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Origins - Tony's view

Those of you who, perhaps as a child, or even better as an adult, read C.S.Lewis's *The Lion, the Witch and the Wardrobe* will know that when the White Witch finally gets to kill Aslan, the lion, she does so by invoking 'deep magic from the dawn of time'. In the very next chapter, however, the great Lion is revived by 'deep magic from before the dawn of time'.

Anyone else, with the exception of Graham Richards and myself, when attempting to write the story of Oxford Molecular would begin their account at, or close to, the recorded birth of the company. For me and Graham, however, the origins of the company go back much further, and whilst I do not want to retain us too long in the pre-history, a brief glance 'before the dawn of time' is essential to really understand the 'deep magic' of Oxford Molecular.

Unlike Lewis' timeless fairytale, the Oxford Molecular story, although a fantastic adventure, with all the promise at one time of being the best of fairytales was to end in tragedy. Our wonderful company, like Aslan, was eventually to be muzzled and tied to that great flat stone called business myopia. Then, surrounded by our own unique versions of the White Witch and her rabble, Oxford Molecular was ritually stabbed to death. Unfortunately for Graham and me, when we needed it most, the 'deep magic' did not come to our aid, as it had done so many times before.

Perhaps now though, in recording our thoughts and memories before they are lost, the 'deep magic' has returned. Through this book, Oxford Molecular, like Aslan, who the children thought was dead, is made alive again, and this time forever.

Despite its many flaws and ultimate demise, Oxford Molecular was special. It inspired a generation in Oxford, in the UK and indeed worldwide. Some were motivated through admiration, most through jealousy, but all strove to emulate our success by setting up their own high-tech University spin-outs, and trying to take them public. In Oxford itself, with the formation of more spin-out companies, came the first Oxford-based venture capitalists, business angels and intellectual property companies, alongside the University's own Isis Innovation. Soon, a whole

new, and highly valuable economic sector had been created, generating huge numbers of highly paid jobs, reviving the prosperity of the region, and at last overcoming the long perpetuated myth that the UK was good at invention but lacked the ability to successfully commercialise the resulting intellectual property.

All this is rushing ahead, however, and my thoughts turn first to my own background, and that very first meeting with Graham.

Graham and I first met on a dark, foggy, Michaelmas (autumn) term evening in Oxford. It was November 1972. I had been invited up to Brasenose College for a so-called Common Entrance interview. I was 16 years old, due to turn 17 the following week, and anything up to two years younger than the other entrance candidates competing for the four undergraduate places to be awarded to read chemistry at Brasenose the following academic year.

I was a grammar school boy; not Manchester Grammar, or Bradford Grammar, or the Bluecoat School, the likes of which showed the best of the English private schools the way home when it came to academic achievement, especially with Oxford and Cambridge entry; but New Mills School, the pride of an otherwise scruffy, working-class town in the semi-industrial, semi-rural, north-west corner of Derbyshire in central England. Indeed, at that time, New Mills had ceased to become a grammar school, and was now one of the newly constituted, non-selected comprehensives.

New Mills, the town, was dirty. It had rows of back-to-back terraced houses, and then the worst *per capita* crime record in England. Its main claim to fame was a sweets and candy factory, which drenched the town daily with its sickly, sugary odour, but nonetheless provided much-needed jobs.

I came from one of the outlying rural villages, and travelled to school each day by bus. As the furthest away we were the first to be collected in the morning and the last to be dropped off at night, so the 7.30 am pick-up from the shelter across from the village church and, if we were lucky, a 5.30 pm return became the regular routine. In winter we left home in the dark and arrived back in the dark; in summer the opposite. There was hardly a January or February when for a few days, at least, we were snowed-in. On those occasions my mother expected no less than that I set off and walk the whole eight miles to school, through the ice and puthering snow, only to arrive and be told by a solitary duty teacher that the whole

school was closed, and then have to walk back. In summer, rather than wait an hour or so for the bus to arrive at home time, I would often choose to walk home, soon leaving the dismal rows of houses behind me, and finding the green fields and fresh air.

I counted myself lucky though. Firstly, I had parents who encouraged me in every way to do my best. My father, Frank, was a part-time farmer and motorcycle mechanic, who worked every hour God gave, and turned his hand to almost anything in order to keep the bills paid. My mother, Millie, stayed at home and became very much the disciplinarian to myself, and two younger brothers, one of whom, Allan, the youngest, will feature later.

I grew up a country boy, happy at school, yes; but happiest in old clothes, running wild on the open expanse of sparse moorland that surrounded our home.

I was fortunate also in the teachers at New Mills, who gave me the encouragement, despite the odds, to aim for the top. But the odds could not be underestimated. The likes of Manchester Grammar School, the renowned MGS, placed a hundred young men a year or more into the UK's top two premier universities. New Mills in those days got one successful kid into Oxbridge every three or four years, if they were lucky. There's no doubt that I felt intimated by Oxford, as in truth did the teachers who taught me.

As for preparation for the Oxford Entrance, I had done my best, but in retrospect that was a long way from the focused 'cramming' which my MGS rivals would have received. Indeed, for much of the time, I was basically self-taught, using only past entrance papers as a guide.

There was, however, the inspiration of the chemistry master at the school, Mr Earp. Gordon Earp should have retired in July 1972, at the end of the previous academic year, but opted to stay on for one more year to see me through the written examinations in October and interviews in late November. His teaching was the same as it had been before World War II; so for chemistry, even in the early 70s, it lacked significant modern content. However, Gordon Earp had a gift or insight, call it what you will, for teaching. In two-hour chemistry lessons he talked more of the Derbyshire Dales and the Industrial Revolution, and the intricacies of homemade wine than of test tubes and chemicals. For example, he would greet the whole class, fresh from the then compulsory religious assembly, with words

such as: 'Well, Marchington, have you been listening to all that Victorian clap-trap again?' And in reference to the modernising headmaster: 'Be under no doubt, Marchington, that man is utterly insane; a complete nutcase!'

In this intellectual environment, even the most hardened anti-chemist amongst us could not help looking forward to the next chemistry lesson. Would it be a two-hour tirade on the raging insanity of the school headmaster? Or, as to the season, boiling chestnuts in laboratory two-litre flasks over Bunsen burners? Gordon Earp had realised, you see, that teaching was about opening minds. Like all great teachers he opened minds by whatever methods were available, or necessary; and then looking down into the awakening intellect, simply poured in as many facts and concepts as he liked. Through boiling chestnuts, insane headmasters, dreams of upland Derbyshire, and a worship of Isambard Kingdom Brunel, Gordon Earp gently opened my mind. That opening soon felt like a cavern into which he, and indeed all the other teaching staff at New Mills, were then able to pour their subject content with alacrity.

Graham Richards has that same ability; just ask any of those who have benefited from knowing him or, better still, having been taught by him. With Graham though, unlike my grammar school teacher, it wasn't Derbyshire hills or the mundane domestic that drew one on. It was new ideas and the sense of being on the very edge of discovery that became so intoxicating. Also, as he and I got to know each other better, our conversations turned, more and more, not just to the science, but how to commercialise it, how to make hard cash from it; discussions that later led to the obvious.

But back now to that foggy night in Brasenose in November 1972.

I had travelled to Oxford that afternoon, ready for an evening interview and overnight stay in College. Sure enough, as I checked in at the porters' lodge, the list on the college notice board already confirmed that Mr A.F. Marchington was required for interview in the Stocker Room at 6 pm. Six o'clock, however, came and went, as did six thirty, and then seven. Obviously things were running behind. Then, at around seven thirty I was called from the nearby common room to the interview.

Inside the said Stocker Room sat at least ten Brasenose dons, but the questions were to come from just two of them. Most came from an older man in his late fifties. This turned out to be Dr John Barltrop, fellow of the college, and

lecturer in organic chemistry. The others were from a much younger man in his early thirties, Dr Graham Richards. What I did not then appreciate was that this was already a dynasty. Barltrop had tutored Richards only a decade earlier, and although I did not know it at the time, John Barltrop would also tutor me in organic chemistry at Brasenose. In the process, like Graham Richards, he was later to become a close and much-loved friend.

The interview came and went. On leaving, I was recommended by Barltrop to try and scrounge dinner in Hall even though, on his own admission, they were running late, and dinner may be finished. Accordingly I sought refuge in Brasenose Hall to be met by what turned out to be the legendary Scot, Jock Wallace, head hallman in his uniform black evening suit.

'Now then, Sir, what will it be? We have some shepherd's pie left over.; I agreed, whereupon I was seated on the High Table, in an otherwise empty hall, and the meal served up to me. It was a moment to be savoured; a dimly lit medieval hall, with its dark oak panelling, heavy guilt-framed portraits of old members going back over 450 years, and the constant attention and warmth of the college servants.

Not long into the shepherd's pie and Graham Richards appeared. 'I'm sorry we kept you longer than we intended' he said. 'I just wanted to ensure you had eaten.'

'Och! Don't worry about this young man, Dr Richards,' came the great, jovial Jock Wallace, 'We're looking after him just fine.'

After dinner, as darkness and swirling Thames fog enveloped Brasenose and the whole of Oxford, I left my rooms and went down into the college quad. Round and round I walked, under each staircase light in turn. Had I got in? Dare I raise my hopes that I might be in for a chance? I so desperately wanted a place. I had convinced myself that I already felt at home. Round and round I walked, until all the room lights were turned out and all the others had gone to bed. Round and round I walked, savouring the moment, and all the time, without knowing it, formulating that 'deep magic'.

I did get in, and three and a half years later, despite too many wonderful nights in Cotswold pubs, too many weekends on the river, and far too many cups of coffee in friends' rooms after lectures - but nowhere near enough lectures! - I salvaged

the situation and managed a Second Class degree in chemistry. It was now the autumn of 1976.

Chemistry in Oxford is a four-year course, with the final year spent on a research project. It was decided that my project, the so-called Part II, for the academic year 1976-77 was to be with Graham, developing theoretical techniques and resulting computer calculations to correlate a chemical's biological properties with its molecular structure, particularly for relatively small, drug-sized molecules.

Graham had been pioneering these techniques since the late 60s and, like many pioneering techniques, 'computational chemistry or molecular modelling' as it was becoming known, had advanced from being regarded in 1970 as 'half-crazy' by academic colleagues, to 'possibly worth a try' by 1976. Clearly, the explosion of ever cheaper and more accessible computer power was a major driving force for a technique, which relied principally on fast computation. In addition, in the US, another Englishman, John Pople, had published the Gaussian 70 suite of computer programs back in 1970. These allowed, for the first time, routine mainframe computer calculations on drug-sized molecules.

The process of increasing acceptance had also not been hindered by a number of promising papers from the Richards' group and others showing that, within carefully selected series, real and potentially hugely valuable correlations, and most importantly predictions, of drug activity were possible. There was also the publication of a fabulous little book by Graham called *Quantum Pharmacology*, brilliant if only for its title; and its logo – the twin snakes of medicine twisted around the Greek capital letter psi. (This logo was later to be adopted by the company.) This clever little book was the first of its kind; one of many such firsts for Graham Richards in what has been, by any standards, a brilliant career. *Quantum Pharmacology* defined the new field and convinced many individuals, and particularly many drug companies, to adopt the methods within their own research. What had been obvious to Graham in 1970 did not dawn on many others for another twenty years, and by then the world and his wife wanted access to the techniques.

For the major pharmaceutical companies the potential rewards for improving the odds of discovering new active molecules was, and still is, enormous. The industry average direct cost of developing a new pharmaceutical is approaching

$750 million. Moreover, for each new drug developed some two to three others fail in relative late stage development, putting the total average cost of research and development expenditure per new drug at over $2 billion. Even minor increases in efficiency can, therefore, produce very significant returns.

By September 1976, at the start of my Part II project, Graham's reputation was such that, as well as a string of pharmaceutical clients, he had also just confirmed a consultancy with ICI Plant Protection Division (PPD) at their Jealotts Hill Research Station, near Bracknell in Berkshire, about thirty miles west of London. Graham, I know, saw this most particularly as an opportunity for his research students, such as myself, and the string of others who would, in time, follow me to acquire hands-on experience of industrial research. In this way we could improve not just our scientific knowledge and understanding, but also hone all those other skills and nuances which separate university research from industry.

Jealotts Hill focused on the development of crop protection chemicals, namely insecticides, herbicides, fungicides and novel plant growth regulators, and was then one of the rising stars of the ICI group of companies, with revenues of about £500 million, but planning to be many times that size within a decade. Most of these revenues came from the sale of paraquat, trade name Gramoxone, the world's most widely applied general herbicide. Paraquat had been discovered a generation early by accident, and the strategy now was to use paraquat, and its relative diquat as cash cows to construct a more rationally based crop protection chemicals business.

Even then it was obvious that ICI PPD meant business. They had a new research director, Dr Peter Doyle, known to Graham, who was keen to introduce the latest methods. Doyle, who features again in the Oxford Molecular story, was formerly a chemist within ICI's well-respected pharmaceuticals division at the renowned Alderley Park Research Station, near Macclesfield in Cheshire. He was clearly ambitious and determined to fill the development pipeline with quality candidate molecules as soon as possible, as his stepping-stone to the ICI main board.

Oddly enough the 'Luddites' at Alderley Park, Doyle's former research colleagues, were to take considerably longer to fully embrace the new technology than their cousins 'down on the farm'. This disparity, due entirely to the enthusiasm

for computational chemistry at Jealotts Hill, was no accident, and stemmed directly from one of the discipline's great unsung heroes, Dr Keith Heritage.

It was often said, in those days, that working hard in ICI was like 'pissing yourself in a dark suit' in that it gave rise to a nice warm feeling but nobody noticed. Keith Heritage worked very hard and was one of the technique's first, really serious, practitioners. In many ways, applying computational techniques to plants and their diseases was more direct and amenable than with pharmaceuticals. Unlike people, plants could be experimented on, at all sorts of doses and conditions, and Jealotts Hill had acres and acres of constant temperature, constantly lit, glass housing full of plants. Indeed, it was said that the pilots of the trans-Atlantic jets coming and going from Heathrow airport just a few miles to the east, used the many acres of illuminated glasshouses at Jealotts Hill as their key night-time beacon for landing and take-off.

Keith was ably supported by his then manager, John Farrington, and later by the talented Rod Morrod. Farrington had been responsible for the elucidation of the mode of action of paraquat, and in so doing had advanced significantly our understanding of photosynthesis and particularly the interaction of photosystems I and II. Farrington was a Cambridge man, a gentleman and, despite being not far off retirement, had an agile and flexible mind. Despite these and other excellent colleagues, Keith, at the time, was still largely ignored by the chemists, who preferred to rely on their own intuition (more akin to superstition) as to what to synthesise next for testing. All that was soon to change.

Following the glorious long vacation of the summer of 1976, therefore, I returned to Oxford to begin my Part II, part of which would be spent assisting Keith Heritage on a project focused on the triazole fungicides. Originally discovered by the German firm Bayer, the triazole class of compounds offered huge commercial potential ranging from crop protection for the treatment of mildew and other fungi on wheat and other major crops, through to athlete's foot and other unspeakable nasties in humans as well as anti-fungal (i.e. anti-wood rot) paints.

That Part II year went so very well. I remember well the regular day visits to the company in Graham's Triumph Vitesse sports car with the soft-top down. Indeed, it was seeing the effect of this beautiful motorcar, particularly on beautiful young women, which more than anything else that year drove me to finally take

and pass my car driving test. Up until then I had relied upon an old 1956 Triumph Thunderbird 650 cc motorcycle to get me about, but for sheer, naked pulling power the uncomfortable bike was nothing compared to its open-topped cousin.

The M40 motorway did not quite reach from Oxford to London in those days. On our regular visits to Jealotts Hill, therefore, we took the old A-class road, the A40, then the M40 motorway for a short spell, exiting at High Wycombe, just after Booker airfield. From there we took the Marlow by-pass, and so into the last few miles of narrow roads, high hedges, and the red brick, red tile, and flint-built houses, that was affluent rural Berkshire.

As you arrived at Jealotts Hill, the agricultural connections were immediately obvious, as ICI still operated a grass and silage production research unit on-site, part of which was a fully functional commercial milk herd. 'There,' said Graham, more than once on our various arrivals, and always with a wide smile on his face, 'don't you feel at home now?'

My interaction with Keith Heritage, and other members of the immediate biochemical and chemistry research teams, proved positive from day one. More importantly I started to glimpse for the first time the commercial opportunities that would result as the new computational technology started to take shape. There were, of course, always the 'Luddites'; some open to sensible discussion as to the merits of computational techniques, others not. Indeed, in my assessment, there was always a direct inverse correlation between intrinsic ability and degree Luddite. How often have I found it so, and in so many other disciplines; many far removed from chemistry. The clever, most interesting, and the very nicest people, are invariably those who are able to comprehend the debate from every point of view. The 'blinkered mares', however, seem destined only to look down their own narrow tunnels, oblivious to what might be possible, or what the world looks like beyond the next hedge. There were plenty of 'blinkered mares' at Jealotts Hill. Indeed, many industrial research establishments seem to be natural stabling for them.

The Part II year was soon over. I completed a short thesis on time and thus concluded the four-year degree process. The question was: What to do next?

I was really enjoying the science. The work on the various new theoretical methods we were developing in Oxford showed promise; and at Jealotts Hill

molecular structures for new triazoles, suggested in the Part II thesis, had been synthesised and shown to have novel biological (anti-fungal) activity. Indeed we had a patent. For a visiting Part II student, I had also been allowed unique access to the company's total compound collection and had formed great relationships with a whole multi-disciplinary team of scientists.

Importantly, in just a year Keith Heritage had also gone from the nice, clever theoretical chemist to whom the synthetic chemists at Jealotts Hill listened politely, but then ignored to go off and synthesise whatever molecules they wanted, to become a key contributor to most research projects.

Clearly, from the science point of view, therefore, I wanted the research at Jealotts Hill to continue. Also, if possible, I wanted to claim another few years in Oxford, a lifestyle I loved dearly. Leaving Oxford at that time, and indeed later, would feel like cutting off a limb. In short, I wanted the best of both worlds.

Brasenose College had been good to me. I felt very much at home in my regular comings and goings between the lab in South Parks Road, to my flat at 19 Beaumont Street, and to Brasenose at the very heart of that wonderful medieval university. I had made many friends over the four years there, not only with the dons and fellow students, but also with the College staff, the porters, scouts and chefs. I had a network, a mafia. I knew the system, and yet I was just at home at a lavish college feast as I was in the back garden of a Cotswold pub on a warm summer's evening playing Aunt Sally, the traditional Oxford equivalent of a coconut shy. To my knowledge Aunt Sally is played nowhere but in Oxfordshire, and certainly Cotswold beer tastes all the better for it.

Equally in the lab there was a great atmosphere. Graham's research team lived in room 365 of the Physical Chemistry Laboratory. The room faced due west, and some of my best recollections are of those Oxford sunsets, intense red and orange against the pale grey Costwold clouds. The honey-coloured limestone of the Cotswold villages can be especially pretty at that time of day, beckoning to us to leave our calculations and seek out a good rural pub. That was of course unless it was a Thursday, when we knew that Graham would be in the Brasenose beer cellar with his current crop of undergraduates, and when on many an occasion, often at my direct instigation, the beer would flow far too freely.

All the occupants of room 365 were, each in our own way, disciples of the

great W. Graham Richards.

Some like the truculent Ian Wilson, the very able Balliol post-doctoral, were performing extremely accurate calculations on very small molecules, which could only exist very fleetingly, if at all, and then only in conditions of temperature and pressure present in deep space or distant stars. One could be forgiven for thinking that this most academic of academic research was just an excuse to indulge in a delightful world of complex mathematics, until it was pointed out that Graham Richards and his team had correctly predicted radio-frequency spectral lines, verifying the real existence of their weird inter-stellar molecules millions of light years away in space. These calculations were at the forefront of rigorous theoretical physics, and it fascinated me that similar computation could be brought to bear on the challenge of new discovery. However, Wilson ragged me constantly about the huge approximations we had to make to try and make sense of our drug and pesticide molecules compared with his aesthetically pure inter-stellar 'diatomics'.

Others like my very good mate Stephen C.R. Moore, the bearded, slightly over-serious Yorkshire man, trod a middle path by looking to apply rigorous calculations to molecules where the problem could be simplified by considering only flat structures. Steve was working on his own long-running doctorate thesis, but also played a pivotal role in the Richards' group, effectively supervising my research when Graham was away or otherwise committed. Steve and I spent much time together, and it is to him, almost as much as to Graham himself, that I owe such a huge debt for the support and encouragement that he gave me at that crucial time.

I desperately wanted to follow the likes of Ian Wilson and Steve Moore onto a two-year doctorate programme. Luckily for me there existed a so-called CASE (Co-operative Awards in Science and Engineering) government grant scheme, which provided extra cash and resources for those willing to spend a proportion of their research time in an industrial lab. ICI, that is Keith Heritage and his now new line manager, Rod Morrod, agreed to sponsor me for the scheme, with Graham as the academic supervisor. Miraculously, therefore, I found myself at the beginning of the new academic term, September 1977, about to embark on another two years of research; another two years of Oxford, Brasenose, room 365, good mates,

Cotswold beer; and not least, computational chemistry. They were great years and they passed far too quickly.

The research on the doctorate continued seamlessly with the Part II, and project-by-project Keith Heritage and I continued to demonstrate the value of the computational approach. Between ICI and Oxford my time was my own, and I became to really appreciate a diary almost entirely under my own control. For the first year I travelled down to Jealotts Hill in a little blue British Leyland Mini van, but then I somehow managed to persuade John Barltrop, the organic chemistry tutor, to sell me his open-topped Triumph Spitfire sports car with wire wheels and racing trim, finished in British racing green. Now I was somebody!

A few weeks after the purchase I saw Graham. 'Hey, I understand you've just bought that wonderful little Triumph Spitfire off Jack Barltrop! You jammy bugger!'

Finally, that last term in Oxford approached. The weather in the May and June of 1979 was exceptional, and without apology I spent as much time as I could in and around Brasenose. I knew I had more than enough to justify the doctorate, having published five papers in the course of the research, including one with Graham and Steve Moore and the American Chemical Society. I had also scored the plenary patent application, 'Triazole Fungicides', together with the Jealotts Hill chemist, Dr Paul Worthington and others. It was time for some deep thinking, however, for I knew I was savouring those very last drops from that wonderful chalice that had been youth in Oxford.

In early June, with three weeks to go, I went out and purchased a fine Panama hat to go with my white flannels and white rowing blazer. From there on, until the last cricket match had been played, the very last 'going down' party celebrated, the very last friend seen off from the station, the very last scout hugged goodbye, and the very last pint consumed in the buttery, I wore that Panama every day. Then, one evening in early July that final evening came, and I took that Panama hat and walked again around the new quadrangle, as I had done six and a half years earlier. Round and round I walked, until all the room lights were turned out, and all the others had gone to bed. Round and round I walked, savouring the moment, for all time. Sure enough, the deep magic was now well established.

Despite the sentiment, however, I knew that my time in Oxford was now over and that it was time to move on. Again I was lucky. Jealotts Hill were not formally

recruiting at the time, but given the importance they now attached to the technique, and clearly to their relationship with Graham, they offered me a job as a technical officer, and in September 1979 I joined Keith Heritage as a full-time employee at ICI. Not only that, but ahead of my recruitment they purchased what was then the most advanced computer for molecular modelling, the Digital Electronic Corp (DEC) PDP 11/60 plus a GT40 computer graphics screen, capable of displaying up to 140 rotating monochrome points and vectors in real time.

The job was, for its day, relatively well paid; if I remember rightly about £12,000 per annum in 1979, equivalent to around £50,000 in 2003, a record starting salary for the Richards' group. Accordingly, from the September of 1979, I buried myself into making computational chemistry a success at Jealotts Hill and very shortly, within ICI generally. It was to prove a grinding fight against the 'Luddites'.

At the same time I was headhunted relentlessly by the other drug and pharmaceutical companies. The competition was so severe that at one time I was even flown across to the US to be interviewed, and then offered a job by ICI's own US pharmaceutical division. Somehow my attendance at ICI, Wilmington, Delaware was leaked back to Jealotts Hill in the UK, and there was hell to play. In truth, however, Jealotts Hill had, at that time, nothing to worry about. If I had wanted to leave there were plenty of opportunities via the numerous, almost daily, head-hunter approaches. At the same time, I was the toast of the conference circuit, giving talks, not just on our own results in computational chemistry/molecular modelling but also to the enthusiastic uninitiated as to how to choose an appropriate hardware and software system.

It was thus that in mid-1980 I became aware that there existed no professional, commercially produced and supported software to address the needs of the developing computational chemistry market. At Jealotts Hill, for example, we had purchased software to drive our then enormously expensive PDP 11/60 from a humble academic at Glasgow University, Dr David White. The David White software was a great advance, but it was buggy and ultimately totally inadequate for a commercial research environment. Getting support from David also depended critically on his day-to-day availability.

In short, there was a clear commercial need for a definitive, well-engineered and well-supported molecular modelling software product. In particular, since

many new research algorithms were being developed in universities, particularly in the UK, a new company would have significant advantage by in-licensing products from UK and US academic research establishments without having to commit to expensive *ab initio* in-house development.

In my second year at Jealotts Hill, starting 1980, Graham asked me to supervise another CASE student, Sandra Robins. Sandra was also from Brasenose, and extremely bright, having taken a First Class degree. Sandra and I clicked immediately. She was clever, imaginative and intuitive. Her research project, consequently, was to be a great success.

Over the next two years, Sandra and I kept returning in our discussions to the requirement for professionally produced and supported molecular modelling software. Now, as well as academic packages from the likes of David White, and a new entrant, Professor Garland Marshall from the Washington School of Medicine, St Louis, the pharmaceutical companies, unable to find what they required, were building their own in-house proprietary systems. We had Dr Peter Gund with the Merck Molecular Modelling System, and Dr David Pensak at DuPont with Tribble, named after his pet dog. A trickle of such systems was soon to become a torrent.

Not only that, but the speed of the computation, and the sophistication of the graphics screens, driven principally by the requirements of the US military, were exploding. It was not long before we could rotate and manipulate protein molecules with thousands of atoms, and all in full colour. DEC, with their PDP and later VAX computers, were already in the field as leaders, but soon came Evans and Sutherland, IBM, Hewlett Packard and a host of others.

In the summer of 1982, as Sandra was writing up her thesis, we met with Graham and made our proposal to set up a new computational chemistry, the world's first. Graham would be chairman, Sandra chief technical officer, and myself CEO. I had also been speaking to Garland Marshall in St Louis, who had become a good friend. Garland had also decided to turn his academic package into a commercial venture, Tripos, and was hoping to win commercial support from Evans and Sutherland. If so, the two new companies would work together, share code and distribute for each other in the US and Europe respectively. On the face of it, it was obvious what we should do, but as usual in life there were potential downsides. For one, my career had got off to a wonderful start. Graham had made

discreet enquiries, and while it was obviously early days, I was very favourably starred. Sandra, equally, had just completed a great doctoral research project, so much so that I had persuaded Jealotts Hill to employ her as a technical officer in her own right. Graham thought we had too much to lose, and we agreed.

You can argue the merits of that decision, as we have done many times subsequently, until, as they say, 'the cows come home'. It is easy to be too critical of us, but the world was different then. There was little or no venture capital available in the UK; where would we get start-up funding? Also, there would be the University to deal with. In 1982, believe it or not, the University of Oxford was vehemently against all forms of commercial exploitation of intellectual property. Previous generation start-ups, such as Martin Woods' Oxford Instruments, were founded under a shadow of secrecy, with founding intellectual property and know-how, developed in university labs being spirited away without reference to the university, and with the latter only too happy to turn a blind eye. How different it all was from the US, where venture capital had flourished since the early 1960s, and all major universities had whole departments focused on invention protection and exploitation. No wonder the UK had acquired a reputation of being poor at intellectual property exploitation; it was all left to accident, to brave pioneers like Martin Wood (now Sir Martin) to bend the rules.

The fact is, rightly or wrongly, we had made our decision; and Sandra and I put it behind us, and got on with our careers.

Some weeks later, however, Sandra called me to say that there was this guy called Keith Davies, a graduate student from crystallography, going round all the departments in Oxford begging software, with a view to compiling an in-house molecular modelling system. It goes without saying that Sandra and I, by this stage, had collected a considerable archive of useful algorithms. However, we had made our decision, and therefore I confirmed my agreement to Sandra that we give him the lot. Not a year later, September 1983, Keith Davies, by then managing director of his newly formed Chemical Design Ltd, was at Jealotts Hill demonstrating his new, all colour, molecular modelling system to us as one of his first prospective sales. When asked by an innocent chemist at one stage in the demo, Keith confirmed, indeed, boasted, that his only competitor worldwide was a firm called Tripos, based in St Louis in the US.

As an aside, it was to give me more than a little satisfaction when fifteen years later (1998) Oxford Molecular Group Plc purchased Chemical Design, by then also a public company.

Not fifteen, but five years later in 1988, one cold late November evening, I was sitting in front of a blazing fire in my parents' farmhouse in Derbyshire. By then I had left ICI, fed up with the big company way of doing things, and wanting to have my own show and be self-employed. For the last two years I had been effectively a travelling showman, taking vintage fairground attractions around the local shows. It never earned much money but I was happy; and each morning when I climbed out of bed in my caravan, I knew the whole day to come was mine with which to do whatever I wanted; a rare, near impossible, feeling for a manager in any large company.

The phone rang. It was Graham, firstly with very sad news regarding his wife, whom I had come to know well at Oxford. 'I am ringing to say that Jessamy has just died.' He was collected and brave, but obviously devastated. What a tragedy. I asked how the two small boys had taken it, and how he was coping with them and life generally. Few would have coped, but Graham did.

'Now something else,' he said. 'Remember that company which we were going to set up? I would like you to give this guy Hiddleston a call. Through my efforts on the University and Industry Committee, and thanks not least to Maggie Thatcher, the University has finally agreed to set up its own intellectual property company under the new government dispensations. The only trouble is no one can think of a strong enough first spin-out candidate company. How about our molecular modelling company? I've got tons of new software. I even have a name, Oxford Biosoft.'

The deep magic was at last kindled. Before long it would become an inferno.