CE separation approaches.

it is an unbiased, universal detector," says Jack Newton, a product manager at Chenomx in Edmonton, Canada, which was co-founded by Wishart in 2000. This attribute, along with NMR's ability to determine structure and perform quantitative analysis is particularly attractive to metabolomics researchers who need a way to compare and exchange results between labs. "The move is afoot — people want to get to that common language of compound names and concentrations," says Wishart, as this will make integrating data sets and obtaining systems-level views of cell physiology possible.

The challenge with NMR is instrument sensitivity — NMR is less sensitive than MS, often identifying far fewer metabolites in the same sample. "For us, the relevant question is how sensitive do you need to be," says Newton. He says researchers at Chenomx have performed many studies in which biologically meaningful differences between samples were easily captured with NMR, even though some compounds in the samples probably fell below the sensitivity limits of the instrument (see 'Dark matter').

MS, on the other hand, is a very sensitive method for metabolite identification and, unlike NMR, is easily coupled to upstream separation techniques. Siuzdak says his group can see thousands of molecules in an MS analysis — and that number can be doubled by changing from positive- to negative-ion mode. And by using both reversed-phase chromatography and HILIC columns, they are seeing more hydrophilic compounds in their analyses than before. "I would venture that we are now seeing over an order of magnitude more than what you would see with NMR," he says.

Detector development

As researchers in the MS camp turn towards TOF and ion-trap MS instruments for metabolite analysis, developers are responding to their complex needs. Bruker Daltonics in Billerica, Massachusetts, has introduced the maXis ultra-high resolution (UHR)-TOF MS system, which can accommodate both UPLC and CE separation. Applied Biosystems in Foster City, California, in collaboration with MDS SCIEX in Toronto, Ontario, have the ion-trap system 4000 QTrap LC/MS/MS that can interface with Applied Biosystem's LightSight software for small-molecule analysis and identification.

WINE-OMICS

G. WOHLGEMUTH

For Kirsten Skogerson at the University of California, Davis, wondering about how chemical composition affects the flavour and body of a wine took her from a degree in viticulture and enology into metabolomics research. When Skogerson arrived in Oliver Fiehn's lab as a postgrad she looked for a project that would marry Fiehn's expertise in metabolomics and her interest in wine.

"There are so many questions in wine science that you could start to answer by doing a global analysis," she says. A deeper understanding of the biochemistry of grape-juice fermentation could help the winemaking industry by complementing the arts of the traditional wine taster. So Skogerson and Fiehn set out to survey wine 'metabolomes', in search of key chemical components contributing to body.

Using proton nuclear magnetic resonance (NMR) and gas chromatography–mass spectrometry (GC–MS), they looked at 17 different white wines with a wide range of body. For GC–MS analysis, they first removed the alcohol under reduced pressure and then ran samples on a LECO Pegasus IV GC TOF MS system and analysed the spectra using the BinBase program developed in Fiehn's lab. Each wine was also directly analysed on a Bruker Daltonics 600 mHZ NMR instrument with the resulting peaks being compared to the commercially available Chenomx NMR database for metabolite identification. "When you think about it, you have the grape metabolome being acted on by the yeast, plus the added complexity from the yeast metabolome, so the metabolite profile of a wine is very complex," says Skogerson.

They found a total of 413 metabolites among the wines — probably only a small fraction of the wine metabolome — of which 108 could be positively identified. And in both data sets, the amino acid proline showed a positive correlation with body as assessed by trained wine tasters. How proline relates to body is not yet clear, however. "That is the hard part of being in metabolomics — you get clues, but the follow-up is the real challenge," says Skogerson. Still, she thinks proline could be used as marker for a wine's viscosity.

Red-wine drinkers have not been forgotten. Bruker Daltonics in Billerica, Maryland, has profiled red wines for important polyphenolic secondary metabolites such as tannins, flavonoids and anthocyanins. This demonstration used the Acquity ultra-performance liquid chromatography system from Waters to separate red wine metabolites for analysis by Bruker's LC-ESI QTOF MS instrument as well as analysis by NMR coupled with Bruker's BioSpin Spectral Base analysis package.

Does knowing the chemistry behind that wonderful bottle of wine take away from the pleasure? Not according to Skogerson. "Science has the potential to bring the art of winemaking to a higher level." N.B.