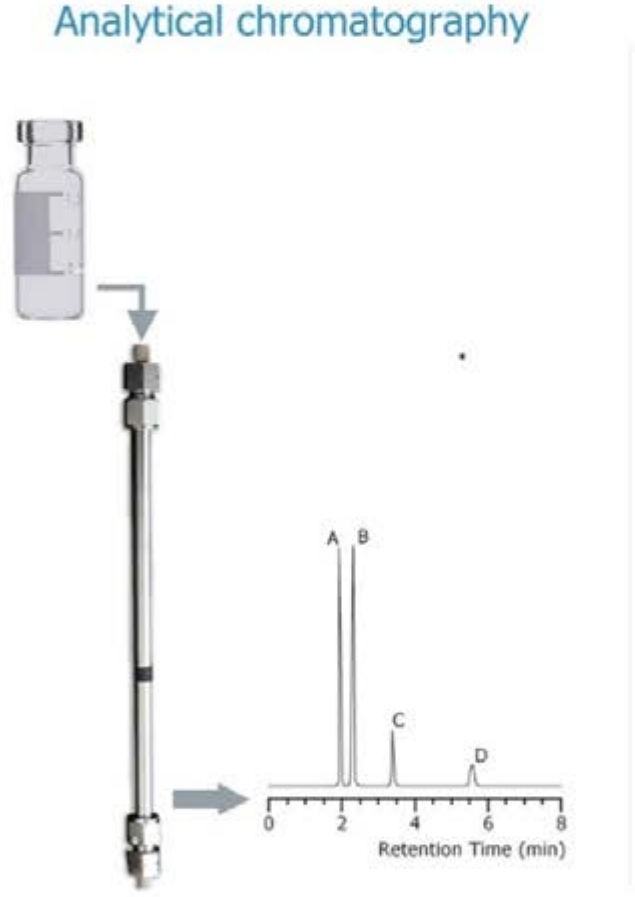
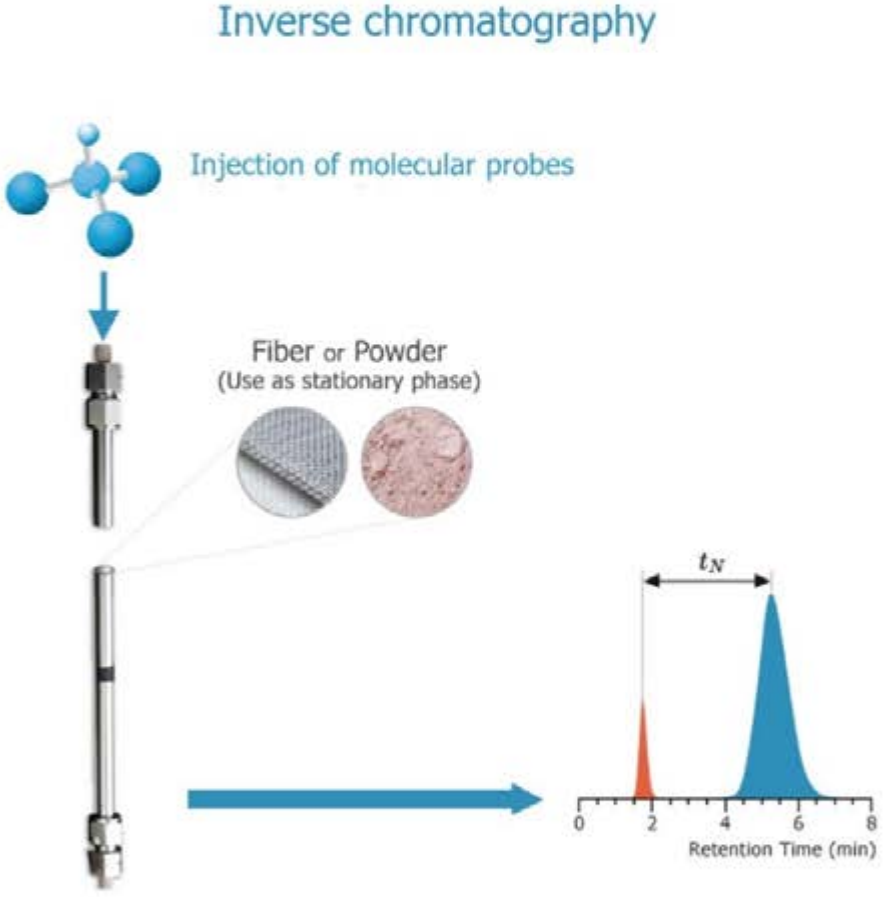
IGC Science
Principles & Practice





Prof Steven Abbott

IGC Science:
Principles and Practice

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Preface

It is unfortunate that Interfacial Gas Chromatography, IGC, is relatively little known and little understood. The situation is changing rapidly for the better and this booklet is my attempt to help even more users to appreciate why IGC is so useful for so many surface, and bulk, investigations.

There is a key reason why IGC has been less popular than it should be: many people who have tried to use it have found it unreliable and unhelpful. This is not the fault of IGC but the fault of some of the machines that are sold as being for IGC but have numerous fundamental flaws that make them basically unusable for effective IGC work (though excellent for other purposes). I personally know many people from academia and industry who have had bad experiences from unsuitable machines and who now find that IGC on a suitable machine is simpler, quicker and much more insightful over a range of real-world problems.

There is another reason - the name itself. The "I" has always stood for "Inverse" which is a genuinely unhelpful word as it conveys only that it is different from "normal" GC. It is far more important to name it after what it does - provide information about interfaces - than to merely contrast it with analytical GC. Of course, all GC techniques are "interfacial". My excuse is that unlike the others, for IGC the focus is on what we can learn at the interface. And as it is the only one with "I" in its acronym, there is no chance of confusion.

I have also had a personal dislike of a key aspect of many IGC analyses: they focussed on "surface energy" (which, as is well-known, I find of very limited value), and featured values that were implausibly high. Most surfaces that we are likely to use are in the 30-50 mJ/m^2 range, yet IGC might routinely find values of 100 or 200 mJ/m^2. It is now clear that in many cases such high values cannot be taken seriously as a measure of surface energy but, when combined with some other key measures, provide very useful information about our surfaces.

So the focus of this booklet will be on what IGC can really tell us about our surfaces and, therefore, how we can use that information for better scientific insight, better formulation, and superior quality control. The key is to ask the right questions using techniques that can give meaningful answers. So asking "What is the surface energy of this material?" is usually the wrong question. A better question is "What can the probe molecules tell me about how this surface compares to the same material prepared or treated somewhat differently?"

As with my other books, all key ideas and formulae are linked to on-line apps so you can explore things live. Just click on the link and you can immediately start exploring. The apps are standard HTML5/Javascrip/CSS3 so they run on phones, tablets and laptops, are safe on corporate networks (the standards prohibit unauthorised access to your device), and are free and free of ads.

Many of the illustrations and scientific analyses come from Dr Eric Brendlé at Adscientis in Mulhouse, France, and Dr Henri Balard who founded Adscientis. They are from the Mulhouse School of IGC science that has been so important over the decades. I would like to thank Eric, Henri and also Dr Ralf Dümpelmann of Inolytix who works closely with Eric.

I also want to thank Sabine Schmelzer who so capably organized a series of IGC conferences where I had the chance to meet and learn from so many IGC experts. Also I thank Dr Rachel Calvet from the Ecole des Mines in Albi who alerted me to a key formula that has helped shape this book. Early in my studies of IGC I learned to appreciate the work of the Poznań school of IGC under Prof Adam Voelkel who led the way in many areas, especially (for me) in terms of HSP measurement. My thanks go to him too.

Finally, I must point out that the views in this booklet are mine. I choose to write in a direct style that gets to the practical core of the issues. So I deliberately miss out subtleties that experts would choose to include. Please blame me for things that you think are wrong. Because this is an eBook I am happy to admit my errors, acknowledge whoever pointed out the errors and quickly publish an updated version.

Steven Abbott
Ipswich, 2018

In April 2020 the eagle eye of Lee McManus spotted a number of issues with the text, most of which I've fixed. A key one was that I had (and this is embarrassing) used "absorption" throughout the book when I should have been using "adsorption".

I warmly thank Lee for his help with this text, plus some glitches on the accompanying apps

Abbreviations and Definitions

5-fold way	Determining γ_d, IM, RIM, ISP, K_a/K_b systematically
AEDF	Adsorption Energy Distribution Function
AFM	Atomic Force Microscope
AN	Gutmann Electron Acceptor Number
BET	Brunauer–Emmett–Teller theory of surface adsorption
DN	Gutmann Electron Donor Number
FC	Finite Concentration, as in IGC-FC
HSP	Hansen Solubility (or Similarity) Parameters
ID	Infinite Dilution, as in IGC-ID
IL	Ionic Liquid
IGC	Interfacial Gas Chromatography
IM	Morphology Index (Index of Morphology)
ISP	Specific Interaction Parameter
Ka, Kb	Acid and Base constants derived via AN/DN
MPt	Melting Point
PEO	Polyethylene Oxide (or PET, Polyethylene Glycol)
RIM	Relative Morphology Index
SEM	Scanning Electron Microscope
Tg	Polymer Glass Transition Temperature
ToF-SIMS	Time-of-Flight Secondary Ion Mass Spectrometry
Vg	Specific Retention Volume
Vn	Net Retention Volume

1 Asking the right questions

The first question is "What is Interfacial Gas Chromatography and why has it always been called Inverse Gas Chromatography?"

In analytical GC, the one most of us know, the stationary phase inside the column is constant and we are interested in finding out, from the retention times and peak areas, what is in the sample we have just injected. In IGC, we inject, known probes such as heptane or methyl acetate one at a time to see how they interact with whatever we have placed inside the column. This is a sort of inverse of normal GC. But it seems unfortunate to define a wonderful technique as being the inverse of a different technique. By calling it Interfacial GC we are making it a positive technique, where we use known probes to find out what is going on at the interface between the sample and the gas phase. A nice analogy is that (when done at infinite dilution) this is a sort of molecular AFM - using individual probe molecules to answer questions about the nature of the surface of a sample.

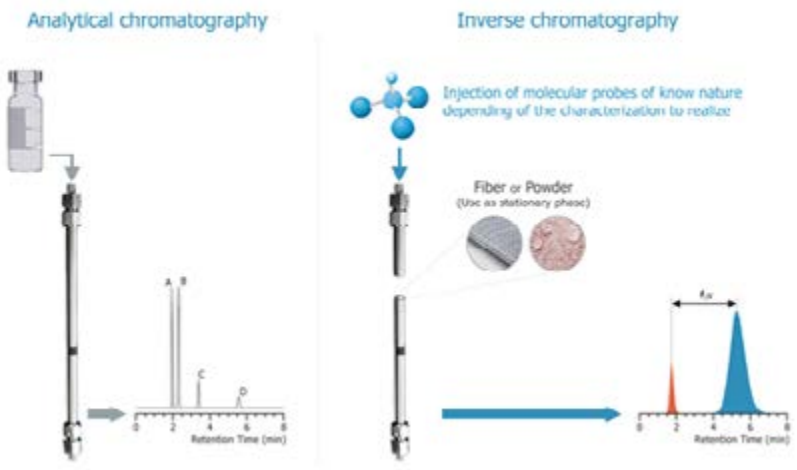

Figure 1-1 How IGC compares to regular GC

So now we have defined the technique, we need to ask why we should use it.

A key attribute of good science is the asking of clear questions and answering them with appropriate techniques. For IGC there are 4 questions each requiring a specific technique to get the good data with which to reach a good answer:

1. How do single probe molecules interact (on average) with the surface of my sample?
2. How do probe molecules desorb from a fully-covered surface?
3. How do single probe molecules interact within the bulk of a thin coated layer of a sample on a neutral support?
4. How can we reliably tell whether we have surface-only interactions, bulk-only interactions or something in between?

There are then matching questions for each technique:

1. Given a set of data about the interactions of single probe molecules, what can we learn about the nature of the surface?
2. From the desorption data, what can we learn about the nature of the surface that we cannot learn by the single probe molecule technique?
3. From the interactions of probes with a thin coating of our chosen material, what information can we derive about the bulk nature of the coating?
4. If we find that our technique and/or our surface is somewhere between the three ideals what, if anything, can we learn about the system?

To be able to answer those questions we need to ensure that our measurement device is fit for purpose.

1.1 The right way to do IGC

Unfortunately, IGC has a history of machines that were re-purposed for IGC measurements, even though they were demonstrably unfit for such a purpose. So we need to define the criteria for a good machine. The reader might find these criteria to be both straightforward and rather obvious. The only reason they have to be stated is that many machines providing "IGC" data fail to meet these basic requirements and the data they produce are compromised, with no hope of "cleaning up" the data to give reliable values.

1.1.1 The right set of probes

For some simpler experiments, just having hexane, heptane, octane and nonane is good enough. But there are far too many experiments that are trying to generate broader understanding of surfaces by using, say, a set of alkanes then a set of alcohols - one providing "non-polar" and the other providing "polar" information. If you are going to inject, say, 8 different probes, you get a far richer store of information by injecting a wide range of chemical functionalities. 4 alkanes and 4 alcohols is a wasted opportunity. The information from hexane, toluene, chloroform, MEK, acetonitrile, ethyl acetate, pyridine and ethanol will be far richer because there is a greater range of van der Waals, polar and H-bonding interactions. As we shall see, a lot of interesting information about a surface can be obtained from a set of linear, branched and cyclic olefins. For looking at the real chemistry of a surface, a range of probes covering Hansen Solubility Parameter space is necessary.

So any machine that makes it difficult and time-consuming to use a wide range of probes is going to force the user to compromise on just a few probes and this will, in turn, either decrease the range of analyses available, or increase the chances that the data analyses miss out on crucial information. The obvious way to allow a large set of probes is to have something like an autosampler

containing a wide range of probe materials, and a smart injection system that can sample from the right vial at the right time.

1.1.2 Infinite Dilution

Many IGC techniques rely on the assumption that the probe molecules interact only with the stationary phase and not with each other, i.e. so-called infinite dilution measurements, IGC-ID. This requires a short, sharp, low-level injection of the probe molecule which in turn requires a fast, accurate injector system capable of injecting very small volumes, and a good, sensitive, detector.

Even with an ideal injection there is a problem. The concentration at the start is relatively high because all the molecules are in a sharp peak. As the front migrates down the column, two effects change the probe concentration.

1. The peak widens via diffusion driven by concentration gradients (broadening is fast at first as the concentration gradients are high) and by fluid dynamical effects, so the local concentrations are reduced
2. The adsorption on the support necessarily reduces the concentration in the gas phase,

Therefore, the conditions are closer to infinite dilution towards the end of the column than at the start. Analysis of the data must take this effect into account[1]. For a given packing, the dilution of a non-adsorbing probe will be less than that of an adsorbing probe so what may be infinitely dilute for one probe may not be for another. The question of how to obtain an objective measure of whether an experiment is, in practice, of ID quality is discussed in a later chapter but a good guide is that the measured retention time and peak shape should not significantly change with an injection of twice or half the amount.

It turns out that on a good machine with a sophisticated injection system it is easy to obtain reliable infinite dilution results. On a poor machine it is almost impossible.

1.1.3 Finite Concentration

An alternative methodology injects a much higher concentration of probe molecules either as a single pulse or, better, via a controlled constant delivery. Either way, the aim is to not just fully cover the surface with a monolayer but to

1 It is also assumed that you have a good measure of the number of theoretical plates, N, to know that you are carrying out a reliable GC measure. In any case, N is required for measurements of diffusion coefficients discussed later.

ensure that multilayer adsorption occurs. The optimal IGC equipment allows these contradictory capabilities: a short, sharp peak for infinite dilution and a controlled square pulse for finite concentration work (IGC-FC). For the first, the injection should be from the head space above the liquid in an autosampler vial. For the second, the syringe injects the liquid itself. In both cases, the systems should be computer controlled to allow accurate timing analysis. For the classic IGC-FC analysis it is important to know that the pressure of the probe molecule is a fixed fraction, typically 0.2 of the saturated vapour pressure which will give the required excess coverage of the surface. It requires a very accurate, slow, liquid injection to reach this stable value without creating large pressure pulses in the system caused by sudden evaporation of the solvent in the injector system.

1.1.4 Perfect peak shape

The shape of the peak at the detector provides lots of extra information for analysis. So we need the shape to depend strongly on the surface we are analysing and to be relatively free from artefacts from the IGC setup.

The shape of the injector pulse has already been discussed. This leaves three other areas for optimisation.

1. Input/output tubing should have minimal effect. The physics of flow in tubing is well-known and the effects on peak shape can, in principle, be de-convoluted. But de-convolution is never perfect, so the tubing shape/length should be optimised for minimum perturbation. Remember, however, that some reasonable length is required to provide thermal isolation if there is a temperature difference between injection port and column.
2. Dead space in the column is, of course, highly undesirable. Because different IGC problems involve different amounts of material in the column, this naturally means that column diameter and length should be chosen to fit the problem at hand. Never use a "one size fits all" column because you will either have too little packing to be meaningful or have empty space in the column which contributes strongly to peak broadening.
3. Different samples pack in different ways and there will be different effects on back pressure and on peak shape. Here there is a mixture of science and art. Packing with tapping, vibration, ultrasonics are options with different trade-offs. The more important peak shape is to your analysis, the more you have to optimise the packing process.

1.1.5 Tuneable flow rates

The gas flow rate is important for any GC and is generally under good control. For IGC it is important for the flow rate to be under good computer control because it is often necessary to vary flow rates in a systematic manner, for example to determine if the probe molecules have had time to equilibrate with

the system being analysed and, as we shall see, measurement of diffusion coefficients depends on a systematic change of flow rate.

1.1.6 The right oven and detector

The ovens in modern GCs are generally excellent with good, accurate temperature control. Detectors are also likely to be good. The only issue with ovens is that a carelessly large oven might mean unnecessarily long input/ output tube lengths (peak broadening) and/or long equilibration times for those experiments that measure the temperature dependence of retention times and peak shapes. Modern systems allow multiple detectors. For IGC-ID a sensitive detector is required for the minimal quantities being injected. For IGC-FC, a less sensitive detector is needed so as to not saturate with the large signal.

The range of IGC analyses would be extended if ovens were available at sub-ambient conditions, but these are less common. For example, those pharma "excipients" with a higher vapour pressure will not remain for long on the support with the flow of gas. At sub-ambient conditions, the vapour pressure might be low enough to enable meaningful analyses, typically, for measuring their Hansen Solubility Parameters (HSP).

1.1.7 Intelligent experiments

Getting meaningful data from IGC requires meaningful experiments which, in turn, require a thoughtful approach to what you are doing. For example, the measurement of HSP values is based on the assumption that the probe molecules have equilibrated with the material on the support and that the support itself is "neutral". To get proper equilibration may take time, so the flow rate of the experiment is important. Too low a rate and your experimental throughput is unacceptably small. Too high a rate and the data are worthless. So at the very least, some tests with a couple of probes (high and low compatibility) at at least two flow rates will be necessary to see if the assumptions are valid.

Whichever analysis you are doing, it requires a similar thought process: think through the assumptions behind the algorithms used to obtain the data, then plan and test to make sure that your assumptions are valid whilst maintaining a reasonable experimental throughput.

All this requires an intelligent machine with good computer control of the test parameters. In regular GC systems it is taken for granted that analyses can be run automatically by smart software. IGC has typically relied on human control of the instrument, severely limiting its productivity and reproducibility. The newer generation of machines is making it far easier to take on challenging surface analyses on a routine basis.

This is especially true when test injections need to be made to first find the appropriate conditions for the correct analysis. Not only does the machine have to be automated, it also has to be intelligent in order to interpret the results of the test injections and proceed with an experiment under the optimised parameters derived from the test results.

1.1.8 Data analysis

The discussions throughout the book focus on idealised experiments. In the real world we need to know if our equipment is approaching those ideals. This means that in addition to the software that does the basic analysis, other aspects of the machine should be monitored for aberrations such as poor peak shapes.

So the optimal system requires data analysis software that can provide not only numbers from the basic analysis (via retention times and/or peak shapes) but also some assessment of the quality of those numbers using other aspects of the data, including comparison with "neutral" test probes that provide information about the general setup - assuming, of course, that the test probe really is neutral.

A good IGC setup

Readers might wonder if I am referring to any specific IGC setup when describing what a system should be like. I'm not. A suitable IGC setup is an intelligent collection of components readily available from the GC world. You can choose from many standard core GC modules (you may already have one), select a high quality (automated) injector system that can sample from many different autosampler probe vials, add switchable detectors for ID and FC use, and choose (or write) your own software for controlling it all. Such a system will be relatively expensive. But compared to the costs of manually running an inferior system and the opportunity costs of missing out on deeper analyses of the data, many in the academic and industrial worlds are concluding that it is a worthwhile investment.

1.1.9 An interesting alternative

It is generally assumed that IGC is carried out on a column containing the material of interest. It is therefore assumed that it would be impossible to analyse the surface properties of a sample of film, a glass sheet or a smooth metal surface. In fact it is rather straightforward to do such analyses using a "column" defined by a serpentine channel in a block of (say) Teflon that can be clamped into contact with the surface of interest.

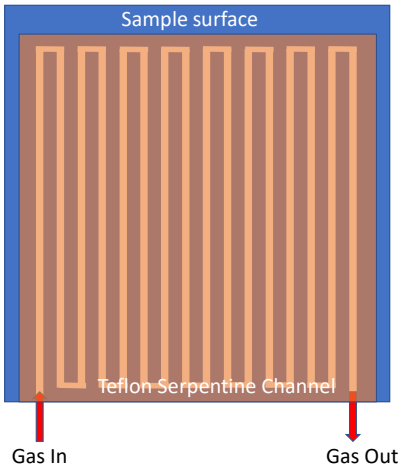

Figure 1-2 The IGC technique for a flat surface

Because the surface area being analysed is relatively small, the technique requires precisely the good system of precise injectors and sensitive detector described above. Because so many systems lacked these necessities, the technique has not been as well-known as it should be.

1.2 Why surface energy is usually not important

I assume that the vast majority of the readers of this book will know, with confidence, that surface energy is of great importance for formulations. So I need to spend some time to demonstrate that it is usually of near-zero importance, especially for adhesion between particles and their matrix.

The reason I am so keen to de-emphasise surface energy is that the fixation on surface energy values has been a serious distraction within the IGC community. Once we can agree that for most of the formulation issues that interest us, surface energy is of minor importance, we can focus our analytical experiments onto those aspects of the surface that make a real difference.

Let us start with contact angle and wetting. From the contact angle of a liquid on a smooth surface we can predict wetting or de-wetting behaviour, and this is clearly of some practical importance. But as soon as we have powders, other issues are far more important, by orders of magnitude. Just changing the roughness of a surface (we're not yet talking of particles) can give large changes to wetting, via Gibbs pinning, Wenzel wetting and other well-known phenomena. As soon as we add particle radius, size distribution, presence of fines etc., the least of our worries is "the" surface energy. And if there is even a small amount of dissolution or swelling of the particle surface (or the treatment on the surface), the effects are likely to be far more profound than anything entailed by a contact angle difference of a few degrees or a surface energy change of a few mJ/m². If you really want to know how a powder wets, then the Washburn technique (discussed in a later chapter) is a good experimental proxy. The formula includes a cos(θ) term for the contact angle. If θ changes from 0 to 60°,

the rate of wetting changes by only a factor of 2, and most surface energies and, therefore, contact angles will give changes far smaller than this. The particle size distribution (rate is proportional to the radius of the pores) is likely to have a far bigger effect on real-world wetting behaviour.

When it comes to adhesion[2], "everyone" knows that surface energy is important. But it is not. Let's do a peel adhesion test involving pure surface energy. The value will be, say, 40mN/m. Now take a PostIt note and do the same test. The value is typically 4N/m. Given that PostIt-style adhesion is designed to be "low", and that it is 100x stronger than surface energy, we have some idea of how irrelevant surface energy is to any real-world adhesion.

People get excited that a gecko can walk upside down on a ceiling thanks to pure surface energy. The way it manages to get pure surface energy adhesion is, indeed, wonderful and interesting. But people then forget that the gecko needs to walk. The adhesion has to be very low so that with a flick of its ankle, the gecko can detach its foot and walk forwards. The gecko is not a proof of the strength of surface energy adhesion, it is a proof of how fragile and delicate such adhesion is. We would not want our particles in, say, a paint formulation, to be so weakly integrated into the paint system - if they were, the paint would readily crack around the particles. For good particle-to-matrix adhesion we need either a modest set of chemical bonds or some form of physical entanglement.

A more sophisticated argument for surface energy is that it can reveal "acid-base" interactions. These can take a surface energy from an overall 40 mJ/m² to, say, 50 mJ/m². Yet if I incorporate maleic acid at a few percent into a polymer so I can get some "acid-base" interactions to improve adhesion, I don't do it to get a 5/4 increase in adhesion. I can get peel strength increasing from 10 N/m to 100 N/m with just a few percent of the acid, then with slightly more acid, the peel strength will crash down to 10 N/m once more. None of this is explicable via "surface energy". [The real explanation can be found in my Adhesion Science book].

What about the behaviour of dry particle powders? Yes, surface energy plays a role, with (again) a maximum factor of 2 difference. Particle shape and size (aspect ratio), proportion of fines, roughness, proximity to MPt or Tg and the effects of minor amounts of moisture will be, in general, far more important.

The fact that surface energy is largely irrelevant to many formulation issues is straightforward and obvious. Yet the IGC community (along with many others!) has obsessed about surface energy to the exclusion of ideas that are far more important. By de-emphasising surface energy and re-focussing on what really matters, IGC will be able to make significant advances.

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2 The free resources on my Practical Adhesion site https://www.stevenabbott.co.uk/practical-adhesion/, or my book Adhesion Science: Principles and Practice, https://www.stevenabbott.co.uk/practical-adhesion/the-book.php provide more details of why surface energy is largely irrelevant and what factors provide strong adhesion.

We shall also see that many of the "high surface energy" values reported for common materials are not reporting high surface energy, but sites where the probe molecule is making multiple contacts with the same surface. This isn't "high surface energy" it is "different surface morphology". To use IGC to investigate changes in surface morphology is an excellent idea. To use it to report on "high surface energy" is not.

1.3 What is IGC really good for?

You have two batches of a powder. Are they going to perform the same in the end-use application? Or an end user reports that batch A is behaving differently from batch B. Or you are trying variations of your particle production process and want to know how the particles might behave in the real world. How can you find out what's happening at the surface?

It turns out to be very difficult to gather meaningful data on the surface of a bulk powder. Electron microscopes and AFMs can give insights into tiny areas of the surface. Light microscopy can tell you about big changes in particle shape and size. BET[3] can tell you something about available surface areas. Those with money to spend can try ToF-SIMS or other fancy techniques. X-rays can tell you about the crystallinity of the bulk particles. But none of these really tell you if there have been subtle surface changes that can affect final performance. Even the basic surface energy (γ_d) measurements, for all their many faults described later, will tell you if something has changed, even if, on their own, they cannot tell you what has changed. A typical example is that of lactose as a pharmaceutical excipient. If its bulk crystallinity changes, a quick X-ray will show it. But changes in surface crystallinity will not show up, yet they can have a big effect on how the powder performs in a pill-making press. A change in γ_d cannot say directly whether the surface has become slightly more or less hydrophilic or more or less crystalline, but a change between batches is at the very least an alert that something is happening.

When we later come to the 5-fold way of measuring a suite of properties in one rather efficient and effective set of experiments we will find that IGC gives us strong hints of what might be going on in terms of functionalities and morphologies. Although, again, IGC provides indirect evidence, the experience of users who can access this 5-fold suite of numbers is that they make sense in terms of what they are doing to their surfaces, and how the particles perform in use.

And when we come to the AEDF (Adsorption Energy Distribution Function) we will see that IGC can give us the big picture of what is happening on the surface. For example, an alkane probe might show a rather dull distribution of binding energies, just as one would expect from a dull surface. But i-propanol might

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3 I assume that everyone has at least heard of BET theory and how it is used to measure surface areas of particles. There is some discussion of it in a later chapter.

show that there is a proportion of discrete high-energy binding sites, meaning that the surface is heterogeneous in a manner that can be investigated further with different probes.

So IGC today, with the right equipment and the right questions, can provide answers unavailable by any other technique and which are of direct use to the producer or user of the particles. The final chapter sketches ideas of how we can ask even more ambitious questions and get good answers.

1.4 GIGO

Whatever the science, it is always garbage in, garbage out. IGC has had an unfortunate history of the wrong questions being asked via the wrong techniques on the wrong machines. If the machine is wrong then life is very tough. If the machine is right then it all comes down to asking the right question and analysing the results to get the right answer. The following chapters address each of our four key questions in turn, before exploring some other issues and ending with a view about the future. As a reminder, here are the questions again:

1. How do single probe molecules interact (on average) with the surface of my sample?
2. How do probe molecules desorb from a fully-covered surface?
3. How do single probe molecules interact within the bulk of a thin coated layer of a sample on a neutral support?
4. How can we reliably tell whether we have surface-only interactions, bulk-only interactions or something in between?

And here are the follow-up sub-questions:

1. Given a set of data about the interactions of single probe molecules, what can we learn about the nature of the surface?
2. From the desorption data, what can we learn about the nature of the surface that we cannot learn by the single probe molecule technique?
3. From the interactions of probes with a thin coating of our chosen material, what information can we derive about the bulk nature of the coating?
4. If we find that our technique and/or our surface is somewhere between the three ideals what, if anything, can we learn about the system?

2 Surfaces and individual probes: IGC-ID

In this chapter we look at how to measure surface properties using, as far as possible, single probe molecules in IGC-ID, infinite dilution.

Let us look first at IGC as a versatile AFM, using a variety of single molecule probes to "scan" the surface.

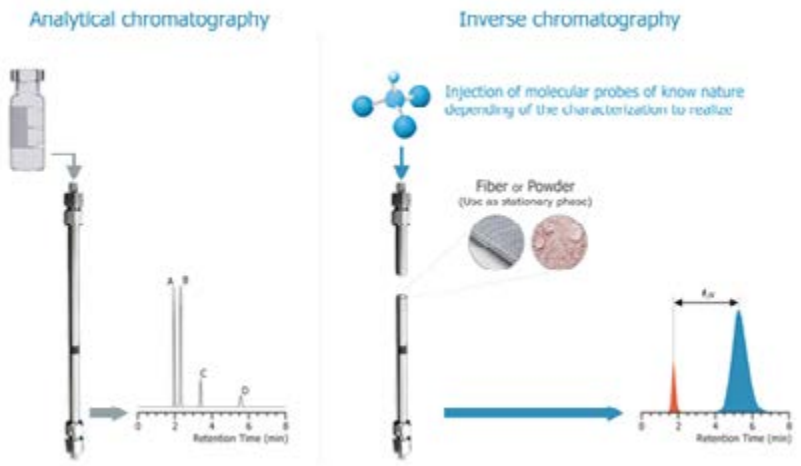


Figure 2-1 How IGC compares to regular GC

The figure, a repeat of the one in the previous chapter, shows that in regular GC we have a known, standard stationary phase and inject our mixture of molecules in order to get separation and quantification. In IGC the stationary phase is our unknown and for each individual known probe, injected one at a time, we measure the elapsed time, t_x relative to t_0 which is the time for the injection front to come through.

For the purposes of this section, we don't care about the peak shape other than an indication of problems within the machine. If there are dead spaces around injection, if there are perturbations to flow via the injection process, if the injection isn't infinitely fast, if the column is badly packed, if the probe is not at infinite dilution, then the peak shape will suffer. But for the moment we are assuming that we have great equipment, run properly. So the only information available from this probe molecule is t_x. As this depends on machine conditions, it has to be translated into a value which can be compared between machines and between runs under different conditions such as flow-rate F (which in turn is corrected for standard temperature and pressure), mass of the stationary phase W and a standard gas compressibility factor J. In this book I have chosen Vg, the specific retention volume, as the standard value for comparisons. It is given by:

Equ. 2-1

$$Vg = \frac{t_x F J}{W}$$

So now we have a standardised volume[4]. How do we derive anything fundamental about the interactions between the probe molecule and the sample? The usual trick is to turn this into a free energy of adsorption, ΔG, via the standard gas constant times temperature term, RT:

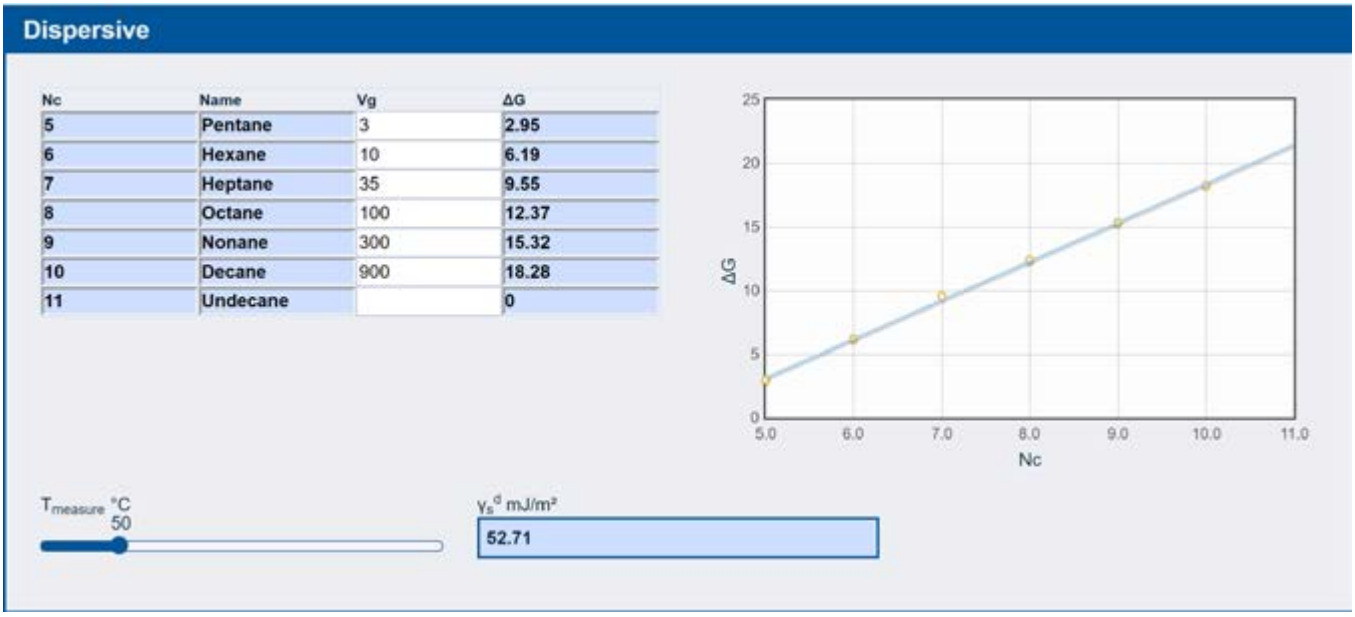
Equ. 2-2 $$\Delta G = RT \ln\left(Vg\right)$$

We have gone from a time to a free energy in two easy steps, and as soon as we have free energy we seem to be able to say deep things about thermodynamics. I find this logic unconvincing for reasons explained later. For the moment, let us accept that it is true and fundamental for the case of an individual molecule. Another way of saying this is that the experiment assumes a case of "infinite dilution" which means that each probe molecule never sees another probe molecule, so probe-probe interactions do not exist. This is often called IGC-ID for infinite dilution.

As we do not have the capability of measuring t_x for an individual molecule, we have to use the lowest-possible amount of injected probe. This in turn requires a good detector and also sharp peaks so there is a strong signal to detect. Many non-optimal machines fail to have good detectors and/or sharp peaks, forcing the user to inject a larger amount and, therefore, rendering the infinite dilution criterion invalid. So the measurements include probe-probe interactions which invalidate the whole idea of measuring a distinctive surface energy. Sometimes this problem is turned into "feature" where it is claimed that you don't just get "a" surface energy but a map of how much of each surface energy there is. For reasons discussed later the "not quite infinite and not quite Finite Concentration" method is not asking a clear question and, therefore, not giving a clear answer.

By adopting a formula such as that of Dorris & Gray (there are various others, but the differences between methods are far less important than having a good machine by which to get the measurements) we can measure the ΔG values for a series of linear alkanes and via the assumption that each CH2 unit adds a fixed amount of "surface energy" we can go straight from the slope of that line to γ_d the dispersion free energy. This is often shown as γ_s^d for dispersive free energy of the surface - but I find these sub/super-script designations too fussy and will use γ_d.

4 Many authors use V_N which is the Net retention volume. The difference is a factor of T/273.



App 2-1 https://www.stevenabbott.co.uk/practical-chromatography/dispersive.php

In this example we have used pentane up to decane and the nice straight line yields a value of 43 mJ/m², a typical value and, perhaps, a meaningful value.

When values from such measures rise into the 100's then we have a real problem. Do we seriously believe that boring CH2 groups interact that strongly with a surface? In my language of "dispersive" (London, van der Waals) interactions in solubility (a topic that will be discussed later), the alkanes are very dull, and you only start to get significant dispersive interactions with cyclic and aromatic hydrocarbons. One measure of dispersive forces is refractive index, which goes in the order hexane < cyclohexane < benzene, so the dispersive component is also in the order hexane < cyclohexane < benzene. But in the world of IGC an aromatic such as benzene is called a "polar" probe. It does not make scientific sense.

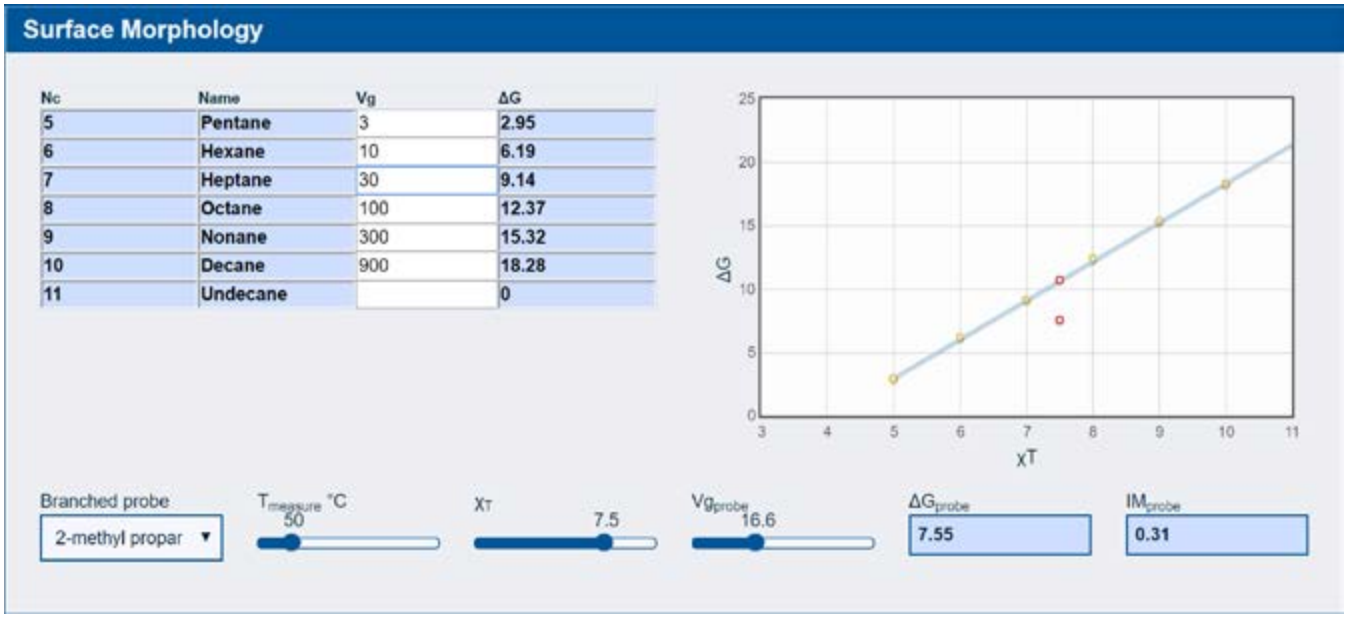
What *does* make sense is that accurate measures of γ_d can be used, at the very least, to highlight differences between samples. As mentioned in the first chapter, the γ_d of a simple lactose powder might have regularly been measured as one value then a "minor change" in production produced a very different value. This happens to be a real-world example and the (unexplained) difference showed up as a very significant change in the dissolution behaviour of that powder - which would have been an unfortunate issue if not spotted quickly, given that this was for a pharmaceutical tablet.

I had often wondered why the size and porosity of the powder hardly featured in discussions of IGC basics. Surely smaller, more porous powders will give larger Vg values than larger, non-porous ones. They do. But if Vg is doubled for a smaller powder, it is doubled for all probes, so the calculated γ_d value is unchanged. More scientifically, the elements in the calculation of the slope of the

Dorris-Gray curve feature area terms in units of m² on the top and bottom so the area cancels out.

2.4.1 The Influence of Shape - IM

The fact that each CH2 group provides a linear increase in ΔG implies that each CH2 in a molecule gains equal access to the surface. Even for linear alkanes this sounds implausible - surely all the rotations and conformations decrease, non-linearly, the average number of CH2 groups in contact with the surface - or maybe they provide a non-linear increase as they can better bend to touch parts other alkanes cannot reach. For whatever reason, the ΔG effect remains surprisingly linear. As soon as we introduce branching and, even more so, cyclic molecules, ΔG values fall below the straight line so the "same" branched alkane, by hypothesis, shows less contact onto the surface. To use this fact, we need to define "same" and "can".



App 2-2 https://www.stevenabbott.co.uk/practical-chromatography/morphology.php

The ingenious answer (what follows is from the original paper[5] on the topic) is to take a surface of a (known-to-be) molecularly flat silica (produced by hydropyrogenation) and for any given branched alkane measure its Vg. From a knowledge of how Vg changes with linear alkane length, the branched alkane can be assigned a "topological index" χ_T which is simply the interpolated equivalent alkane number. So if a branched molecule has a Vg 50% between hexane and heptane, it will have a χ_T of 6.5. The use of χ comes from standard connectivity indices (Wiener, Randic) so the T means Topological and a good estimate of the χ_T of a new molecule can be made from those indices.

5 Eric Brendlé and Eugène Papirer, *A New Topological Index for Molecular Probes Used in Inverse Gas Chromatography: 1. Method of Evaluation*, Journal of Colloid and Interface Science, 1194, 207–216 (1997)

Note that the interpolation can be made directly on the curved Vg versus alkane number plot or indirectly via the linear ΔG plot.

If we use this branched alkane on another surface and its Vg remains at the same relative position we know that the surface is flat - a very easy way to determine flatness! More usually we find that the Vg is significantly less, which means that the surface is too rough for the branched material to make good contact. From the ratio of Vg values we have a Morphological Index which, spelled in French order, is IM:

Equ. 2-3 $$IM = \frac{Vg_{Branched}}{Vg_{Linear}}$$

If we use a cyclic molecule (e.g. cyclooctane) as well as a branched one (e.g. isooctane) we can calculate IM values for each, allowing us to calculate a Relative IM, RIM, given by:

Equ. 2-4 $$RIM = \frac{IM_{Cyclo}}{IM_{Iso}}$$

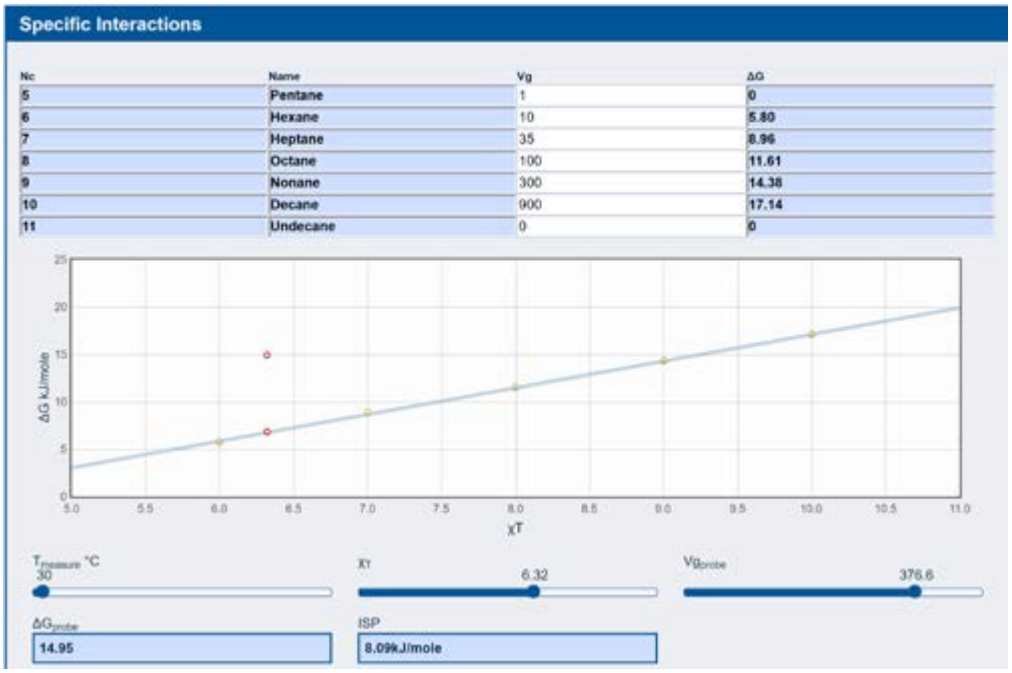
We will make good use of RIM later.

As a specific example of the use of IM, the surface of Aerosil 130, generally regarded as being fairly smooth, has an IM ~ 0.98, depending slightly on the probe, and a γ_d of ~40 mJ/m². For H-magadiite, known to be not at all flat, the γ_d is a super-high (and implausible) 260 mJ/m² with an IM ~ 0.7, showing the inability of the branched or cyclic probes to interact with whatever is causing the linear alkanes to linger longer on the surface.

2.4.2 Beyond alkanes - ISP

Alkanes can only interact with surfaces via dispersive (van der Waals) interactions. As soon as we add other functionalities, other interactions such as polar and hydrogen bonding become possible. This has allowed a tradition of measurements that distinguish between "dispersive", "polar" and "acid-base" interactions. This is clearly wrong. By any rational criterion, benzene has a much larger dispersive energy component than an alkane. Whether it has a "polar" component depends on one's definition and it can certainly participate in hydrogen bonding according to the relatively recent IUPAC redefinition of hydrogen bonds. It seems to be a fundamental flaw of surface energy analyses that components are put into arbitrary boxes ("dispersive", "polar", "acid-base") then argued about endlessly. If we want to measure γ_p, γ_a and γ_b values (polar, acid, base), we should do it not so much for their insights into relatively meaningless concepts but for their ability to distinguish between batches of powder that otherwise look rather similar.

However, no such values exist. If a non-alkane probe has a Vg of X, how can we work out how much of this is due to "dispersive" and how much to non-dispersive interactions? Again we can work out some χ_T for our probe molecules which tell us what the Vg would be if the molecule was a linear alkane, and any difference (calculated from the experimental Vg) in the ΔG value from the "alkane" one can be put down to "specific interactions" though as we know that shape also has an influence it is not obvious how to disentangle the shape-related and specific interaction effects.



App 2-3 https://www.stevenabbott.co.uk/practical-chromatography/specific.php

In the app example, the probe is toluene with a χ_T of 6.3 and alll we can say is that it has a Specific Interaction Parameter, ISP, given in kJ/mol. There does not seem to be a valid way to extract a meaningful γ_p.

With even more effort, using ISP values for a series of probes with varying ratios of Gutmann Donor and Acceptor numbers (DN and AN), it is possible to extract K_a and K_b "acid and base" numbers for the solid surface. However, one extreme probe with a high DN/AN is ether and at the other extreme is nitromethane, neither of which we would consider a classic base or acid respectively, so one has to wonder what K_a and K_b mean scientifically.

An excellent overview of the multiple problems involved in measuring acid/base values is found in a critical analysis[6] by Fekete and colleagues of the measurement of these values for calcium carbonate. We might think that it would be obvious that calcium carbonate is basic, yet it takes a lot of work to

6 Erika Fekete, János Móczó, and Béla Pukánszky, *Determination of the surface characteristics of particulate fillers by inverse gas chromatography at infinite dilution: a critical approach,* Journal of Colloid and Interface Science 269 (2004) 143–152

obtain a reliable value. First there is the problem that calcium carbonate can give absurdly high γ_d values unless pre-conditioned carefully. The reasons for these high values (which are not related to the "true" nature of calcium carbonate) are discussed in the next section. In this particular work, the measured surface energy values keep changing up till about 10 hours of measurement - i.e. removal of residual moisture and/or surface rearrangements require those sorts of times even at the elevated temperatures (100°C or greater) used. Then there is the problem of agreeing on an acid-base scale as there are so many to choose from. Then there is the choice of using ΔG values (convenient) or ΔH values which map more correctly onto acid-base theory but which require ΔG measurements made at several temperatures, plus a plot of ΔG versus 1/T to remove the entropy term.

After an immense effort, the authors found that they could extract some reasonably stable K_a and K_b values and K_b was higher than K_a, meaning that calcium carbonate is indeed basic. By coating with stearic acid, the surface energy decreased somewhat then started to rise, and the surface became net acidic.

The paper itself is excellent because it is such a cautionary story of how hard it is to get good data. But we have to ask ourselves why we would use IGC to tell us that calcium carbonate is basic and that adding too much stearic acid to a surface makes the surface acidic. What formulator is going to be able to formulate better with such insights? This brings us to a more general point.

On a good machine, able to cycle quickly through a variety of probe molecules, with good software able to do the simple calculations based on a good dataset of χ_T values it is easy to get ISP and K_a and K_b values. Because (via χ_T) the values have some element of standardisation, there is a good chance that ISP and K_a and $K_b$values can be compared meaningfully between samples, and therefore allowing a wider range of varying surfaces to be distinguished. Differences and similarities may help sort out good batches from bad batches, or it might be possible to get QSAR fits that relate to end-use performance. This is all valid.

Where I take exception is to a "therefore" following from some measure of polarity or acid/base as part of a causal chain between such values measured for particles, and dispersibilty or adhesion of those particles within a real formulation. The physics of dispersion (i.e. of particles in formulations, not of the dispersive forces discussed above) and adhesion is so far removed from naive ideas of surface energy (even if we had genuine surface energy values, which we don't) that there is no "therefore" to be used.

It is easy to be critical. To be positive we can note that ISP-type experiments, as with other IGC tests, excel at picking out variations between different batches of material, providing potentially important information. Whether the differences

appear in aromatics, esters, alcohols, or in K_a/K_b values allows some idea of what the changes might mean.

To be even more positive requires a methodology to extract real chemical information from the interactions of multiple probes. Some suggestions are provided in a later chapter.

An even greater challenge is to relate probe-dispersant interactions in the gas phase to the same interactions in the liquid, formulation phase. Again that topic will be addressed in a later chapter.

2.4.3 Why are values so variable?

We can interpret this question in two ways. The first is optimistic. It says, truthfully, that IGC is very sensitive to small changes in samples which allows us, for example, to distinguish batch-to-batch variations. This section is about the pessimistic, and far more realistic interpretation.

The first cause of variability is the "conditioning" phase. When a column is packed it will contain plenty of extraneous components such as bound water. So some time spent with a flow of super-dry carrier gas will be needed to remove any bound surface contaminants. One way to do this is at the desired measurement temperature for a long time. Another way is to condition at a higher temperature for a short time. The trouble with the former is that there is no obvious way to know how long is long enough or too long, other than doing repeat measurements till the measured Vg values stabilise. The trouble with the latter is that plenty of powders (a typical example is the much-studied lactose used in pharma) can change their form (e.g. crystallise) at higher temperatures, so the measured value does not represent the real sample. This problem is manageable. The next type of problem is not.

It is often noted that the surface energy changes (in general increases) when particles are milled to a finer particle size. Bland explanations say that the milling "exposes more high surface energy portions of the material" or has "induced more microporosity". There is nothing wrong with the explanations, both might be possible. The problem is the implication that the high surface energy parts are some sort of mild exception or that microporosity is a nuisance compared to the "real" surface area.

If there is an increase in high energy sites, what percentage might it be in order to raise the measured surface energy from 40 to 160 mJ/m²? Some work (discussed in detail later) based on selective coverage of high energy sites by polymers or surfactants shows that even 0.1% has a large effect. To check if this is plausible requires a few steps. Let us suppose that 99.9% of the sites have an interaction energy E (we're not talking about surface energy) of 15kJ/mol and that 0.1% have an energy of 40kJ/mol, which is a considerable increase

in energy as we shall see when we discuss Adsorption Energy Distribution Functions, AEDF. The time taken for a probe molecule to get through a column depends on a base time, t_0 and then an exponential term representing the weighted (n_i) average of the sites.

Equ. 2-5 $$t = t_0 \sum_i n_i e^{\frac{E_i}{RT}}$$

Later we will use an app to do the calculations on a full energy distribution. The point here is to get the general idea. If we take RT as 2.3kJ/mol and t_0=1 then for 100% of the low energy surface, t=exp(15/2.3)= 679. With 0.1% of high energy at exp(40/2.3)=3.6.10^7 we have 0.999*679+0.001*3.6.10^7 = 35000 which means that the retention time is overwhelmingly responding to the 0.1% of high energy sites. The steps from large t to large surface energy are not simple, but the point is still valid that a small fraction of sites with strong interactions have a disproportionate effect.

This simple calculation tells us that most reported "high surface energies" are nonsense. They are telling us only that our probe molecules can easily get trapped in a very few sites with interactions from more than one direction. A graphic gives some idea of what these different sites might be.

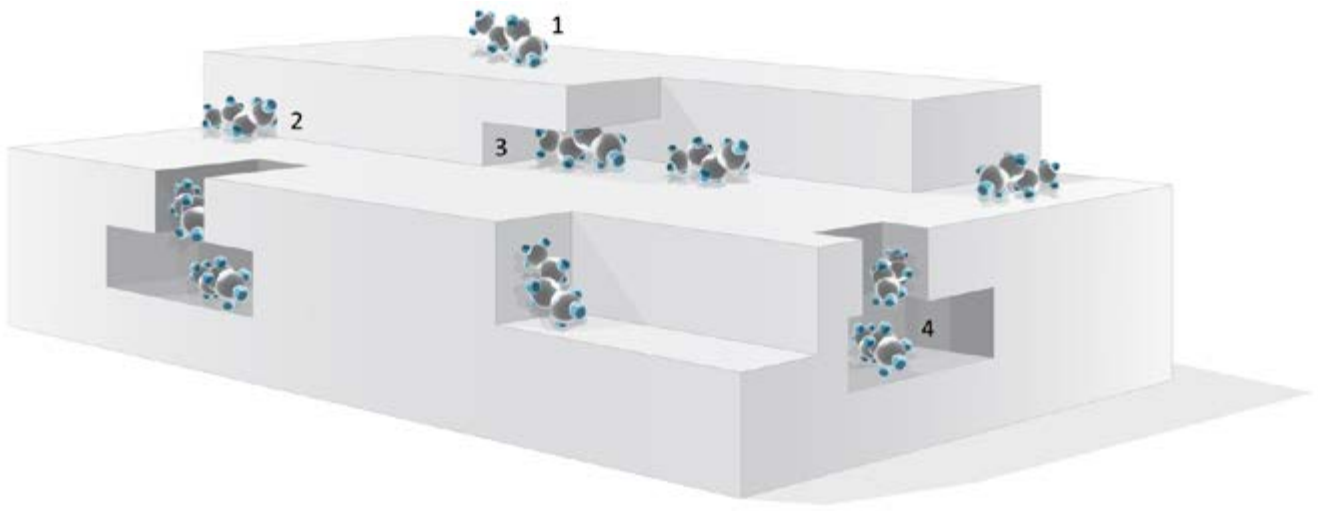


Figure 2-2 We have molecules on the surface (1 interaction direction), at a step (2 interaction directions), in a cavity (3 interaction directions) and in a pore (4 interaction directions).

There is much confusion about what such sites might be and the naming is also confusing. So let us number them 1-4 to capture four rather different types of sites. They will be called X/4 sites because the first type allows only 1/4 of the possible surface energy interactions and the fourth type offers 4/4 of such interactions, i.e. the whole surface of the molecule can interact. The numbers on the image show examples of each of these different sites.

2.4.4 1/4 Interactions

Here we have the classic assumed behaviour in IGC. The probe molecule interacts with the flat surface and so only 1/4 of the surface area of the molecule is involved in interactions. Whether we call these plane surfaces or smooth surfaces, and whether the surfaces are atomically smooth or not doesn't matter at this broad level of definition. Only 1/4 of the molecule can interact.

2.4.5 2/4 Interactions

Here we have some sort of step on the solid surface. Now the probe can interact with 2/4 of the total area. Whether these are called step sites or some other name, the key feature is that only 2/4 of the molecule can interact.

2.4.6 3/4 Interactions

Now we have some sort of cavity or slot between layers or maybe a large void in the crystal surface. The probe can interact with 3/4 of the total surface area so the overall energy of interaction is going to be much larger. Whether these are called slot sites or cavities or voids, the key feature is that 3/4 of the molecular surface can interact.

2.4.7 4/4 Interactions

Finally we have some sort of hole or pore (see the box for the confusing nomenclature for pores) into which the whole molecule can fit. The probe can interact with 4/4 of the total surface area so the overall energy of interaction is going to be the largest of all. The probability of a molecule falling into such a hole is, of course, rather small, yet even a small fraction of such interactions can have a large effect on the measured Vg and, by implication, the supposed γ_d. Whether these are called holes or pores, the key feature is that 4/4 of the molecular surface can interact.

Now we can see that the "high surface energy" of samples such as zeolites is clearly nothing to do with the surface itself having an especially high surface energy. We know that the same components, as flat surfaces, have rather routine surface energies. Zeolites are of interest precisely because they are full of small pores of approximately the size of typical small molecules, so a probe is likely to be interacting with more than one surface as it gets (almost) stuck in a pore. For simplicity we can call zeolites 4/4 structures and should get out of the habit of saying that they have high surface energies.

Pore nomenclature

The naming of pores is very confusing. One scheme is logical, so that micropores are micron sized and nanopores are nanosized. But in much of the particle world, including IGC, macropores are above 50nm, mesopores are 2-50nm and micropores are <2nm. Mesopores give rise to complexities such as capillary condensation. Micropores involve strong multiple interactions with any molecules that can enter them, giving the false impression of high surface energies.

2.4.8 The formulation difference between 1/4 high- & 4/4 low-energy

This is not to say that genuinely high-energy sites do not exist. There can, on average, be surfaces with specific functionalities with higher energies, especially with respect to polar probes. Such 1/4 sites might turn out to be super-important within a formulation, for example as points of binding into the matrix. The point is that the IGC community has far too often taken measured values as proof of high energy in general, rather than indication of a small subset of high energy sites. The differences, in practice, are large.

In a formulation, there is often no great reason why 0.1% of high energy sites will be of importance, whereas a whole surface with a higher energy would be likely to have very different interactions. And if the measured "high energy" is due to 4/4 sites, this is probably irrelevant to how a formulation (polymers etc.) will interact with the particles as the sites might be completely inaccessible to anything other than (irrelevant) alkane IGC probes.

This means that it should be routine to check what the situation really is, using techniques that properly reveal the adsorption energy distribution. In a later chapter we will see an example, using the irreversability index, I_{irr}, where a rather straightforward experiment showed that a "high surface energy" site was attractive to hexane rather than to i-propanol, making it likely that the high energy was due simply to the ability of hexane to fit into a site (maybe 3/4 or 4/4) to which i-propanol (and presumably other interesting molecules in an eventual formulation) could not gain access.

2.4.9 The 4/4 system summary

The above points are illustrated nicely via a paper[7] from Calvet and colleagues that attempts to specifically "poison" the active sites on a surface using various polymers and surfactants. It turns out that 0.08 wt% of polymer is sufficient to transform "high energy" talc into a typical modest surface energy material. But

7 Marie-Pierre Comard, Rachel Calvet, John A. Dodds, Henri Balard, *Inverse gas chromatographic study of the surface properties of talc impregnated with different acidic and basic polymers*, Powder Technology 128 (2002) 262– 267

it is not just a case of polymer smothering the surface[8]. Although a polyethylene oxide, a polyethylvinyl ether and the surfactant CTAB were more-or-less equivalent in poisoning the surface (the differences in behaviour are interesting but are not important in this context), polystyrene, which by hypothesis cannot get its bulky side-chains into high energy sites, requires 2% of polymer before the "surface energy" reduces.

If the IGC community had some way to easily poison the few % of high-energy sites, then it would become possible to use a wide variety of probes to better understand those parts of the surface (the overwhelming majority) that will influence the interactions with other parts of a real-world formulation. Because "high surface energies" sound interesting, the IGC community has spent more time measuring these (usually) artefactual values than it has spent working out how to measure those parts of the surface that will truly influence their formulations.

2.1 Topology and Chemistry - the 5-fold way

We can now switch from a generally negative tone to a totally positive one. While any individual value is of little intellectual or formulation value, the combination of values is very powerful because we can work out if differences between samples are due to topology, chemistry or both.

Let us say that γ_d varies between samples. This might be because the surfaces are of genuinely different chemistry or because there is a different topology - varying numbers of 2/4, 3/4 or 4/4 sites. We have no way to tell. By doing IM measurements we might get hints about the topology, but this won't tell us if the chemistry is also playing a role. Although the idea of RIM (Relative IM) is not explored properly till a later chapter, we can briefly say that it is a measure of unexpected interactions. If RIM is greater than 1 it is telling us that some extra interactions are taking place and these can only plausibly be ascribed to chemical interactions between the probe and molecules from surface treatments such as dispersants or surfactants. It might be that for the alkane probes the extra chemistry provides no extra attraction - after all, alkanes don't interact much with most polar chemicals. If we now measure polar probes and ISP, they still cannot tell us unambiguously about chemistry because the X/4 sites might contain specific interactions absent from the bulk surface. So we need the RIM equivalent for the polar probes. As a specific example, if the surface has been treated with a PEO-type molecule, the RIM value for an alkane will be small yet it will be large for, say, i-propanol which interacts well with PEO. Finally, by performing some sort of acid/base analysis to measure K_a/K_b, we might find that changes between samples are caused by a shift in acid/base functionality.

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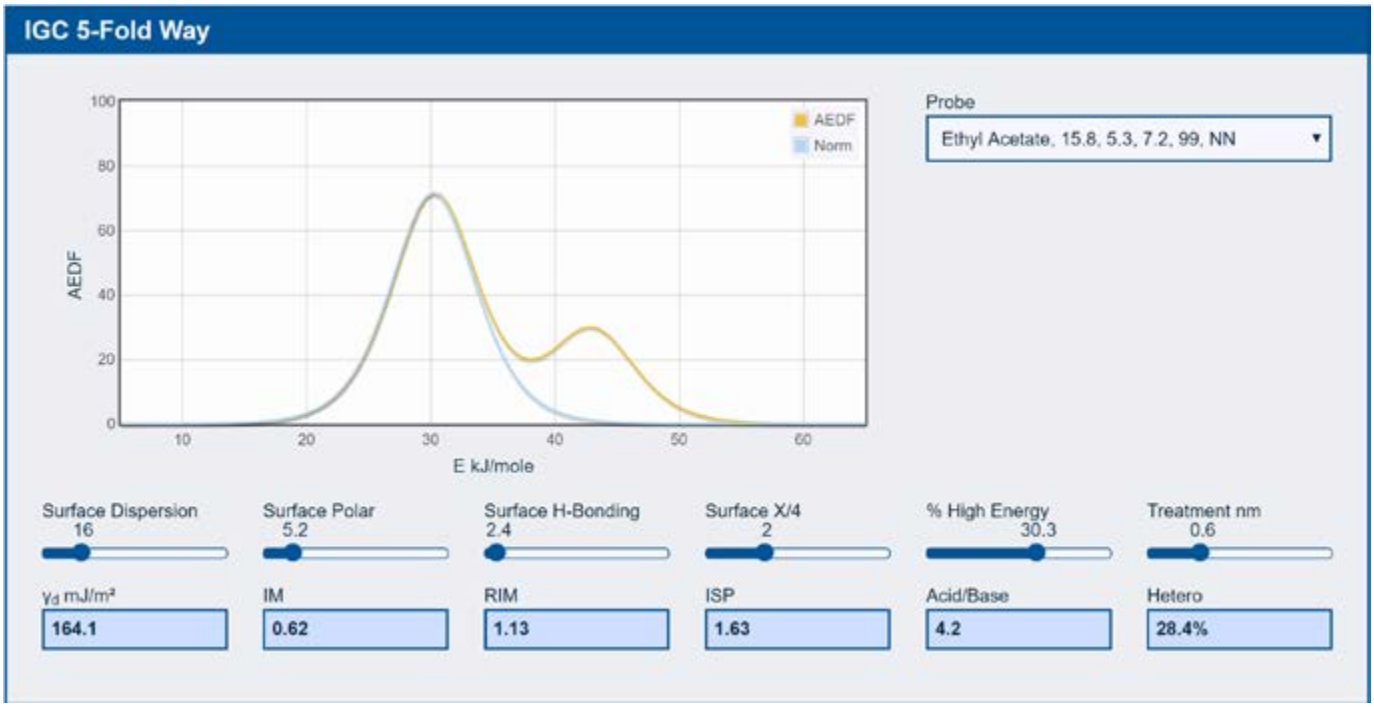
8 I'm not able to work out what % of the surface of the talc is covered with polymer at 0.08%, but because the effect is so specific, as opposed to the polystyrene, I assume that it is "small".

To get all 5 measurements: γ_d, IM, RIM, ISP, K_a/K_b might sound a lot of work. On unsuitable machines it is. But with modern, high performance, automated IGC systems it is not at all difficult. This means that we can routinely use the 5-fold way to get a fingerprint of changes between samples (comparison between different types of surfaces are probably less valid), giving us actionable ideas about whether the surface shape (topology) has changed or if the changes are due to functionality (chemistry) - or some mix of both. No other technique is capable of providing such insights. The criticisms about the value of the individual measurements remains; currently, IGC provides indirect insights. Yet the theory tells us, and practice confirms, that this 5-fold approach helps us understand what happens to our materials after changes of preparation, treatment, handling, storage, and use.

An attempt to capture these complexities in a plausible but merely illustrative manner is contained in the 5-fold way app. The app text goes carefully through each variable and how it affects the AEDF (Adsorption Energy Distribution Function) which is described in the next chapter and from which the retention time is derived by the sum of the exponentials, weighted by the AEDF. The reason for the app's existence is discussed in the final chapter.



App 2-4 https://www.stevenabbott.co.uk/practical-chromatography/IGC-5.php

The inclusion of the AEDF might plausibly suggest a 6-fold way, but in reality the AEDF is the one calculation that binds them all so it really stands on its own.

The app is attempting the impossible: going from the AEDF via a chain of logical interactions to the values currently measured. I have written it because I think that doing something along these lines is better than doing nothing. The fact

that a sound theoretical basis for doing this does not (yet) exist is a challenge discussed in the final chapter.

As long as we use IGC as a sensitive control between different batches, the causes for different measured surface energies or parameters do not matter too much. If we use naive interpretations of these individual values as if they tell us something about surface energy or polarity or hydrogen bonding then we are using pseudoscience, something that is not helpful in the long term. If we can find a direct way to interpret measurements, along the lines suggested in the app, then we will have a revolution in IGC. In the meantime, the 5-fold way at least gives a routine way to examine a surface from different perspectives and correlate changes in a plausible manner with other aspects of the system.

3 Surfaces Fully Covered - IGC-FC

We now move to a totally different set of questions and ways of asking them. The core question is: "If the surface is completely covered with probe molecules, interacting with themselves and with the surface in a complex, probably co-operative manner, what happens to those interactions as the molecules desorb down to a bare surface?" Although we can ask an equivalent adsorption question, in practice the technique is much harder to implement in IGC, so we will only discuss desorption.

For this we use IGC-FC, Finite Concentration, and the experiment is apparently simple: add a big slug of probe to the column and watch how the detector signal changes over time. There are, inevitably, two sub-questions: how big is the slug needed to adequately cover the solid?; how do we best add that amount?

The answer to the first question used to be that it is difficult to know in advance so some intelligent guesswork was needed, along with a few experiments to confirm that there is a significant difference in the elution profile as you go from "too little" to "just right" and no change (other than a longer wait before desorption properly starts) between "just right" and "rather too much".

The answer to the second question is "fairly slowly and evenly" otherwise you risk large-scale perturbations such as a big pressure wave as a large slug of liquid suddenly evaporates in the injector port.

Fortunately a more rational answer to both questions is available[9]. The analysis of the desorption curve typically starts when the vapour pressure of the probe, P, is 0.2 to 0.3 relative to the saturated vapour pressure at that temperature, P_0. This takes us well into the BET region (discussed below) which means we can do a full, relevant analysis of the sorts of interactions that interest most of us. So let's inject that quantity of probe from a simple calculation based on MWt, temperature, T, density ρ, corrected flowrate D_C and $P_{0:}$

Equ. 3-1
$$\frac{P}{P_0} = InjSpeed \frac{RT\rho}{MWt.D_C.P_0}$$

With a modern controlled rate injector at speed InjSpeed, this produces exactly those conditions in the column, provided the injection is sustained for a time needed to provide a stable P/P_0 environment in the column.

Analysis of the desorption starts the moment the signal starts to fall.

9 The analysis here follows a paper presented by Brendlé at the 2018 IGC Symposium in Köln.

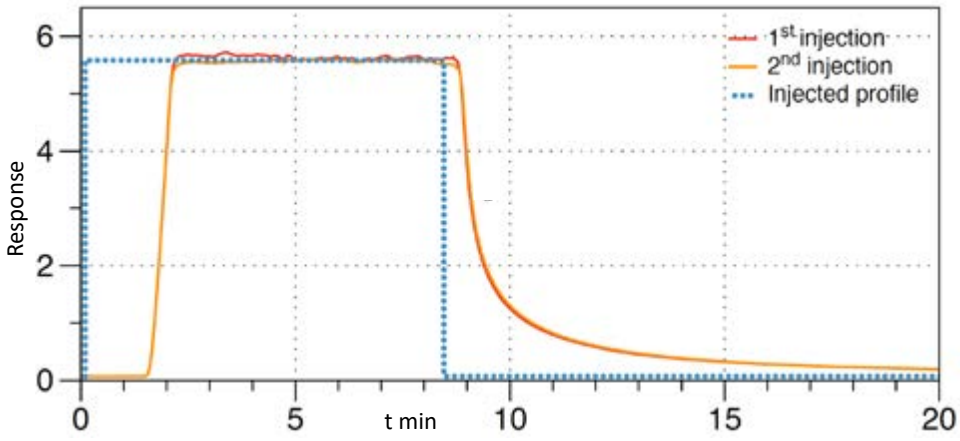


Figure 3-1 A gentle injection of just the right level of probe, allowing an analysis of the desorption curve after about 9 minutes.

Before discussing the analysis of the desorption curve we need to check on an important issue. In the figure above, the curves from the two injections are identical.

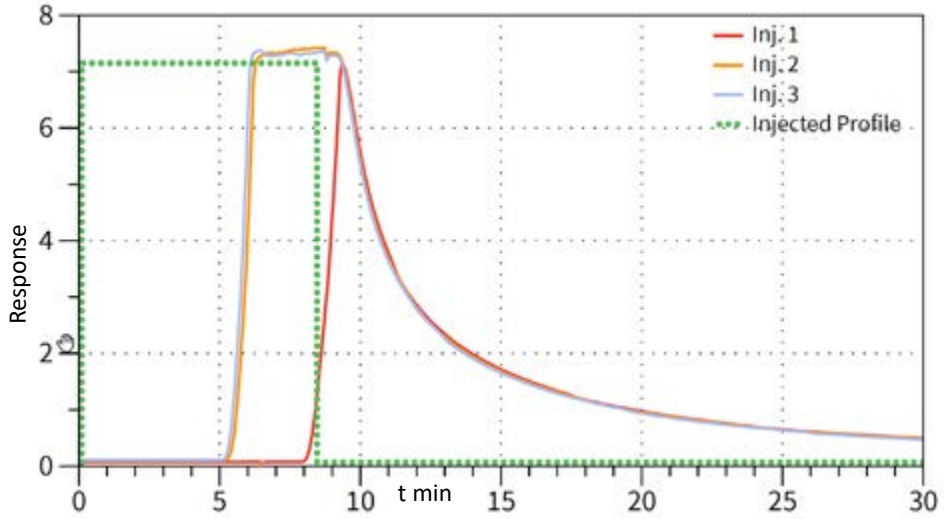
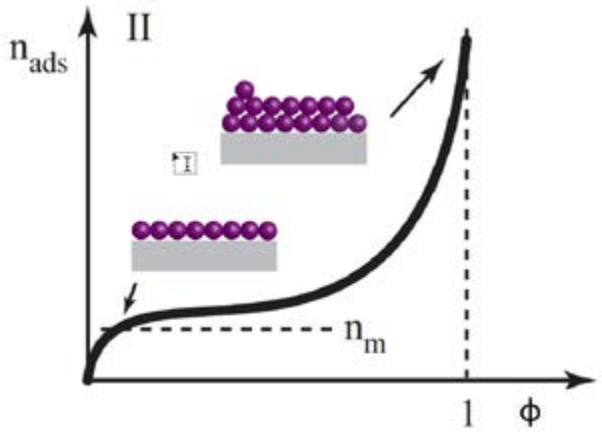


Figure 3-2 The second and third injections are identical but clearly the probe molecules from the first injection showed strong (irreversible) adsorption.

In this figure, clearly the sample irreversibly adsorbed a large amount of probe molecule because it takes longer for the first injection to produce the P/P_0 concentration. This example is extreme, but it should be routine to carry out at least two injections to look for (and calculate) the irreversible adsorption. A subsequent temperature ramp can elute the peak indicating (from the temperature) how strong that "irreversible" adsorption is. From the size of the peak an "irreversibility index" can be calculated, as discussed in a later chapter.

3.1 Analysing the Desorption Curve



What we want from the desorption curve is the isotherm - how the number N of molecules on the sample depends on the pressure P or, as in the diagram[10] how it depends on $\phi=P/P_0$. What we know at each point of the IGC curve is the Vg and (from the size of the signal) the P at that point. Surprisingly, it turns out that Vg (with some minor constants) gives the derivative $\delta N/\delta P$ of the isotherm. So we can obtain the isotherm by integrating from the end of the desorption curve up to our starting P. And from the isotherm we can work out the key BET adsorption parameters, one of the standard ways to consider available surface coverage. And from the isotherm we can also work out the AEDF, Adsorption Energy Distribution Function - i.e. how many low energy up to high energy binding sites we have on the sample.

It turns out that going from desorption curve to AEDF is rather difficult as it is an ill-posed problem with multiple solutions. If you have good software on your system, and can get good data (we shall see that this is trickier than we might like) you will be able to get these values with no need to understand the theory. Here we solve a simpler problem: to create an AEDF and see how that affects the BET curves and the desorption curve. This allows us to get a good feel for what is going on.

The app follows the analysis by Balard[11], and has four graphs showing the four key bits of information. We will look at them one at a time, in reverse order from an IGC measurement.

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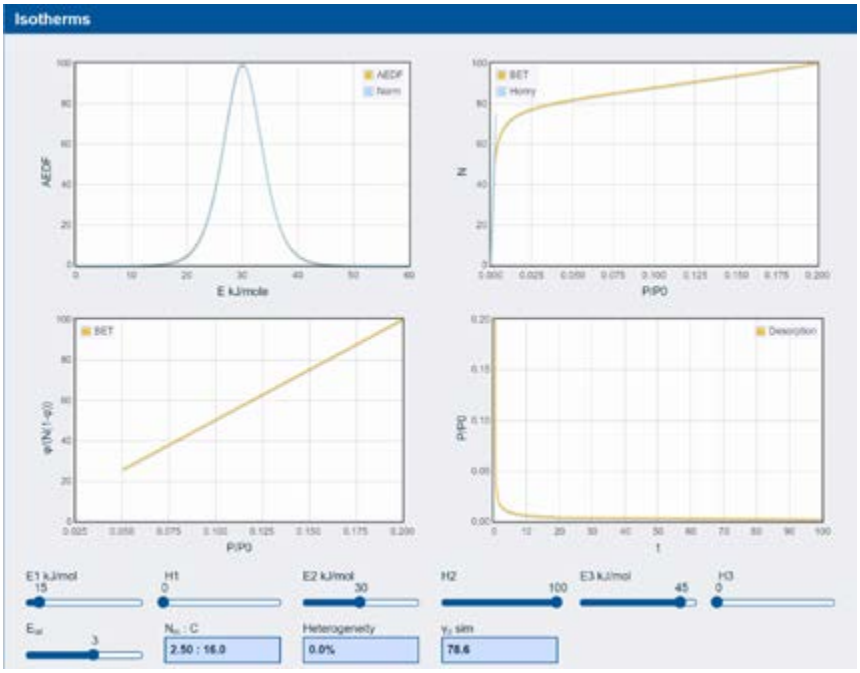
10 Taken, with kind permission, from the PhD thesis of María Graciela Cares Pacheco, *Caractérisation de solides organiques par chromatographie gazeuse inverse : potentialités, confrontation à d'autres techniques*, University of Toulouse, 2015

11 Henri Balard, *Estimation of the Surface Energetic Heterogeneity of a Solid by Inverse Gas Chromatography*, Langmuir 1997, 13, 1260-1269



App 3-1 https://www.stevenabbott.co.uk/practical-chromatography/isotherms.php

3.1.1 The Adsorption Energy Distribution Function

The image shows a simple AEDF. There is a distribution of adsorption energies nicely centred at one energy value E2. To a casual observer, the shape looks like a Gaussian curve but in fact it is the fundamental shape of a Langmuir isotherm of energies ε centred around ε_C, in this case 30kJ/mol:

Equ. 3-2

$$AEDF_{\varepsilon} = \frac{e^{E}}{RT\left(1+e^{E}\right)^{2}} \text{ where } E = \varepsilon_c - \varepsilon$$

If we slide E2 then we can go from low to high energy and see the effects on the other graphs. We can also add low energy elements by increasing the value of H1 (Height) from zero. And we can add high energy elements via H3. Of course we can move the peaks via E1 and E3. There is no option to change the peak width because the Langmuir isotherm leads to a fixed width, independent of ε_C.

3.1.2 The BET Isotherm

The second image shows us how the number of molecules, N, on the surface increases as we increase the pressure P relative to the saturation pressure (100% probe solvent vapour) P_0. If, for simplicity (technically we assume a Type II isotherm), we assume a BET constant C then a curve from a single AEDF energy, E is given by:

Equ. 3-3

$$N = N_0 \frac{C\varphi}{(1-\varphi)(1-\varphi+C\varphi)}$$

where N_0 is a reference value and $\phi=P/P_0$.

When we have multiple values of E we simply sum all the C values derived from the original energies, weighted by the AEDF, so we can imagine that N_0 varies (as in the app) from 0 to 100 depending on the AEDF. The individual C values come from:

Equ. 3-4 $$C = \frac{\exp\left(E - E_{lat}\right)}{RT}$$

where RT is the gas constant times temperature and E_{lat} is the lateral interaction energy a monolayer of the probe molecule on top of those molecules adsorbed by energy E. Values of E_{lat} could in principle be the enthalpy of vapourization of the molecule though in practice the values must be lower because typical values of such enthalpies are comparable to typical values of E, and BET assumes that E_{lat} is always at least a factor of 10 lower than E.

The very early part of the BET isotherm plot is a linear domain called the Henry region because Henry's law applies. It is usually so small a domain and so hard to extract meaningfully from the data that it is merely indicated (as in the app) rather than discussed in detail.

By introducing multiple energies, we are already implying that we are going away from ideal BET. In fact, although many people obtain BET values from automated equipment, they are not aware that their values may hold only a loose link to BET theory because the realities of their particles (e.g. not flat, containing micropores) go entirely against the assumptions behind BET. So a typical automated BET measurement produces "apparent specific areas". An advantage of the IGC, AEDF approach is that although the analysis assumes simple isotherm behaviour, which means that absolute values are unlikely to be realistic except on smooth particles, the AEDF gives you an idea of how much variation there is on the surface, rather than standard BET which sweeps everything together into the single "apparent specific area".

In the app P/P_0 extends to 0.2. If you choose to go to a higher value then things might get more complicated, especially if there are mesopores that can encourage capillary condensation. A check on whether the BET plot (next) remains linear across your chosen domain will provide an alert to other phenomena at higher pressures.

3.1.3 The BET Plot

The BET isotherm (or BET-like isotherm given the effects of real particle surfaces) can be translated into a linear plot of P/P_0 versus $\varphi/(N(1-\varphi))$ where, again, $\varphi = P/P_0$. From the slope, A, and intercept, I, of the plot it is possible to calculate N_m the monolayer coverage and the overall BET constant C. By knowing the cross section of the adsorbed molecule and its molar volume it is possible to calculate the *specific surface area*, S_{BET}, in units such as m^2/g. The app does not attempt to do this as the calculations are with normalized rather

than real units. Because S_{BET} is proportional to N_m you can get a feel as to what would happen as AEDF values change according to how N_m changes. Using real IGC desorption data is a good way of getting specific surface area values[12]. Most "official" BET values are from nitrogen measured at 77K. In general the IGC BET surface areas are similar, within the assumptions of the cross sections of the adsorbing molecules. In general, too, the BET constant, C, is lower (i.e. less binding) simply because IGC experiments are done at room temperature or higher, while nitrogen BET values are obtained at 77K.

3.1.4 The Desorption Curve

It is surprisingly easy to translate between the BET plot and the desorption curve. The BET plot is N versus P and from this it is easy to take the derivative $\delta N/\delta P$. It turns out that $\delta N/\delta P \sim Vg$ (there are some minor corrections). Given that we know P (via P/P_0) and we know $\delta N/\delta P$ from Vg, we can work out N for each value of P. That's the good news.

Here's the bad news - that is obvious in retrospect but not intuitive (at least to me; when I first noticed it, I was very surprised). The dramatic part of the desorption curve takes place once the P/P_0 injection has finished. The data from this part are concerned only with the rather boring right-hand portion of the BET curve. The dull part of the desorption curve is that long tail heading towards zero. This is where all the interesting information is contained, describing the left-hand portion of the BET curve. If you have a poor-quality machine with an unstable baseline and/or with noise down at these low signals, and/or you stop the run too early, then you miss out on the key BET information.

This means, unfortunately, that there are a lot of bad BET datasets out there from machines that failed not only with the initial P/P_0 setup but also failed to gather good data in the long tail.

3.2 Different probes

Standard BET is done with nitrogen as a nice, boring probe molecule. It is perfectly valid to do IGC-FC with simple alkanes as boring probe molecules. What is not yet routine in the IGC world is to do the AEDF work with a variety of different probes. This means that we are missing out on a lot of useful information. Suppose we have an acid/base surface. The AEDF from an alkane probe may well be rather dull. Yet with a suitable "acid" or "base" probe we might find a very different AEDF depending on how many basic or acidic sites happen to be at the surface. From my own reading of the literature i-propanol is the most common non-alkane probe, showing high energy peaks in surfaces with more functional groups. Because alcohols are both donors and acceptors, they don't tell us what mix of acidic and basic sites is at the surface, so we are missing

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12 Although I said that IGC-->AEDF is difficult, IGC-->BET is straightforward, so IGC BET values are as valid as the assumptions behind BET.

some key information that could, in principle, be gathered rather easily, using probes that are respectively pure base and pure acid.

3.3 Routine IGC-FC, plus the 5-fold way

A single AEDF may or may not be insightful. But the *comparison* of AEDFs should become routine for those concerned about changes in their product due to process, treatment, handling, storage or use. By seeing, for example, a consistent decrease in a high energy portion, or by seeing an unchanged AEDF for heptane but a significant change for i-propanol, there is an immediate view of the big picture of what is going on with the sample. In some cases the user will immediately be able to hypothesise why such changes are taking place. In other cases it might require specialist analytical tools such as ToF-SIMS to see what is going on. Given that the AEDF data has been obtained via IGC, and that a machine able to acquire AEDF data is likely to be suitable for the IGC-ID measurements, then investment in the 5-fold measurements may well be a first step to work out whether the changes are topological or chemical, or both.

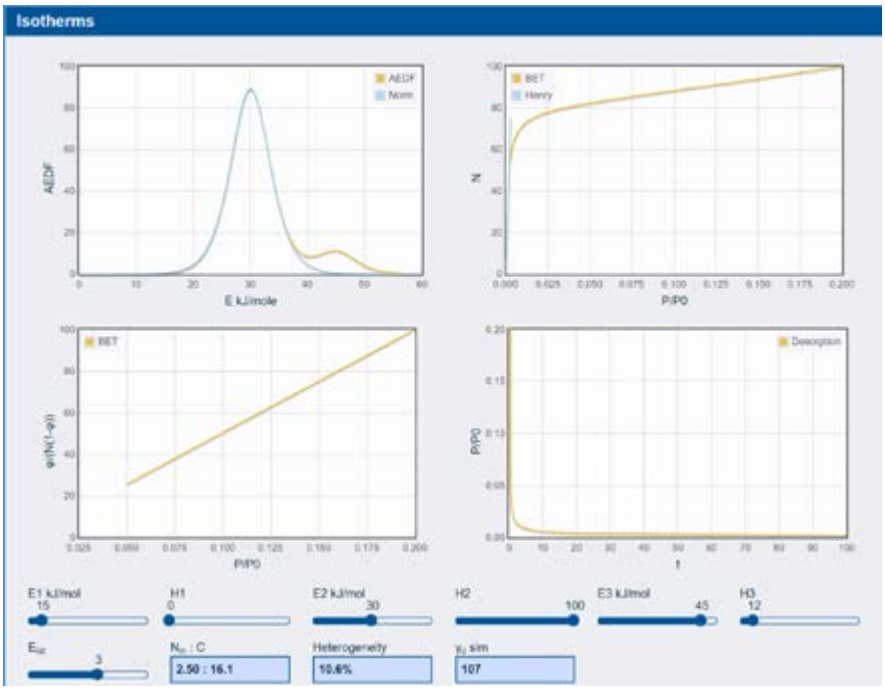


Figure 3-3 Now the AEDF has a small high energy peak with a Heterogeneity of 10.6%.

What constitutes a change big enough to trigger further investigations? Currently the only generally-accepted metric is the Heterogeneity. In the (idealised) example from the app, there is a main peak that contains the normalised main peak, plus an area outside it representing other adsorption energies. The ratio of the area under the extra peak to the total area, is the Heterogeneity. Other analyses can be imagined and can be implemented by the user from the raw data curve.

3.4 Not to be confused with...

There is a well-known technique that purports to measure something that in principle relates to the AEDF. Via injections of different amounts of probe to span a range of particle coverage, the technique results in a plot of "surface energy versus coverage". Given that the technique is relatively simple in principle and these coverage plots are commonly reported in the literature, why would anyone bother with IGC-FC? There are three reasons:

1. As discussed in the later Surface versus Bulk chapter, the reason that IGC-FC is preferred is that the "surface energy versus coverage" plot does not measure surface energy nor does it do the measurement with respect to coverage. The technique produces data that are simply not analysable in terms of fundamental parameters, because the actual interactions along the column during the required experiments are unknown and unknowable.
2. A single, or at most a confirmatory second, injection provides the whole of the AEDF data. For the surface energy versus coverage plot the "surface energy" has to be measured via multiple injections of linear alkanes for each injection of different nominal coverage amounts, so it is a lot more work.
3. The AEDF data can be collected for a wide variety of probes with different functionalities, making it possible to explore the different types of probe/ surface interactions. Only linear alkanes can be used for the other technique (needed for the "surface energy" calculations), meaning that we miss out on a lot of interesting knowledge.

3.5 Summary

IGC-FC, when done properly, provides crucial information lacking from other techniques. The ability to discover the AEDF and how it varies with the probe used is a fundamental step up from the rather simplistic information available from any single IGC-ID measurements. What is holding it back is the lack, up to now, of a broad base of IGC machines able to do these measurements routinely and (mostly) automatically. That is gradually changing; once the technique starts to be routine, and starts to be combined with the 5-fold method from IGC-ID, people will wonder why they haven't always been using it.

4 Bulk interactions

So far, we have used IGC to look only at the surface of the sample. Now we see what happens when the surface is sufficiently "liquid" for the surface effects to be irrelevant (we hope!) and for Vg to depend on how much, or little, the probe molecules diffuse into the bulk surface.

This means, first of all, that we should create the bulk material on the surface. The standard method is to take a (hopefully) neutral support and via some sort of melt or solution process, cover the support with, say, 20-30 wt% of the test material. The ideal coverage is when the surface of any carrier is covered 100% but still resulting in a “dry” powder to allow it to be packed for a good gas flow and conditioned as normal.

There are many analyses that can be performed under these conditions. We discuss two in detail and mention some others in outline.

4.1 Diffusion coefficients

When a molecule enters a bulk material it moves randomly and the net effect of those random movements is diffusion along a concentration gradient, from high to low. The average speed of movement is controlled by the diffusion coefficient which depends on how much free volume is available within the material. This in turn depends on the material (e.g. crystalline versus amorphous), how much it is crosslinked (chemically or via entanglements) and temperature. It also depends on the probe molecule. Smaller, more spherical molecules diffuse faster than larger branched or cyclic molecules. Measuring diffusion coefficients is often rather difficult so it is good that IGC offers one possibility.

Assuming that you have a column packed nicely with the material covering an inert support then the experiment requires the careful measurement of how peak width changes as the flow rate is systematically changed. The theory follows a number of steps.

The first relies on the Van Deemter equation which tells us that the theoretical plate height, H, of the probe molecule depends on the flow rate u via three constants, A, B and C:

Equ. 4-1 $$H = A + \frac{B}{u} + Cu$$

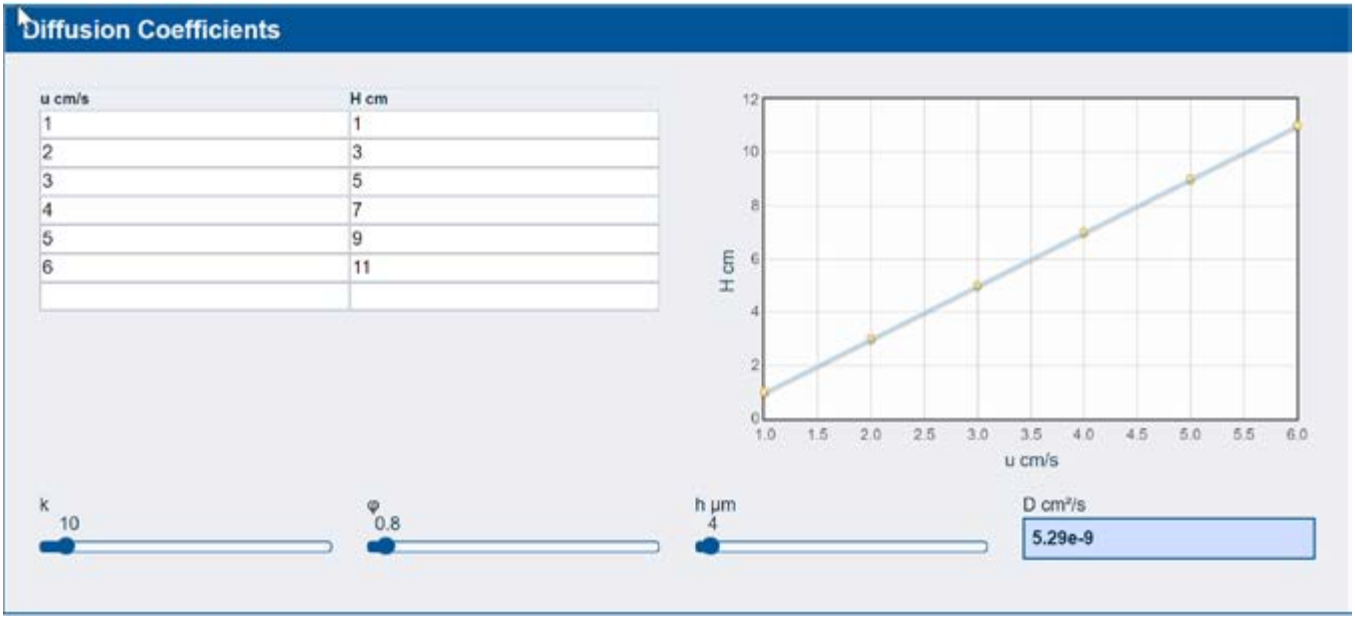
The plate height is measured from retention time, t, peak width d and column length l via:

Equ. 4-2 $$H = \frac{l\left(\frac{d}{t}\right)^2}{5.54}$$

Assuming the B/u is small (a more sophisticated fitting algorithm can remove this assumption), a plot of H versus u gives the slope C from which we can derive the diffusion coefficient, D:

Equ. 4-3 $$C = \frac{\varphi k h^2}{D(1+k)^2}$$

The calculation requires φ which is a geometrical factor generally taken to be 8/π², h which is the thickness of the polymer coating on the packing material and k is the "partition coefficient" which is $(t-t_0)/t_0$, i.e. the ratio of the elution time after the injection peak appears and the time of the injection peak appearing.



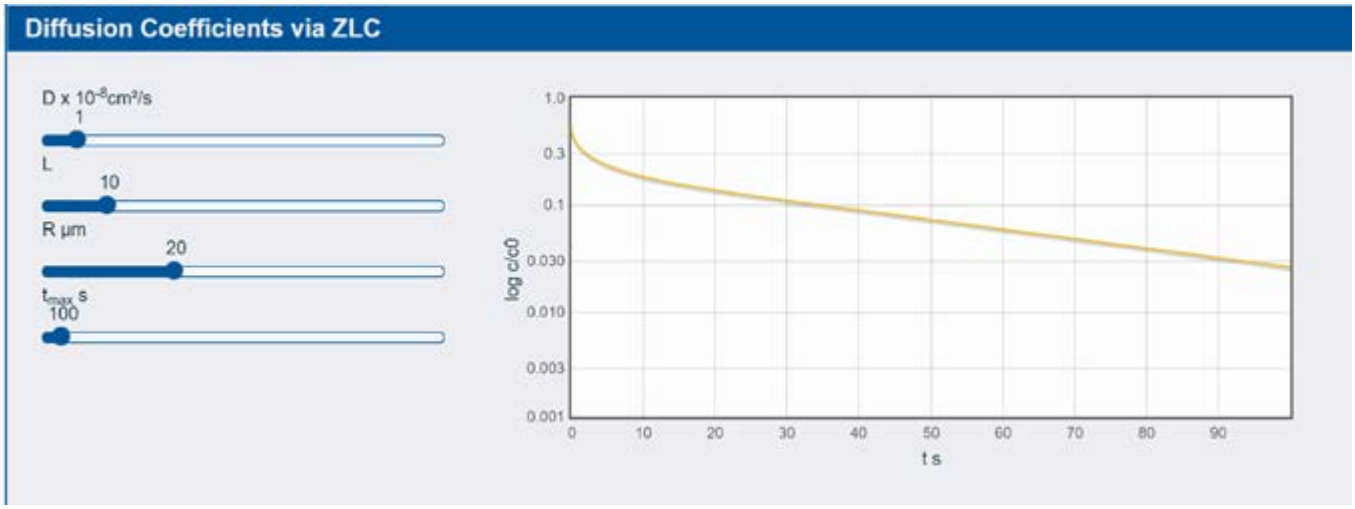
App 4-1 https://www.stevenabbott.co.uk/practical-chromatography/igcdiffusion.php

The app shows an idealised version to illustrate the principle.

As diffusion is important for many things I do, I was very excited to discover this new (to me) way of measuring D values. Unfortunately the technique is not widely used for two reasons. First, those materials that are easy to coat onto the support are generally not of much interest to those who need diffusion coefficients. Second, it is not easy to cover a support with a very thin, even layer of a polymer for which many of us would like to know diffusion coefficients. If someone can solve this problem then the IGC method will become very popular, because although it might be worth the effort, using conventional techniques, to measure D for one or two solvents in a polymer, no one wants to measure the values for many solvents, something that would be easy with an IGC capable of injecting many probes, and software to organise a sequence of flow rates and peak width measurements.

4.2 Diffusion in powders

Although it isn't strictly an IGC procedure, a quick and easy way to measure the diffusion coefficient of probes in powders is performed rather well on a modern IGC machine with a well-controlled pulse injection. The technique is called Zero Length Column, ZLC and has been extensively developed by Brandani and Ruthven[13]. The experiment is very simple! Take a single particle of a known radius R and trap it between two frits allowing gas flow in and out. This is the zero length column. Via a slow, careful injection, saturate the particle with the probe gas. Then follow the desorption curve. It depends on the diffusion coefficient, D, the flow rate F, the volume of the particle, V and the Henry constant K. The analysis is made in terms of a factor $L = FR^2/(3KVD)$. The shape of the desorption curve is rather complex near the start because it depends on a sum of a series depending on the factors β_N which are the solution to $\beta_N \cot(\beta_N)=1-L$. Fortunately this can be done readily in an app[14] and rather rapidly the curve becomes a simple exponential depending on t, β_1, D, R and L. This means that from the linear portion of a log plot of c/c_0 (the ratio of the concentration to the starting concentration) the key values can be derived. In the app we treat D as the input and we ignore V and K because these are subsumed into L. Although L depends also on D and R, for simplicity we make it an independent variable. In practice it varies from 2 (less than 2 and the experiment is invalid) to a few 10s.



App 4-2 https://www.stevenabbott.co.uk/practical-chromatography/igcdiffusionzlc.php

The effects of the two key parameters are straightforward. Increasing the radius or decreasing the diffusion coefficient leads to a reduced slope in the linear domain.

13 Stefano Brandani and Douglas M. Rutheven, *Analysis of ZLC Desorption Curves for Gaseous Systems*, Adsorption 2, 133-143 (1996.)

14 I am grateful to Clément Brendlé for an expert critique of early versions of this app.

In reality, to make sure that the data are in a domain of valid L values, it is necessary to perform the analysis at two flow rates and those who wish to be super-cautious can also vary the initial injection pulse to ensure that the sample was fully saturated - taking into account the fact that the time required to saturate is, for a large L, $0.42R^2/D$. Once these minimal conditions have been validated, it is straightforward to measure diffusion coefficients of many probe molecules and, therefore, to gain insights into how different molecules interact as they move through the sample.

4.3 Other polymer properties

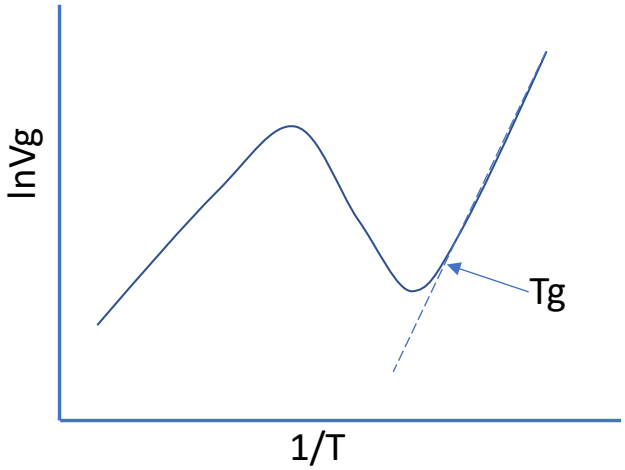
IGC has a fine tradition of investigating other properties of polymers. The topic of Hansen Solubility Parameters, so important for modern formulators takes up the next section. Here we look briefly at other properties that have been measured via IGC. The reasons for the brevity are that such properties do not seem to be of high importance for the formulation world that is the target audience of this book, and because an excellent, full review[15] is available from Yampolskii and Belov. What now follows is a summary of the relevant portions of their review.

The first point, well-known in other "partitioning" chromatography techniques, is that if the probe concentrations in the polymer and gas phase are C_p and C_g, then the equilibrium partition coefficient between the polymer and the gas phase, K is, with a temperature correction, equal to Vg:

Equ. 4-4
$$K = \frac{C_p}{C_g} = Vg\frac{T}{273}$$

A key property that is derived from Vg (plus known parameters such as the molar volume and pressure of the probe and B_{11} its second virial coefficient) is the infinite dilution activity coefficient of the probe in the polymer. Via a similar calculation, the more practically useful Flory-Huggins χ parameter is derived. Very briefly, a χ parameter of 0 means that the probe and the polymer are perfectly happy together, a value of 0.5 means that they are "neutral" to each other (in solvent terms, this would be the theta solvent state) and a value greater than 0.5 means that they actively dislike each other. This is a convenient scale used throughout polymer science, though in practice formulators tend to use χ converted to the even more convenient Hansen Solubility Parameter Distance value discussed in the next section.

15 Yuri Yampolskii and Nikolay Belov, *Investigation of Polymers by Inverse Gas Chromatography*, Macromolecules 2015, 48, 6751−6767



The next popular methodology is to measure Vg as a function of temperature. A plot of lnVg versus 1/T gives a distinctive Z-shaped curve. At low T (high 1/T values) there is a linear decrease in lnVg with increasing temperature until the polymer approaches its Tg. The probe can now readily enter the polymer and lnVg increases significantly. The point at which the curve deviates from linear gives Tg. At higher temperatures the polymer is sufficiently open that lnVg reverts to a linear decrease with increasing temperature.

In the review, the behaviour of the probes around Tg is linked to discussions about, for example, excess enthalpies of mixing and free volume effects. Such matters seem of relevance mostly to polymer theoreticians. Most of us would choose to measure Tg more directly via differential scanning calorimetry but it is good to know that IGC can provide an alternative set of insights into what is happening in this important region.

Subsequent sections of the review cover solubility parameters, which we are discussing next and then diffusion coefficients in an in-depth theoretical manner for those who require analyses deeper than in the previous section.

4.4 Hansen Solubility Parameters

There is now an explosion in the use of IGC to measure Hansen Solubility Parameters, HSP. The reason for this success is the exact opposite to the (comparative) failure of the diffusion coefficient technique. Lots of people want to know the HSP of their oligomers, excipients, emollients, ionic liquids. and other lower molecular-weight semi-solids. For solid materials such as polymers, an existing technique (using a bunch of test tubes and solvents) works very well and there is no good reason for using IGC. Indeed, for polymers below their Tg, IGC cannot be used because the probes cannot diffuse into them. But for the softer samples, the standard technique is difficult to use, and IGC is very effective.

As a reminder, HSP are three numbers to describe the essential solubility/ dispersibility/similarity between solvents, polymers, nanoparticles, excipients etc. The three numbers are:

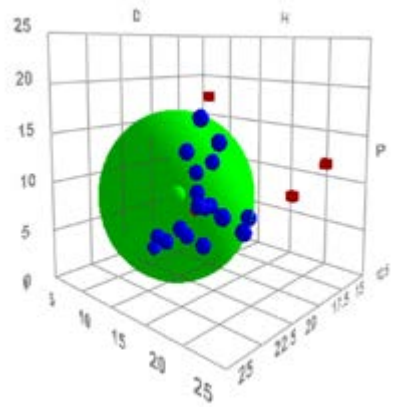
1. δD, the dispersion parameter which describes the polarizability of the electrons within a molecule; the van der Waals interactions that result from

this electronic polarizability, are the main source of cohesion between molecules.
2. δP, the Polar parameter which describes classical polar attractions via a dipole moment.
3. δH, the Hydrogen-bonding parameter which describes the hydrogen bonding capability of a molecule.

The reason the technique is so powerful is that the degree of "likeness" or "unlikeness" can be calculated via the Distance, D, between two substances (e.g. polymer and solvent, or particle and solvent) based on their respective HSP values [δD_1, δP_1, δH_1] and [δD_2, δP_2, δH_2] via the classic formula:

Equ. 4-5 $$D^2 = 4(\delta D_1 - \delta D_2)^2 + (\delta P_1 - \delta P_2)^2 + (\delta H_1 - \delta H_2)^2$$

This equation for D^2 is used extensively by HSP users and will re-appear in terms of IGC measurement.



The classic way to measure the HSP is to put a solid sample into, say, 20 different solvents of known HSP and to find which solvents are "good" (dissolve or swell the polymer) and which are "bad" (leave the polymer unaffected). A fitting procedure finds the HSP value for the polymer which is a sphere that includes all the good solvents (blue in the image)and excludes all the bad ones (red). The centre of the sphere is the HSP value of the polymer. The blue solvents have a relatively small D and the red ones have a larger D.

If the experiment is tried with an oligomer, excipient etc. the range of solvents that are compatible is very large so there are too many good solvents and too few bad solvents to define a meaningful sphere.

The IGC technique uses the long-established principle, discussed in the previous section, that the Flory-Huggins χ parameter, which is a measure of how like or unlike two materials are, can be calculated from the Vg value of any probe. The definition of the χ value maps straight on to that of the HSP Distance, so if we can measure χ we can know D^2 via:

Equ. 4-6 $$\chi = \frac{MVolD^2}{4RT}$$

To measure the HSP of a sample we therefore coat it onto a suitably inert support and measure the Vg values for a range of probes spanning HSP space.

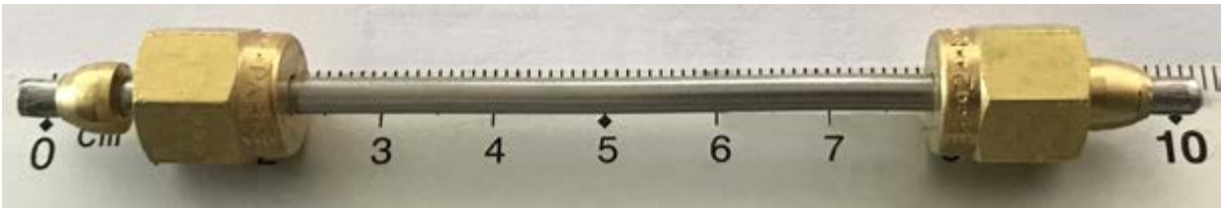
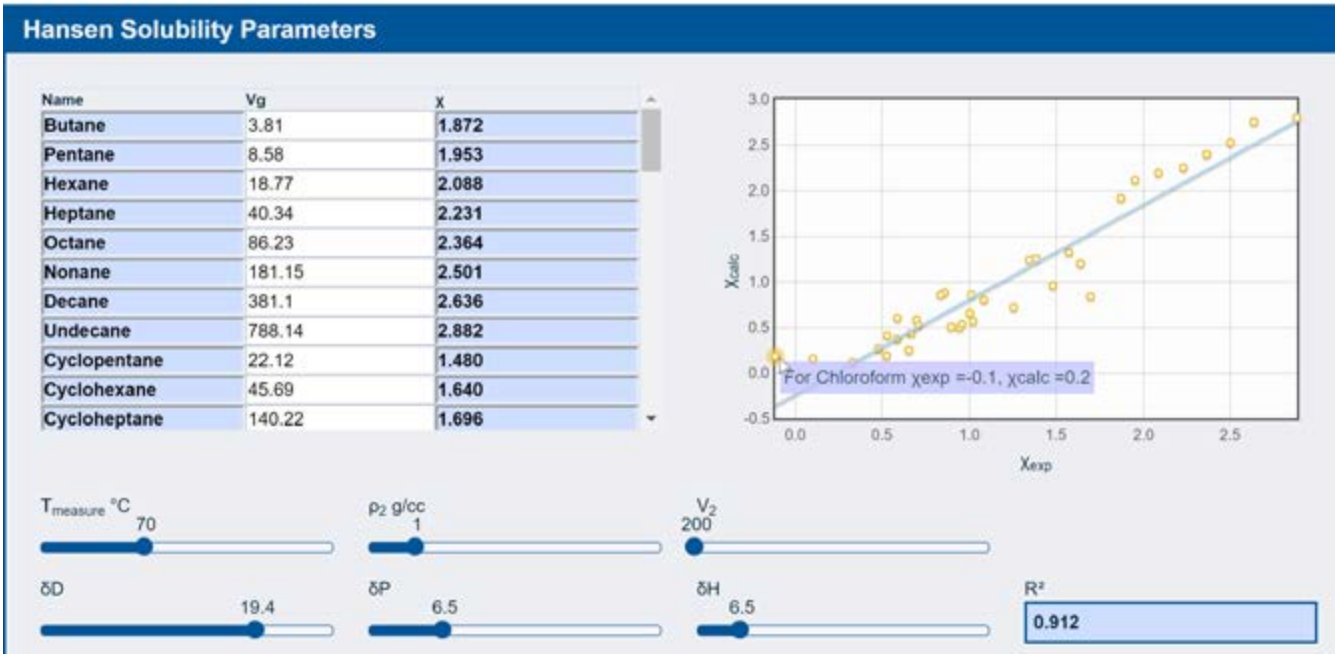


Figure 4-1 A 10cm by 2mm IGC column for HSP measurements.

The image shows a typical short column, 10cm with an internal diameter of 2mm into which a few 100mg of sample are packed. The support material is coated with ~20% by weight of material. This translates into between 10 and 100nm of coating which is a very thin layer. The implications of this are discussed shortly.

In the past there were attempts to use "δD probes", "δP probes" and "δH probes" to calculate the individual HSP values. This makes no sense because most probes have a mix of all three parameters. And if the tests are done with groups of alkanes, esters and alcohols, large parts of HSP space (chlorinated, ketones, nitriles, sulfoxides...) are being ignored so the fitting cannot be good.

Once we have the Vg values and, therefore, the experimental χ values, we need the calculated χ values based on an estimate of the HSP of the sample. Via an optimization algorithm, we can find the HSP values that give the closest match to the experimental data.



App 4-3 https://www.stevenabbott.co.uk/practical-chromatography/hsp.php

The app shows a manual data fit (sliding the 3 HSP sliders) of a dataset obtained by Munk for polycaprolactone at 70°C, above its Tg so that the data

are meaningful. The mouse readout shows that chloroform is predicted to have a larger χ (less compatible) than the experimental value, with an error larger than most other probes. As discussed below, for reasons currently unknown, chloroform shows the same error over a wide range of samples.

A more sophisticated, fully automated analysis is contained within the Hansen Solubility Parameters in Practice (HSPiP) software.

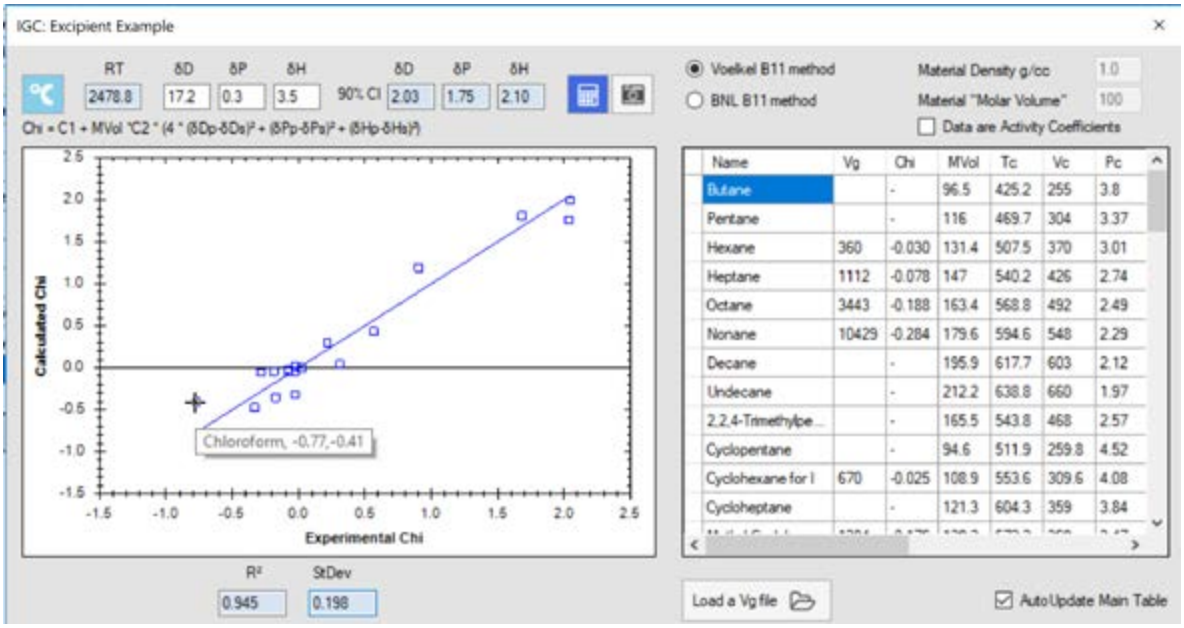


Figure 4-2 A typical excipient automatically analysed via HSPiP. Note that chloroform shows a similar error on a very different, non-polar sample.

The example[16] is a cosmetic excipient (the data suggest that it is a rather simple oil), and is a typical example of the use of IGC to measure the HSP of these otherwise difficult materials which are generally mixtures.

A different dataset shows what happens when assumptions are not valid, because the data are from a polymer measured below its Tg.

16 This and the following example uses data kindly provided by Laetitia Hell of Adscientis.

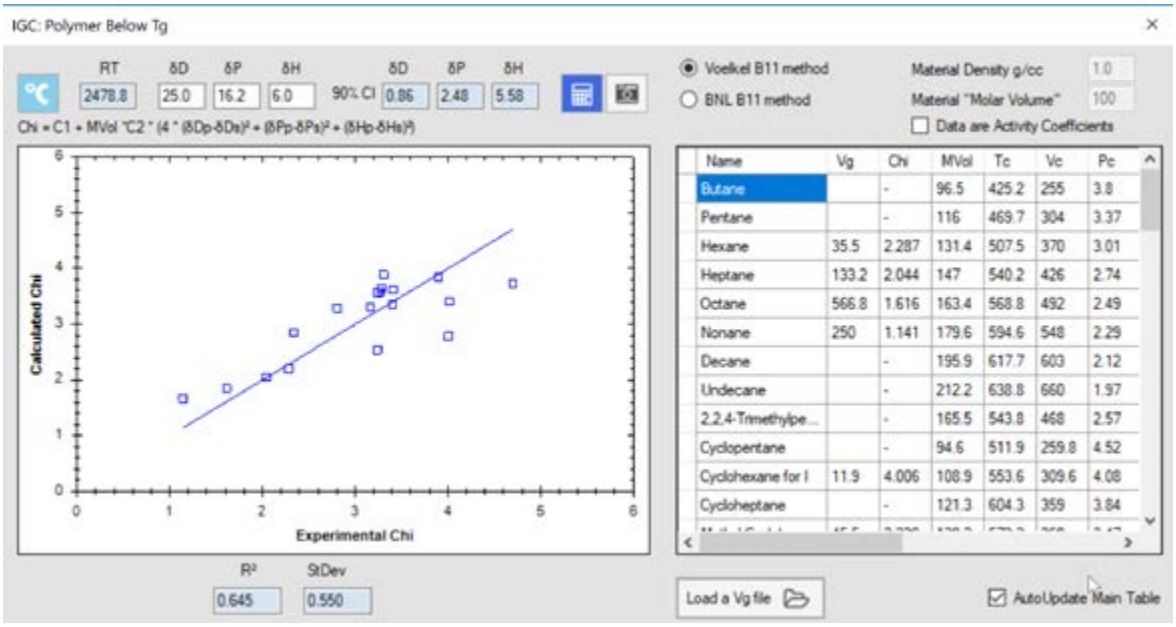


Figure 4-3 A rather poor fit to a polymer below its Tg. Not only is R^2 rather low, but the δD value is implausibly high.

The fit is obviously poor both in terms of quality of fit and implausibility of the fitted δD value. The reason is that the probes could not readily diffuse into the polymer so the Vg values are an unknown mixture of surface and near-bulk effects. In a way, it is good that the results are so bad because they are an immediate flag that something is very wrong.

4.4.1 Problems with HSP measurements in IGC

There are a few problems when measuring HSP via IGC. It is worth stating them clearly so that people can either avoid them or find ways to solve them.

1. This problem is connected to the fact that if the material coated onto the stationary phase is not sufficiently "liquid" then the analysis is not valid. When the material is not at all liquid then the results, as in the example above, are obviously bad so are not a problem. But what about "partly bad"? At the time of writing there is a need for an independent assessment of whether the sample meets the requirement for validity. In many cases such as excipients and plasticisers, there is no real doubt that the sample is sufficiently liquid. Until there is an agreed objective measure, the experimentalist has to use common sense to decide.
2. If the sample is too volatile then it will evaporate during the analysis, invalidating the experiment. This is only fixable on machines with ovens that can go to sub-ambient temperatures.
3. If the intrinsic nature of the sample depends on a low level of water then either the carrier gas has to be pre-treated to the required humidity or the experiment abandoned. There is a special issue with ionic liquids, ILs. It is rather difficult to dry them completely and many experimental data on the performance of ILs are taken (knowingly or not) with small quantities of water

present that can have large effects on the IL properties. If an IL is properly conditioned before IGC measurements then it is likely to be super-dry which is good for analysing the HSP of the pure IL but may be irrelevant in terms of real-world IL performance.

4. If there are too few probes and/or they do not span a good range of HSP space then the data are likely to be of low quality.
5. Chloroform regularly gives an experimental value of χ lower (better associated) than expected from chloroform's HSP values. There is currently no explanation for this (diethyl ether is similarly unreliable) and we greatly look forward to the day when an explanation/fix is found.
6. The support is assumed to be neutral but this is clearly not true in many cases. My own experience, working with Adscientis, is that Chromosorb PAW DMDCS is an unacceptable support as the data obtained from samples coated onto it are consistently meaningless. One hypothesis is that the silanated support is difficult to coat evenly (remember, we are trying to get 10-100nm which is challenging) so the probes interact with the sample *and* the silica support which has a high polar content. Much more successful is the use of Carbopack C which is poorly polar and interacts much less with polar probes. Besides, insufficient coverage is easily spotted by the high disperse surface energy of the carrier itself.

4.4.2 HSP and IGC Summary

At least in Europe, an HSP measurement community has evolved that is open about the best technique to be used. For solids and typical polymers, the classic HSP "20 tube" test is clearly preferred. For pigments and particles, IGC is less relevant unless the particles are fully covered. For many plasticizers, emollients, excipients, oligomers and ILs, IGC is clearly preferred. As the community gains more experience and continues to solve problems, IGC measurements of samples will become even more routine.

5 Surface or Bulk?

If we have a plain silica particle, there is no question that any analysis will be "surface" only, with some caution about what happens in nano/micro-porous particles. If the silica has a thin small-molecule layer of dispersant/stabilizer, maybe we can still think of the analysis as being "surface", though we might expect a dual-peak AEDF, and should be prepared to analyse the data accordingly. If we have a polymeric dispersant/stabilizer, what behaviour should we expect: "surface" or "bulk"? As far as I am aware, this question has not been answered satisfactorily. Finally, if we have Carbopack coated with 20 wt% of an excipient, we can be confident (from the HSP data analysis) that the analysis is "bulk".

The intermediate cases seem to be scarcely considered in the IGC community. This is unfortunate. My view is that this is a huge opportunity for IGC because many of us have no interest in our "pure" particle but in how particle plus dispersant/stabilizer might interact with a formulation. Who cares about "TiO_2" when in reality we use "Stabilized TiO_2", with many different stabilization treatments.

One way that such particles are studied is via standard HSP techniques, where the stability of a particle in different solvents is measured as a function of sedimentation rate: slow = compatible, fast = incompatible. Such information translates directly into formulation strategies. Why can we not get relevant information from IGC?

A step in the right direction has been taken with the development of the RIM/IM plot by Brendlé. My personal view is that this is an important, but limited step in the right direction. Suggestions for a generalisation of the technique are made once RIM/IM has been described.

5.1 RIM/IM

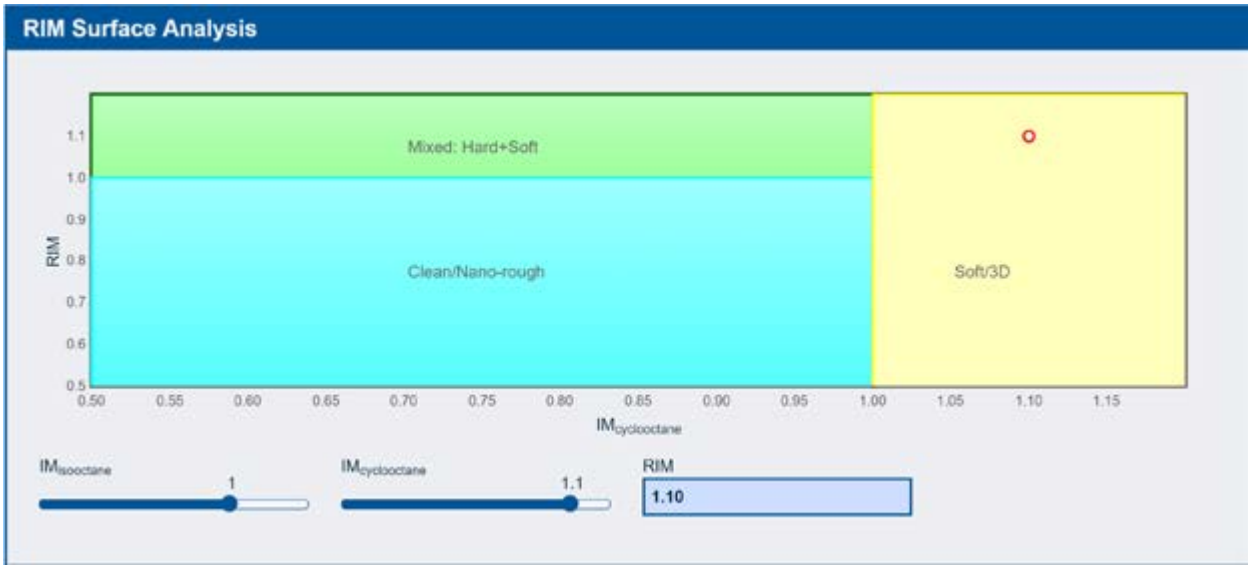
IM, index of morphology, was discussed in the IGC-ID chapter. When a branched or cyclic probe with a carbon number equivalent to a linear alkane shows a Vg lower than the linear alkane, that tells us that it cannot attain the good contact of the linear alkane, meaning, in turn, that the surface is nano-rough. As IM falls from 1 to, say, 0.5 we know that the surface is increasingly nano/micro-rough.

Sometimes the IM of a cyclic probe such as cyclooctane is *larger* than 1. This tells us immediately that something interesting is happening. And sometimes the IM of cycloctane is larger than that of isooctane, again telling us that something interesting has happened, given that cyclic molecules respond, in general more badly (lower IM) than a branched equivalent.

So by measuring $IM_{Isooctane}$ and $IM_{Cyclooctane}$ you can calculate a Relative Index of Morphology.

Equ. 5-1
$$RIM = \frac{IM_{Cyclo}}{IM_{Iso}}$$

The previous paragraphs and the definition of RIM give us a plot with three areas:.



App 5-1 https://www.stevenabbott.co.uk/practical-chromatography/RIM.php

In the screen shot, the IM of cycloctane is higher than 1 and the red circle show that its RIM also places it high in the Soft/3D region. Had its IM been less than 1 but its RIM greater than 1 then it would have been in the Mixed zone.

What does "Soft/3D" mean? It means that a large, stiff probe is happy to be in a region on the surface that does not make sense in terms of classical ideas of what a pure, hard surface should be and it invalidates the assumptions behind whatever "surface energy" might be calculated. The most natural interpretation, given that many particle surfaces contain a dispersant/stabilizer, is that the cyclooctane is positively happy to be in a "softer" or "3D" environment. If we talk in HSP terms, cyclooctane has a higher δD than octane, so a polymeric chain (which generally has a higher δD than a simple alkane) will be more compatible ("like dissolves like") with the cyclooctane than with a linear or branched alkane.

The beauty of RIM/IM is that it requires just two extra probes beyond the few linear alkanes that are used for standard surface energy measurements. If IM and RIM are both low then for the minimal effort of two extra probes we have confirmation that standard surface analyses are likely to be OK. And if we are in either of the two softer zones then we can assume that "surface energy" values are meaningless because the assumptions behind their calculations are invalid.

"Just two extra probes" implies that you have a machine where it is no trouble to add them; without such a machine, IGC is arguably too tedious to be worth doing.

5.1.1 Beyond RIM/IM

In the world of HSP, a particle plus its stabilizer is a single entity, with its own set of HSP values. HSP is silent on how much of the overall value is due to the particle and how much is due to the stabilizer. This is at the same time a strength (we just care about what works) and a weakness (we're missing understanding).

It seems logical that IGC could start to untangle the differences if we had a methodology that could distinguish between "particle" and "stabilizer". In principle, γ_d, IM and ISP information combined suitably could say a lot about the surface and some combination of RIM/IM and HSP-style χ measurement could say a lot about the stabilizer. This would mean doing RIM-style analyses with probes other than alkanes. So a linear ester might be compared to a cyclic lactone.

The combination of the 5-fold way and the AEDF is the most powerful current approach to understanding surface interactions. Can we find a better approach?

Given my remarks about γ_d measurements not really measuring surface energy, and given that IM and RIM are derived via a series of "surface energy" measurements, maybe it is time to throw out the whole γ_d infrastructure and create analyses starting with the real physics which we saw before:

Equ. 5-2 $$t = t_0 \sum_i n_i e^{\frac{E_i}{RT}}$$

From our t values we have insights into the energy distribution of the interactions of each probe with the surface. You can't deconvolute the Σ of interactions from a single t, but surely there are smarter ways of extracting information than pretending that there is "a" surface energy for the sample. Suppose that a small fraction (~1%) of higher-energy sites dominates the t values, while we are generally interested in the properties of the 99%. This brings us back to the need to "poison" the 1% so we can focus on the 99%. This cannot be so hard. There is already a tradition (mentioned briefly) of measuring the "irreversible" adsorption. This can be done in two ways. When there is a large fraction (which is not our main interest here) then comparison of peak areas of consecutive IGC-FC runs can provide an answer. When there is a small fraction, then a large temperature ramp after an IGC-FC injection can remove the "irreversible" fraction so that its peak area can be measured directly. Donnet and co-workers[17]

17 H. Balard, D. Maafa, A. Santini, J.B. Donnet, *Study by inverse gas chromatography of the surface properties of milled graphites*, Journal of Chromatography A, 1198–1199 (2008) 173–180

have proposed an "irreversibility index", I_{irr}, as the ratio of the area of this thermally desorbed peak to that of the total area of the chromatogram. In that specific paper, the index is measured in terms of the milling time for graphite. It would seem rather obvious that oxygenated functions would increase with milling time and that I_{irr} should be much larger for a functionalised probe such as i-propanol than for a dull molecule such as hexane. Yet the exact opposite is found. This tells us once more that the "high energy" sites often have nothing to do with being high energy and are much more connected to the probe molecule being trapped in some site where it can make contact with two or more (normal low energy) surfaces. The work shows that there is a strong correlation between the evolution of a "high surface energy" as measured via the standard alkane probe technique and the availability of these rather dull irreversible binding sites.

So for smart evaluation of surfaces we need to choose our poisons carefully. In some cases they might be dull linear alkanes to fit into steps, cavities or pores (2/4→4/4 sites), in other cases they might involve specific acid or base sites which, in turn, might be shape dependent (as in IM experiments). A few smart experiments with linear, branched and cyclic probes with a range of functionalities would tell us a lot about high energy sites. Once those sites have been blocked rationally with a small amount of the right probe, we can use other probes to see what the majority of the surface is really like.

Such ideas are not so much serious proposals as a stimulus to thought. We know that much of "surface energy" measurement in IGC gives bad values because the community is not routinely thinking about what a high value really means. We also know that the HSP IGC community is currently basing its hopes on the assumption that the support is effectively neutral, with no coherent plan for dealing with the cases where there is a thinner layer of material or where there is a stabilizer partially or wholly covering a particle.

With the newer generation of "smarter" machines, allowing highly-automated running with a wide range of potential probes, maybe we can all start asking smarter questions. Some suggestions are included in the final chapter.

Which brings us to a different topic which, regrettably, has to be included. It was mentioned briefly towards the end of the IGC-FC chapter.

5.2 How not to do it

We have so far made a distinction between "single molecule" infinite dilution experiments and "full coverage" finite concentration experiments. What about something in between?

The right question might be: "Can we measure the different energies of a surface (effectively, the AEDF) by measuring the Vg values for the surface

covered with different amounts of each probe molecule used for the Dorris Gray analysis ?"

The right answer is "No". Unfortunately, others have imagined not only that the right answer is "Yes" but that it can be obtained via a series of injections with different amounts of probe, equivalent to different surface coverages.

We therefore have many publications with plots such as the following:

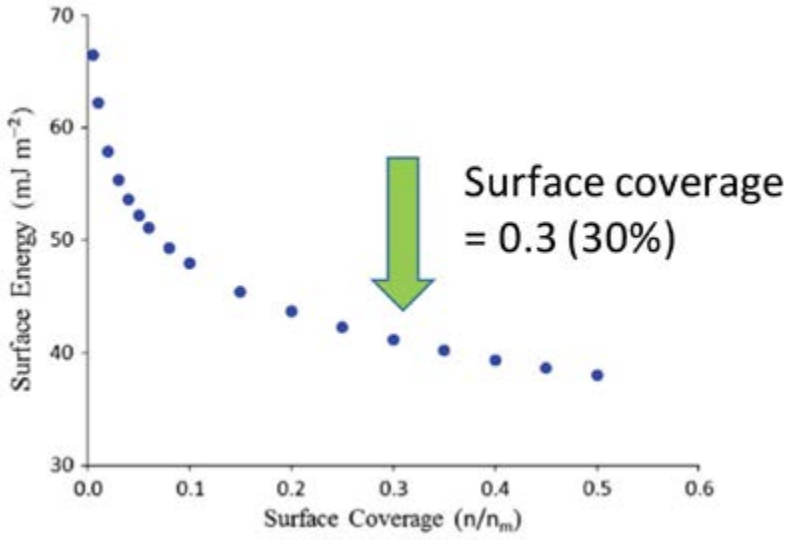


Figure 5-1 A classic "energy versus surface coverage" curve that is, unfortunately, not measuring either.

What is wrong with this technique? The key issue is that at no time has the surface experienced the "surface coverage" assumed by the analysis.

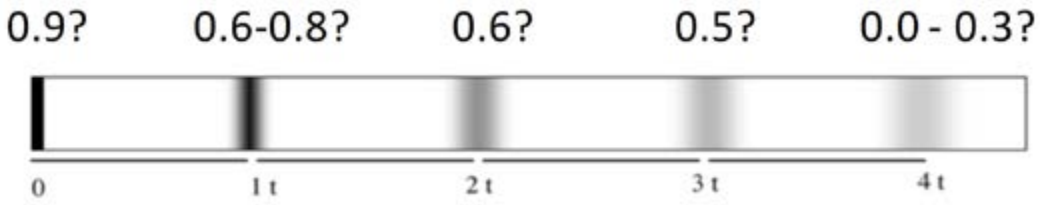


Figure 5-2 The core problem of the "surface coverage" technique.

Let us suppose that the experimental point was intended to measure the Vg at 30% coverage. On injection, we might have a rather even 90% coverage, after one unit of time, it might be a broad 60-80% and near the elution point it will be somewhere in the 0-30% range. So the Vg contains information from everything in the 0-90% range and is, therefore, not providing information about the interactions at 30% coverage.

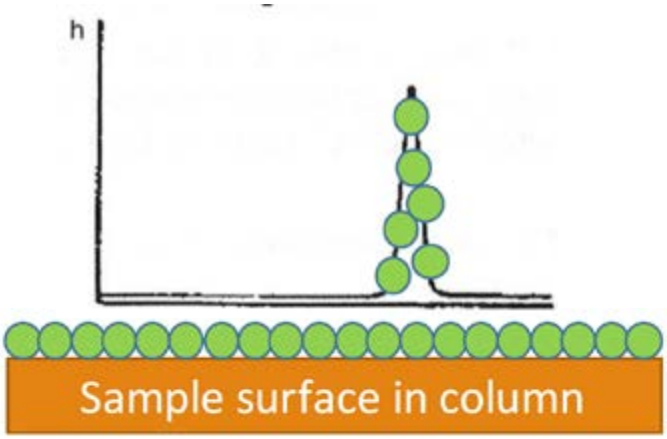


Figure 5-3 It is not possible for a "30%" peak with 6 molecules to travel down a column where 20 molecules = full coverage.

To put it another way, if we imagine that 100% surface coverage requires 20 molecules, then a peak containing 30% coverage would have ~6 molecules so this 6-molecule peak has to travel perfectly down the column, with no possibility of high energy sites retaining some of them, leaving fewer in the peak to probe the lower-energy sites. Putting it like that shows that the technique refutes its own assumptions.

Some theoretician might be able to disentangle the required answer from a mixture of Vg and peak width/shape, but I have not found any publications claiming to do that. So the papers that report the "energy versus surface coverage" are, there is no other way to put it, wrong.

That is why the book has been structured in a specific way: asking the right question using the right technique to get a clear answer. The "surface coverage" technique has asked the right question. It would be wonderful to get such data directly rather than via the AEDF. But it is using the wrong technique so the answer itself is wrong.

While we are challenging wrong assumptions, how about those claiming that their experiments are at infinite dilution. Surely they suffer from a version of the above problem: at the start of their short, sharp injection there is a finite concentration that invalidates their assumption of single molecule, AFM-like probes. The little image below repeats the one from the first chapter:

This criticism is entirely justified in theory; the question is how serious it is in practice. We have an objective answer to the question. A non-ID injection cannot give a symmetrical peak shape, because the molecules are reporting from a different part of the desorption isotherm. In addition, the retention

time will change according to the injected amount. By deliberately injecting an unnecessarily large amount (but still small by FC standards) in an "ID" experiment, unsymmetrical peak shapes, at concentration-dependent retention times, are clearly observed. The objective test, therefore, is to inject smaller and smaller amounts till the peak becomes symmetrical and the retention time is unchanged, indicating that in practice the ID criterion is obtained. With a poor machine with too much dead space and turbulence, with bad packing or with a low-quality detector, the ID criterion is never met because the (asymmetrical) peaks get lost in the noise. On a good machine, the ID criterion is readily and routinely obtained.

6 Links to other techniques

IGC has strong links to other techniques. When the measurements agree then we don't learn much; when they disagree with each other we can learn something interesting.

6.1 BET surface area

We have already discussed the comparison between the specific surface area values from classic nitrogen BET and those obtained by IGC. For nice smooth surfaces they are similar within the limits of the estimate of cross section area of the probe and any ordering the probe might make which in turn would change the cross section. The BET constants C are, generally, lower for IGC because the values are measured at 300K or higher while nitrogen values are measured at 77K.

The classic BET measurement can be via vapour pressure measurements after introducing controlled amounts of gas (manometric) or by monitoring the weight of a sample when gas is introduced (gravimetric). Nitrogen can be replaced by argon or even krypton for measuring low specific surface areas. Differences in techniques and probe gases are in the practicalities and accuracies rather than in the isotherms themselves.

For most real surfaces, the standard BET test is working outside its own assumptions so the measured value is only an "apparent specific surface area". The AEDF from an IGC-FC measurement still gives you an apparent BET, but also provides deeper insights into particle-probe interactions.

6.2 Washburn surface energy

Take a capillary tube, fill it with your powder, dip it in the liquid of interest and measure its mass m over time t. The well-known Washburn formula which depends on contact angle, θ, the surface tension, density and viscosity of the liquid, σ, ρ and η, and a constant c gives us:

Equ. 6-1
$$\frac{m^2}{t} = \frac{c\rho^2\sigma\cos(\theta)}{\eta}$$

For a test liquid we know σ, ρ and η, so from a plot of m² versus t we can find c.cos(θ). To determine c we do an experiment with a liquid with an assumed zero contact angle (e.g. hexane). If we assume that c is a constant across all test liquids we can work out the contact angle for other liquids. That is not controversial, though whether these angles mean anything on a powder *is* controversial. The bigger problem is that the contact angle, via Owens-Wendt (etc.), is converted into a surface energy. Whether an idealised, bulk surface energy on a flat surface (Owens-Wendt) has any significant relationship to that of a micro-rough or even micro-porous surface is contentious, especially as

there are competing schools of interpretation of contact angles on controlled-roughness macro surfaces.

As a technique for attempting to understand a surface and/or batch-to-batch variations of that surface, Washburn looks to be too crude to be of much help. It is also a frustratingly difficult technique to make reproducible. For any powder (such as a pharmaceutical) where the solvent can interact/swell, the technique is clearly inappropriate. Though if your end-use application is as a powder that has to be wetted, why bother with IGC when Washburn provides the direct answer?

6.3 SEM and AFM

IGC cannot tell you the shape and size of your powder, whereas SEM and (to some extent) AFM can. On the other hand, it is very hard for either of those techniques to tell you at the molecular level how the probe molecules are interacting with, say, nanopores or amorphous versus crystalline regions.

For straightforward materials, the measured IGC properties changes remarkably little over a wide range of shapes and sizes of particles. In such cases, IGC is blind to large changes. For others, even small changes in the particle surface, hard to spot in SEM, can lead to large IGC differences. The reason was discussed earlier in terms of the overwhelming (exponential) effect of a small amount of "high energy" attraction on the retention time. Often we can only speculate as to what has happened to cause the IGC differences[18] (if we could directly identify the changes, we would not need IGC), but such information is often vital for practical applications.

Calling IGC a molecular probe AFM-like system is a little exaggerated, but it captures a key insight into the potential of IGC to investigate the fundamentals of a surface.

So the techniques are clearly complementary rather than competing.

6.4 DSC, TGA, x-ray etc.

If we are interested in gross changes in our particles such as from amorphous to crystalline, from below to above Tg or via loss of molecules such as water, then standard thermal, Differential Scanning Colorimetry (DSC), Thermal Gravimetric Analysis (TGA) and structural techniques are the natural choice (though those who are keen can measure Tg via IGC as described in the Bulk chapter).

IGC is more useful in showing "minor" differences at the surface which will not show up in the bulk techniques but which might have a major impact on how the particle behaves in a subsequent process such as tablet manufacture. As with

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18 At present we have a double-speculation until we use the 5-fold way to systematically understand what causes high energies: sites of genuine high energy (polar, acid/base) or slot/cavity/pore sites loved by alkanes.

the previous section, the IGC data can only indicate that significant changes have taken place, without directly saying why. A good example is where DSC shows no change between samples, whereas the measured IGC γ_d values might change significantly showing, for example, that there has been a phase change (a localised Tg or MPt) at the surface, not detectable by a bulk technique.

6.5 Correlations

The surfaces of the particles have direct impacts on dispersibility, packing, flow, static, chemical reactivity, adhesion etc.

The general use of IGC to help understand how the surface affects such properties has resulted in modest levels of insight. At the very least, a change in γ_d might signal that something strange might be found in a subsequent process, though because γ_d can change for multiple reasons, a correlation might be hard to find.

With a better set of measurements (5-fold + AEDF), obtained in not too much more time thanks to a better setup, it is becoming clear that correlations based on more interesting (sets of) parameters are being found, with greater predictive capabilities.

Once IGC's true capabilities are better understood then it will become far easier to make the right choices of which techniques to use for which aspect of understanding and quality control of our particles.

7 The future of IGC

The future should start with IGC throwing away the negative word "Inverse" and replacing it with the positive word "Interfacial". A GC technique that helps us to analyse what is going on at interfaces sounds immediately appealing - which, indeed, it is.

The future should also start with an admission that the absurd focus on "surface energies" has provided astonishingly little benefit. It is clearly the case that retention times depend on a mix of molecular shape, size, functionality and on surface shape, size and functionality, with rather small fractions of higher-energy sites having a disproportionate (exponential) effect on the values for parameters such as γ_d.

As is increasingly becoming apparent to those with access to the sort of modern machine that IGC deserves, the 5-fold way, measuring γ_d, IM, RIM, ISP, K_a/K_b, provides a rich picture of the surface. Importantly, the different insights from the different probes are being linked straight into the formulation knowledge of suppliers and users of the materials.

It is true that there is some merit in knowing that γ_d of one batch is different from γ_d of another. Because these values can change for multiple reasons, this is only suitable as a rough quality control - better than nothing, but not actionable information for those who need to fix the root cause of the change. If, for not much extra effort (given a highly-automated setup), all five parameters are known, then it is possible to see whether things have changed because, for example, the surface chemistry is significantly different or because the surface topology has changed (causing interactions on more parts of the probe) or because a few percent of some high energy sites (e.g. some new exposed functionality) have appeared.

The need for this type of analysis means that IGC has to move away from older machines that cannot meet the basic requirements set out in the first chapter:

1. ability to inject a small, controlled volume for truly infinite dilution, ID, measurements
2. ability to inject a controlled large amount for proper finite concentration measurements and the ability to extract AEDF data, FC,
3. sensitive detectors that work with the small injections of ID yet can cope with the large signals from FC.
4. freedom to fit the exact length of the right-sized column for the specific analyses
5. low volume input/output systems to minimize peak shape distortions
6. intelligent computer control and automated analysis of measurement quality and the derived parameters.

It also has to be acknowledged that the basic physics shows that so-called "surface coverage" techniques do not, and cannot, measure what they say they are measuring. We have objective techniques for analysing true infinite dilution, ID, and true full coverage, FC. At present we have no objective technique to go from the data gathered using "surface coverage" techniques to any of these objective values.

The need for a high-quality machine is also apparent when it comes to the move away from surface properties to bulk properties such as diffusion coefficients or Hansen Solubility Parameters. The early work from Munk described the minimum criteria for reliable HSP (and other bulk property) determination. But my own observations from looking at numerous papers purporting to measure HSP via IGC is that such advice has been largely ignored. This means that there are quite a number of worthless IGC HSP measurements out there, slowly being supplanted by rather good values obtained by those who use due caution and take advantage of technology beyond that available to Munk.

The current resurgence in the use of HSP in the formulation world in general means that there is a real need for accurate HSP measurements. The classic "20-tube" technique is excellent for many solids. The recent interest in centrifugal sedimentation techniques for nanoparticles has opened up new opportunities for measurements in that field. For cosmetics, pharmaceuticals and much of "soft matter", IGC is the only viable method for measuring HSP, and a rapid growth in the use of IGC is inevitable.

So even without any intellectual breakthroughs, IGC clearly has a lot going for it. Which is why I have put in the effort to write this book.

7.1 Beyond "more of the same"

Even though the future of IGC is more encouraging now than it has been for some time, it seems to me that there is an opportunity for it to do much more.

There has to be more to IGC than the somewhat ad hoc ideas behind IM/RIM, ISP and the acid/base values. These values are calculated from comparisons to a set of dull, standard alkane probes. Who cares how hexane interacts with a complex oxide or carbonate or carbonaceous surface? Why do we use the least-interesting molecules as the basis of our measurements?

The core problem is that we focus on Vg because it is the most natural thing in the world to measure retention times. Yet we know that the same Vg values can arise from many different surfaces, depending on the ratios of the interaction energies of different sites.

So maybe we should accept that the default option for IGC should be a set of AEDF measurements made with a sensible variety of probes spanning a range

of shapes, sizes and functionalities. By knowing the energy distributions of this range of probes we immediately learn a lot more than we can gain by trying to interpret Vg values as if they carried direct information about interactions.

Even if we can gain these AEDFs we still do not know directly (though the use of branched and cyclic molecules will help) if the higher energy sites are due to strong specific interactions or to multiple interactions between the probe and steps, cavities or pores. Some creative thinking is required here. Smart poisons might allow us to identify specific high energy sites if we can hypothesis specific functionalities that the right poison would selectively bind to. Or polymer poisons might be used to exclude surface sites while allowing pore and cavity sites to be probed.

Or it needs fresh ideas from a fresh mind willing to tackle a major issue, with major upsides if the ideas work out.

7.1.1 Even more

Let us assume that the analysis of pure particles has been solved and the analysis of bulk properties (e.g. for HSP measurements) has also been solved.

That still leaves the majority of practical particles unaccounted for. These are the ones with organic/polymeric dispersants on them.

That is somewhat unfair to the IGC community. Many such particles are analysed using the normal techniques and RIM/IM is starting to show that there are extra ("polymeric") interactions. I just don't think that the standard analyses begin to address a key question: how will the dispersants help or hinder the integration of the particles into a formulation?

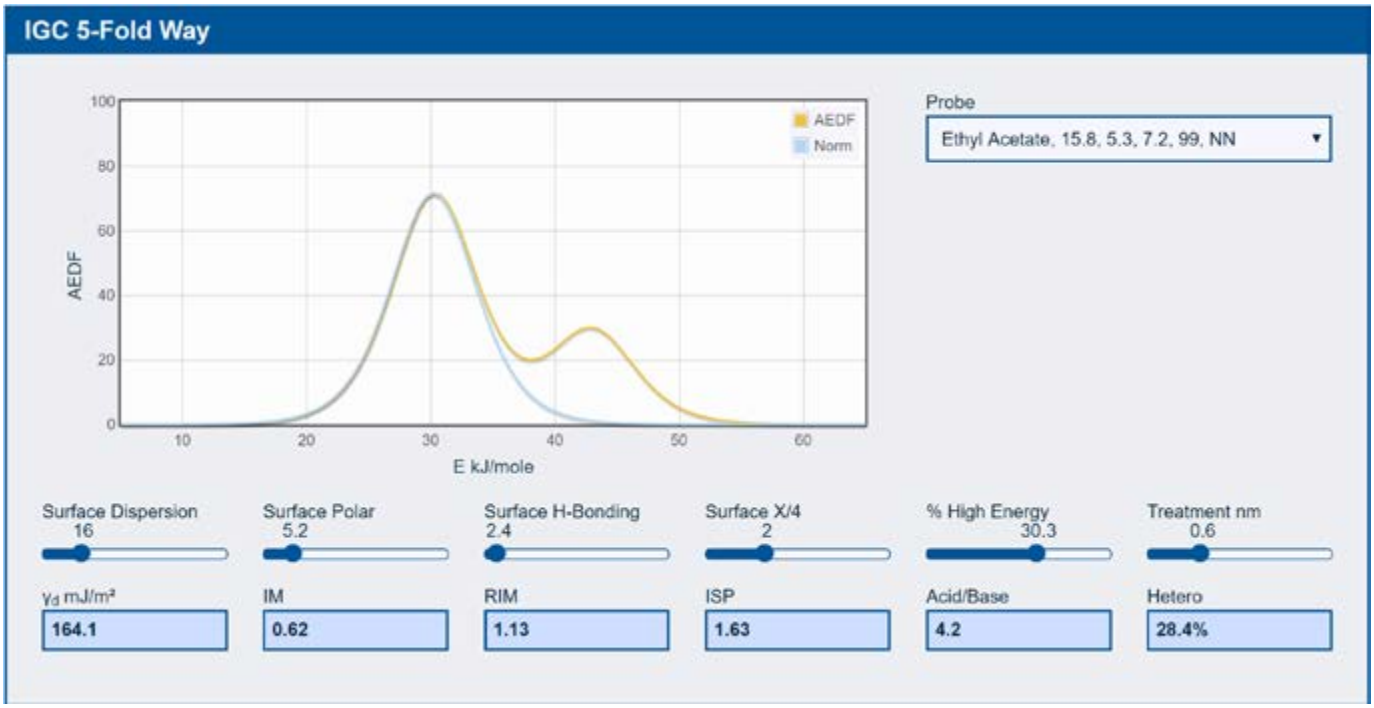
The current standard way to answer that question is by the classical measurement of the HSP of the particle/dispersant combination. This is, admittedly, a matter of intellectual controversy; how can the measurement of "solubility" parameters apply to a particle, with or without some (fractional) coverage of dispersant? One answer is that a suitable theory (Kirkwood-Buff) is under development. The more convincing argument is that it works in practice and has done since the 1970's when Hansen first applied the theory to paint pigments.

How wonderful it would be if this mixture of particle surface and organic material could be analysed via IGC in a manner that mapped straight into formulations.

At present there seems little hope of this. As discussed in Chapter 5, IM/RIM certainly hints at the ability to detect sites into which cyclic molecules prefer to go (because their δD values are higher than linear equivalents). Bulk HSP measurements via IGC show that the chemical nature of a polymer layer can be

analysed effectively. The key problem is that because Vg depends on (usually) irrelevant steps, cavities and pores, this means that we currently cannot get direct measurements of the key surface chemistry interactions.

My own, simplistic way to approach this is via the 5-fold way app, re-shown here, that takes a number of dubious, but plausible, logical steps from key parameters (pseudo HSP values of Dispersion, Polar and H-Bonding), some estimates of the X/4 nature of the surface, the % of high energy sites and the thickness of any treatment. It then provides estimates of what the measured parameters might be.



App 7-1 https://www.stevenabbott.co.uk/practical-chromatography/IGC-5.php

This at least illustrates the potential for what IGC might achieve with improvements to the chain of logic between raw data and calculated values.

Those who are adventurous might want to start a process like this with some relatively simple surfaces such as smooth silica (where we know there are no Vg distortions from structural effects) and systematically change the coverage and chemistry, using a rational range of probes designed to seek out chemical interaction trends, especially polar and hydrogen bonding. The pioneering work of Papirer and colleagues[19] in the 1980's showed the promise of this approach, by grafting systematically longer chains of PEO onto silica. The γ_d went down and the ISP went up with increasing chain length. That decrease in γ_d seems to me not evidence of a lower "surface energy" but evidence that alkanes don't like

19 E. Papirer, H. Balard, Y. Rahmani, *Characterization by Inverse Gas Chromatography of the Surface Properties of Silicas Modified by Poly(ethylene Glycols) and Their Models (Oligomers,Diols)*, Chromatographia, 23, 1987, 639-647

to hang around next to relatively polar PEO chains. Unfortunately, this sort of systematic approach does not seem to have been much followed, which seems to me to be a 30-year-old missed opportunity.

The idea of controlled poisoning of a small percent of highly active sites (such as pores) might allow a similar exploration of more interesting surfaces.

Once some basic datasets have been built up, perhaps it will be possible to devise a methodology for understanding the relationship between, say, Vg values and the subsequent interactions of the particles with their desired matrices such as paints, coatings or pharmaceuticals and their excipients.

A different view is that an AEDF approach would be more convincing because a surface covered (initially) by probe molecules is closer to a particle in a formulation than a surface which sees individual probe molecules in ID mode. To the extent that the probe molecules start to solubilize any polymer chains on the particle, the assumptions behind the AEDF start to fall apart. Perhaps this would show up as a non-linear BET and the non-linearity could be analysed in terms of solubility.

Perhaps these specific ideas are wrong. That's not the point. Interfacial Gas Chromatography has, up to recently, been rather poor at delivering on its promises. With the 5-fold way and routine AEDF measurements it is at last providing key insights into changes in the surfaces of particles, something that no other technique can currently manage. As the equipment required to make these measurements routine and automated becomes more widely available, users will naturally be asking "Is there more we can learn?". It seems obvious to me that the answer is "Yes".

All it needs is someone with the vision, talent and determination to take IGC to the next level.

I've not admitted it earlier, but the real reason for writing this book is the hope that someone will read the previous sentence and decide that they are going to be the one to take the big step forward. Perhaps it is you.