

Resolution Revolution

Can GC×GC be considered a super-resolution technique?

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We posed the question above at the Riva del Garda ISCC/GC×GC symposium in May – perhaps somewhat rhetorically given that the audience was made up of committed GC×GC researchers. Today, “super-resolution” is a term apparently reserved for the Nobel prize-winning spectroscopic technique that is defined by achieving spectroscopic imaging at wavelengths less than those of light. This feat is accomplished by a combination of the “blinking” of fluorescent emitting centers – for instance, located along a fibril – and the mathematical localization of the center of the emission, which effectively reduces the dispersion of the light and centers it better on the emitting moiety. In this way, a biological feature comprising the emitting centers can be defined with much greater precision.

So, does GC×GC qualify as a super-resolution technique? We define the separation power of GC in terms of peak capacity – the total analysis time/peak width measure. Or, in other words, how many peaks can be fitted in the chromatogram. For example, if we consider the limit for well-resolved

peaks to be separation by 4σ (the width at baseline), then we might fit 400 peaks in the total chromatogram. If we relax (reduce) the peak width measure for defining separated peaks, then we can fit in more peaks. There is a natural limit to how small the peak separation measure can be before we are unable to distinguish neighboring peaks, which is exacerbated as peak response magnitudes become increasingly different. For a regular (non-MS) GC detector, we rely upon peaks being adequately resolved.

For GC×GC, we use a second column, decoupled and independent from the first. The total resolvable peak number is often quoted as being the product of peak capacities on each dimension – ${}^1n_c \times {}^2n_c$. If ${}^1n_c = 400$ and ${}^2n_c = 25$, then total resolvable peaks will be 10,000. When modified by the sampling of first dimension peaks, it will actually be about 8,000, but still significantly expanding upon the 1D GC peak capacity capability. In addition to total capacity, the manner in which GC×GC presents data as ‘structured retentions,’ grouping similar compound classes in a structured manner, is informative.

However, peak capacity is not everything. We argue that for a technique to be considered super-resolution, it is important to consider the ability to provide peak localization and, ideally, identification. Localizing a peak in 2D space depends on the detector used. A flame ionization detector (FID) generates a peak defined by its dispersion in both 1D and 2D, given, for instance, by its width at baseline in each dimension. The peak maximum in 2D (known as 2t_R) is readily obtained, but marginally decreases for each successive modulation due to the incrementing oven temperature. Defining the peak in 1D is somewhat less clear, due to the discrete modulation period sampling employed.

Some years ago, we reported a method to predict the 1t_R value based

on fitting a Gaussian distribution to the modulated peak profile, which allows a better characterized ${}^1t_R/{}^2t_R$ set of peak coordinates – something that has been picked up by other users. With a reliable set of peak coordinates in 2D space, a better-defined peak apex plot can be generated (the apex plot is defined as a plot that presents just the 2D peak coordinates; to do this precisely, accurate identification of the coordinates is needed). The peak apex plot clearly offers considerably greater peak ‘capacity’ than those of classical definitions based on peak widths at baseline, as the peak apex should be ‘definable’ to a much narrower width – although the magnitude and uncertainty of the apex plot is not normally stated.

Mass spectrometry detection further refines the total peak identification that is possible. If based on the total ion chromatogram, the consideration is effectively the same as for FID. But if a unique extracted ion is available for a compound, then the compound corresponding to that ion can be further isolated from other compounds that might be located with very similar 2D coordinates. Using the approach of precise prediction of the 1t_R value, and locating the 1D and 2D peak 2D apex, it is possible to obtain a truly ultra-high resolution GC technique. Does this mean we should be able to call it “super-resolution”? I believe so.

The GC community has accepted the high resolution provided by capillary GC as the gold-standard in separation of volatile compounds. By adding a suitable second dimension in GC×GC, the expanded separation power provides a degree of chemical resolution that is unprecedented – in essentially the same time. The addition of mass spectrometry further enhances the ability to isolate the response of individual compounds. The resolution provided is simply ‘super’.