

A Tutorial & Introduction

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Technology of multidimensional gas chromatography (MDGC) and comprehensive two-dimensional gas chromatography (GC×GC)

MDGC and GC×GC are advanced operating modes of GC.

Whilst MDGC (or 2DGC) has been available for many years, the comprehensive version – GC×GC – technique has emerged as one of the most exciting development on the GC scene.

Both of these methods require special interfaces in order for their successful implementation.

Analysis Dimensions:

The terms 'dimension' in the above titles refers to the use of a 'dimension of chromatography' – or put more simply, a column. In the broad sense, a 'dimension of analysis' is any technique that provides independent analysis capability. So FTIR, MS, and GC are discrete dimensions; they can be operated independently to provide some measure of analysis / identification. Provided the separate dimensions are compatible and can be 'hyphenated', we can construct two- or multiple-dimensional systems, such as GC-MS. The only benefit in doing this is to provide the analyst with more information than is possible from either of the separate dimensions.

According to the above definition, thus a two-dimensional separation system employs two separate and independent columns. We might find such a multidimensional separation system comprised of LC with GC. They are independent experiments. But for GC, they may be housed in a single GC oven. The interface is located between – or near the join of – the two columns. We revisit this concept later. But by this definition, simply linking or coupling two columns together is not a multidimensional system.

Multidimensionality in Gas Chromatography:

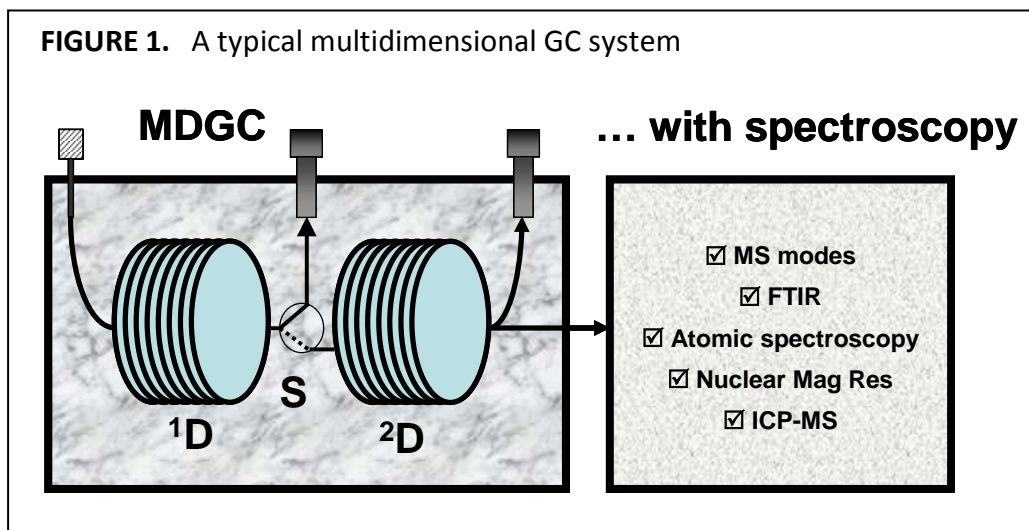


Figure 1 shows a schematic diagram of a MDGC system (**ref 209**). The usual mode of MDGC is straightforward. A valve or selection device (S – switch mechanism) allows some small region of components that emerge from the first column (1^{D}) to be switched to the second column (2^{D}). This can be called a ‘heart-cut’. The selected compounds then elute on the second column, where the aim is to attain better resolution or separation. This may be, for instance, where certain peaks must be analysed in a sample, and each region where they are expected is heart-cut to the second column. The second column then provides the improved separation performance that allows each compound to be resolved. This method might be commonly used for samples that contain many compounds (a ‘complex sample’) such that most peaks are unresolved. The peaks are better resolved on the second column by virtue of the fact that we use a column of different ‘selectivity’ or phase coating. This shifts the peaks around compared to the first column, and so – hopefully – any interfering peak are separated from the desired components on the second column.

An obvious application of MDGC is chiral analysis. Here, a chiral column is used as the 2^{D} column. Enantiomers are unresolved on an achiral column, and so appear as one ‘peak’ to be heart-cut to the enantioselective column. On this column, they are then resolved into their component enantiomers.

Figure 1 also shows that a variety of spectroscopic detectors can be used to provide additional characterisation of compounds that elute for the column.

A landmark development – the LMCS:

In our research, we make extensive use of a device that we have patented, called the longitudinally modulated cryogenic system (LMCS; **refs 52, 55, 57, 60, 61**) – **Figure 2**. This device is a cold – cryogenically cooled – cylinder that oscillates back and forth along the capillary GC column. It is essentially a trapping device that acts somewhat like a gate. Volatile compounds cannot pass the gate until it is moved along the column (in this case, towards the incoming carrier flow), so that compounds trapped at the cold spot can then be heated and released into the gas

phase. The cryotrap unit protrudes into the oven of the GC, and the column passes through the centre of the cryotrap 'shuttle' (the part that moves back-and-forth along the column). The range of applications to which this device can be applied is very broad, from aiding injection, to modulating peaks just before the detector, and most importantly, unique ways to hyphenate two columns within the chromatographic channel. One of the key tools we use this for is MDGC. The other is comprehensive two-dimensional gas chromatography (GCxGC) - more of that later.... Given that the concept of moving a cryogenic zone longitudinally along the column was previously not described, and not was our prior description of moving the column back-and-forth through a fixed cryotrap, we owe much of our success to the development of our LMCS system in the 1990s. The use cryogenic modulation has now become a common approach around the world for implementation of the GCxGC method (see below).

Figure 2. The LMCS Unit

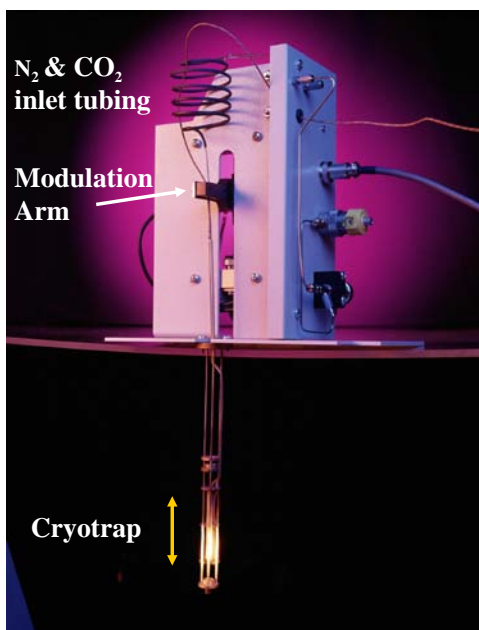
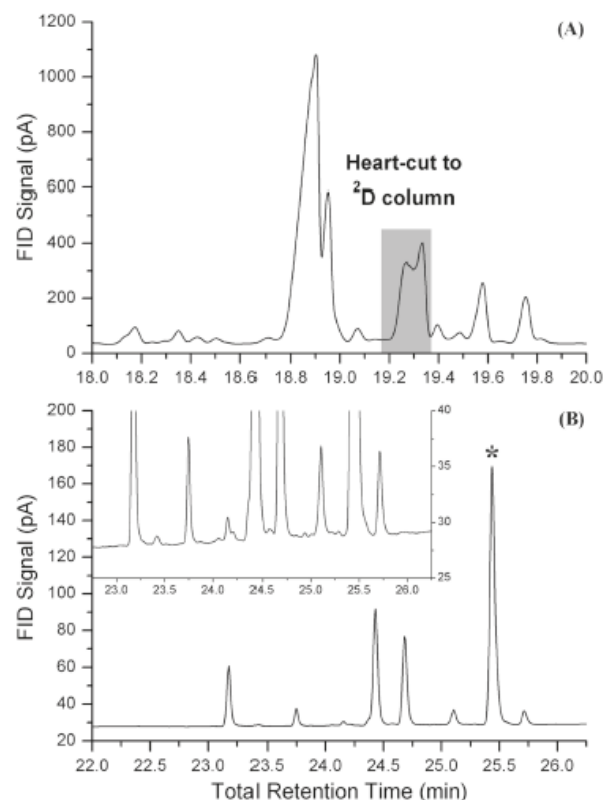


Figure 3. MDGC Application

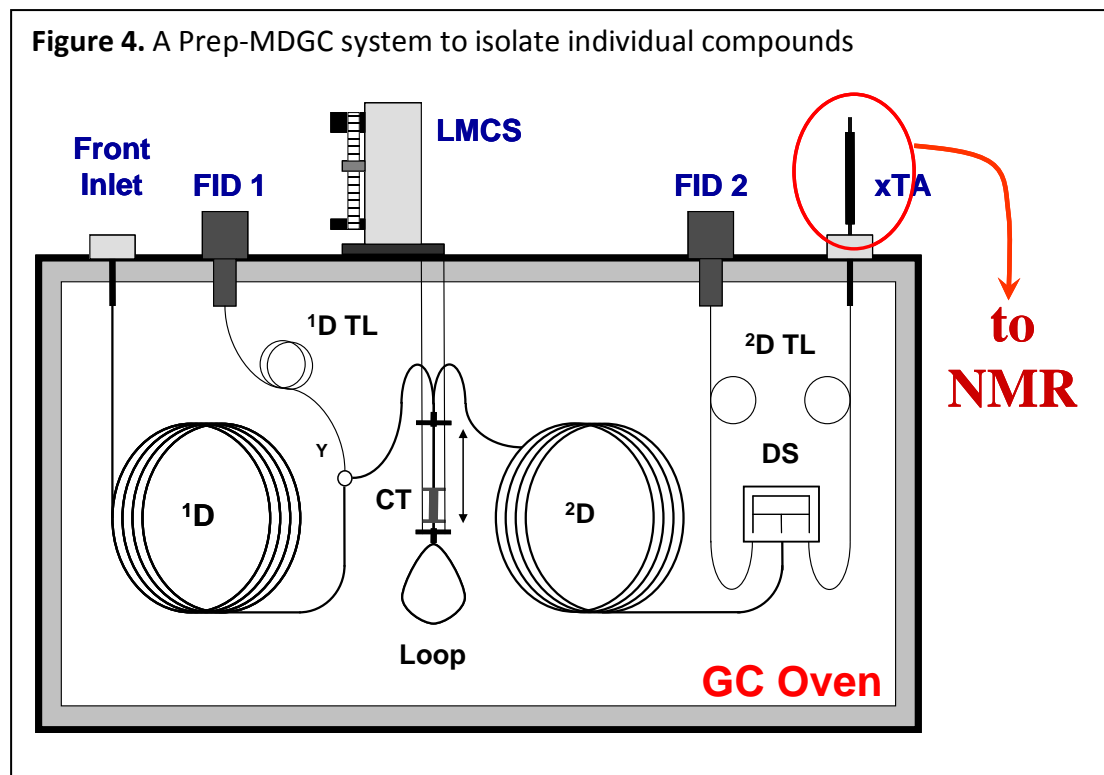


In **Figure 3**, MDGC analysis shows that an unresolved region is cut to a second column, and better resolution results. Here the asterisked peak gave rise to a spicy aroma, according to olfactometry analysis (**refs 132, 157, 162**).

Extending the capability of MDGC – advanced separation with spectroscopy:

Through our research, we have endeavoured to introduce many new GC systems that we believe can – or may – have some role in improving chemical analysis (in this case for volatile chemical samples) - i.e. to provide relevant solutions to the complex analytical problems that face both researchers and industrial technologists. This is aimed at pushing the boundaries of classical analysis, and finding new approaches that have not been possible or thought of. The only arbiter as to whether our innovations are successful at delivering new capability, is through the uptake of our – or similar methods – in research and industrial analysis. It is interesting to contemplate whether a new conceptual approach – even if publishable – meets the ultimate goal of being truly relevant to contemporary analysis, and by extension, how useful innovation in chemical analysis ultimately proves to be!

Recently we have developed a new capability for MDGC as shown in **Figure 4**. This system is an ‘analytical’ scale preparative GC system, which can target small sections of a sample separated through the ¹D column, trap this section in the loop which is isolated in space from prior and subsequent peaks, and then release the peak(s) of interest to a ²D column. Multiple peaks in the target section are then separated. At the end of the ²D column, a Deans switch (DS) can further be used to heart-cut one single peak to a external trapping assembly (xTA). By making repeat injections, it is possible to concentrate the single peaks into sufficient amount to allow spectroscopic techniques such as NMR to be used for characterisation of the peak. This is a powerful addition to classical mass spectrometry methods to add significant identification capability for chemical structural assignment.



We make wide use of Deans switches and related devices promoted as Capillary Flow Technology by Agilent Technologies (see for example <http://www.chem.agilent.com/en-US/Pages/Homepage.aspx>; and search Capillary Flow Technology). This is shown as DS in Figure 4.

The above system allows the improved separation of heart-cuts, accomplished by selection of overlapping target zones in the loop which are then passed through the ²D column, to be switched into the DS. Ideally this gives a single compound product which, when the sample is injected many times, is concentrated up to a mass that allows various spectroscopic methods to be employed. One of these is NMR. The list of publications reports various such applications (**refs 188, 200, 201, 210, 213, 228**), used to demonstrate the basic method.

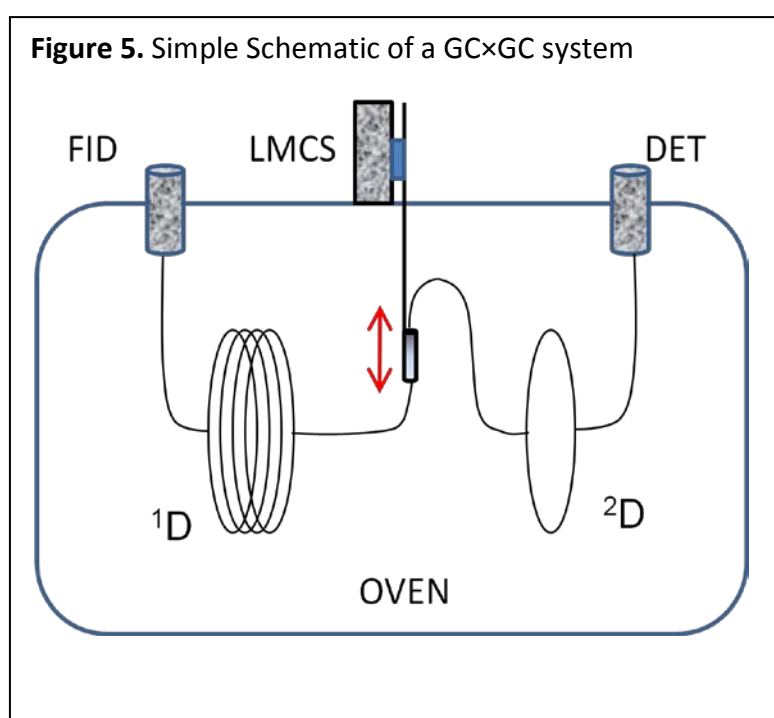
Comprehensive two-dimensional gas chromatography:

Our most widespread recognition has come from the development of comprehensive two-dimensional gas chromatography (GC \times GC), for which we almost universally have use the LMCS device. The first publications on the LMCS and its role in GC, was in 1996 and 1997. Soon after, it was demonstrated for use in GC \times GC, for which a rotating heater element was used in prior research. Soon after, cryogenic methods largely supplanted the use of the ‘sweeper’ system in commercial GC \times GC instruments (**ref 80, 88, 96**).

Since these early demonstrations of what we felt at the time to be a new basic operational mode of GC, it has been our continuing interest to develop fundamental

considerations and relationships (ref 76,143, 150, 154, 183), define new nomenclature (ref 98, 205), research detector technologies (ref 144, 149, 153) and apply GCxGC as widely as possible (ref 146, 185, 186, 192, 199, 203, 224). Clearly interested researchers are often attracted by methods that provide different – or new – informational content for application case studies with which they are familiar, and so we have deliberately tested GCxGC in as wide a range as possible in order to establish a solid ‘beach-head’ for the technique. This was critical in the early years, when it was felt that GCxGC needed a few serious champions who were convinced of its importance to the area of volatile chemical analysis. We hope that today there is no doubting the position of GCxGC in the panoply of analytical GC methods.

Figure 5 is a simple schematic diagram of the GCxGC method, as reported in our implementation of the method.



The LMCS performs its function by oscillating back-and-forth along the column, but there are important differences between the Figure 1 and Figure 4 arrangements.

1. The ²D column in GCxGC is relatively short. Contrast this with the long – or more classical length ²D column – in MDGC. One may feel that the short ²D column will not have much separation capacity, but this fails to recognise differences in GCxGC. MDGC has a few discrete heart-cut events. Normally the heart-cuts might be all collected together (in a cryotrap) and then the oven cooled and the ²D column eluted in one run, over the time frame of a conventional GC analysis. It is also possible to put the ²D column in a second oven, and/or to pass the heart-cuts to the 2D column without cryotrapping.
2. The short ²D column in GCxGC means that the ²D analysis is completed in fast – very fast – time, eg. 2-6 s. This now permits ‘modulations’ of the

interface device (LMCS here) to be conducted very rapidly, maybe every 2-6 s. We call this the modulation period, P_M . Since the two columns are in direct fluid connection, all the sample peaks exiting the 1D column enter the 2D column. And part of the peak that enters the cryotrap is focussed into a sharp band since (ideally) the cryotrap acts as a collection zone – or as a ‘gate’. The sharp band can then be passed to the 2D column simply by modulating the LMCS. Here, two effects can be noted.

First. If a peak width exceeds the modulation period ($1w_b > P_M$), then that peak entering the modulator will be modulated into more than one peak on the 2D column. We refer to this as the modulation ratio, M_R , the peak width of the 1D peak / P_M . This is a significant departure from classical GC where normally each single compound will have a single measured response. In a data system, we now have to have some way to deal with MULTIPLE PEAKS from a single compound.

Second. The 2D column should – MUST – have a phase coating that is different from that of the first. This is the basic tenet of multidimensionality. Since we have two GC columns, one might argue that this cannot constitute a multidimensional system (ie. two independent techniques do not exist – as in the case of GC-MS). But we can fall back on the idea of polarity of a GC column to discuss multidimensionality further. If two compounds elute at the same time from a first column, can we know which compound will elute first from a second column? If we do not know their ‘polarity’ or better expressed as their retention mechanism on the 2D column, then we will not be able to predict their retention. Thus we can now state that multidimensionality exists if the ‘mechanism’ of one dimension is different to that of the second dimension, then we can have independent analysis properties. Just as the mechanism of GC is different to that of MS, then the mechanism of a polar column is different to that of a non-polar column. Of course, we still have ‘boiling point’ as a primary mechanism determining retention in GC.

This discussion then extends to ‘orthogonality’ of the multidimensional experiment, and we’d say that true orthogonality does not exist in MDGC or GCxGC, but the important thing is that GCxGC provides opportunities for separation that simply do not exist in a single column nor MDGC experiment.

Figure 6 describes the process above in a pictorial sense (ref 92). The modulator results in the individual peaks in (A) generating the narrow peak pulses in (B). Since they have the same total area, the peaks in (B) must be significantly taller. They are also modulated into discrete zones according to the P_M value, and their 2D retention. Different peaks that occur at the same 1D time but have different retention properties on the 2D column will be separated on the 2D column. Conversion to a 2D presentation format, they will appear as separate peak zones in the 2D plot, which is shown in (C) for the two peaks here. The 2D plot is essentially a ‘map’ of the chemical properties of all compounds in the sample, as suggested by Fig.6(D). Here, a 1D non-polar; 2D polar column set is indicated.

Figure 6. Process for generation of a 2D GC×GC plot.

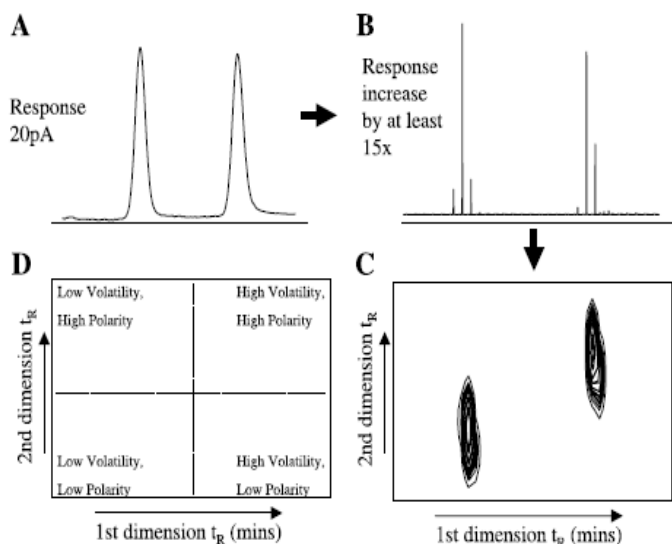
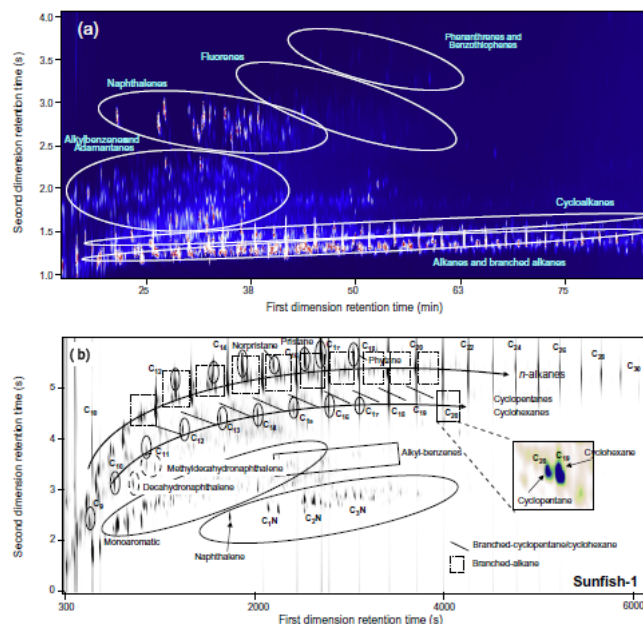


Figure 7. GC×GC plot of a crude oil sample,



Finally, a more substantial example is given in **Figure 7**. Our study of biodegradation of crude oil classically produces an ‘unresolved complex mixture;’ in GC (Geochim. Cosmochim. Acta, **ref 233**). This appears as a big ‘hump’ in the chromatography result. To adequately resolved this has been a challenge to GC researchers for many years. In 1D GC analysis, the result would be like collapsing all the peaks in the GC×GC plot of Fig. 7 onto a single axis – with therefore no separation! Here, an exquisite chemical class separation is revealed, with ‘horizons’ displaying different class polarities – alkanes, cyclic compounds, olefins, aromatics.

We invite you now to look through our compilation of publications, primary research literature, reviews, and book chapters.

We also hope that you will find some interesting applications related to a number of our studies – essential oils, petrochemicals, illicit drugs, derivatised compounds – flavonoids, metabolites - FAME, perfumes, traditional Chinese medicines, incense.

We hope that you will find answers to any questions that you might have regarding the basis of GC×GC, and MDGC. If you have any questions regarding the research we have conducted, or would like to follow up further opportunities to participate in the research we conduct, contact us below:

Contact us for research innovation in gas chromatography, mass spectrometry and hyphenated GC analysis.

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