**PREFACE** 

By Michael Lee, January 2024.

Family: I have one brother who went to Lincoln College, Oxford and is artistically inclined. Ann and I have two sons and six grandsons. It is a curious fact that I also have only male antecedents going back two generations.

Education: started in a primary school just before the war, and continued partly in tunnels made from (unused) sewer pipes partially buried in the school playing field and covered with grass.

Secondary school was at Harrow County School for boys which started in the second form, and consequently we also took the general schools and higher schools examinations a year early. One of our teachers suggested that I apply for a job at the Post Office Engineering Research Station. The application was successful, I continued studying one day and three evenings each week and gained a B.Sc. General degree at Chelsea College , which is about 10 miles each way by bike.

Next was two years national service. The first nine months were in Catterick Camp in Yorkshire. I was in the 3% selected for officer training which was exceedingly arduous. One pleasant memory was that I was the only officer cadet to beat our Captain on the revolver firing range. I fired from the hip (having read too many westerns when I was young).

Afterwards I spent several weeks at Garrets Hey where signalmen (private soldiers) were trained in high speed Morse code. The officers mess consisted only of me and a major- general (normally in command of 3,000 men). The food was fabulous.

Next I was posted to 1 Wireless Regiment, in Brunswick, West Germany.

After two years National Service I returned to my parents in NW London and commenced two years at Imperial College in London.

A friend and I decided to take an activity holiday. Luckily my future wife was also on holiday there at the same time. After a couple of years we married and bought a maisonette in west London, and had two sons.

Together with Vince Grispo and his wife we started Research Instruments Limited.

While all this was going on I had written a PhD thesis concerning tunnel diodes, and submitted it to the University of London. They replied that I should submit the thesis again in a revised form, which I duly carried out. This revised thesis was rejected. All this took many months, and I remained very dissatisfied. With considerable help from Bob Robinson I found that a decision of the University of London could be challenged. Bob and I wrote a series of letters over a period of months, eventually I received a letter, sent on behalf of the Queen, announcing the decision of her Privy Council, in our favour!

We found out later that the "Chief Clerk" of the University of London had written a letter to the second examiners stating "you have no alternative but to fail this man". We found that this "Chief Clerk" had been sacked.

### A company started in the 1960s

#### The history of Research Instruments Limited

By Michael A Lee A.R.C.S., Ph.D., FInstP.

#### Acknowledgements to my wife Ann and to Vince Grispo

© 2023 M.A. Lee. All the material in this book is subject to copyright. The contents may not be reproduced, stored or transmitted, in whole or in part, in any form or by any means, electronically or otherwise, without the prior written permission of M. A. Lee.

### CONTENTS THE SIXTIES

The UK Sixties economy. Workshops. A factorypage 3Micromanipulators. Probers. Sales. Product rangepage 5Sales promotion and exporting. Microscopepage 9Exporting. Competition. Productionpage 10Moving from London to Cornwallpage 15A summary of the sixtiespage 15

#### **THE SEVENTIES**

Postal strike. Severe recession	page 16
Miner's strike. Self-build factories. Cattle breeding	g page 17
Cloister stage. Lever stages	page 18
Groovac. Accounts. A smaller factory	page 19
A summary of the seventies	page 24

#### THE EIGHTIES

Miner's strike. Self-build factories. Cattle breeding	page 25
Human IVF. PZD and SUZI. Puller. Forge	page 27
Micropipette making. Exhibitions. Lectures pa	ge 29
A summary of the eighties pa	ge 32

#### THE NINETIES

Economic and industrial landscape	page 33
The future of RI. Recruiting graduates	page 35
New IVF micromanipulation techniques	page 35
Bourn Hall workshops. Exhibitions at symposia	page 37
SMART award. Sonic sword	page 38
EU fourth framework grant. Dolly the Sheep	page 39
Transfer to the new directors	page 41
A summary of the nineties	page 41

### THE SIXTIES

My good friend Vince Grispo and I were not finding our jobs very interesting, so we decided to set up our own Company for manufacturing a new type of micromanipulator. This instrument reduces hand movement to facilitate carrying out fine work under a microscope.

### The UK Economy in the Sixties

After the austerity of the war years, the UK economy was largely prosperous, although growth was weaker than in other European Free Trade Area (EFTA) countries. In 1960 EFTA was established as an alternative to the European Economic Community (EEC). Although trade between EFTA members more than doubled in the sixties, this was much less than that enjoyed by countries within the EEC. Attempts by Britain to join the EEC were vetoed by the French president Charles de Gaulle.

Annual inflation rose to 5%. The bank rate rose from 3.5% to 5%. Low growth led in 1967 to the pound being devalued from \$2.8 to \$2.4.

Married life for Ann and I started in a first-floor maisonette in a block of four in West London. Fortunately the maisonette came with an attic in which Vince and I built a tiny workshop to house a second-hand metalworking lathe and a drill which we used for making prototype instruments.



Malcolm, the best man at our wedding, won £400 competing in Criss-Cross Quiz on Granada TV. He very kindly lent us £100, and also helped with sales and marketing for some months. By 1962 more space was needed for machine tools, so we set about building a small shed at the bottom of the garden to our maisonette. The shed had very good

sound insulation which avoided machine noise annoying the neighbours. It was painstakingly built by ourselves, with brick



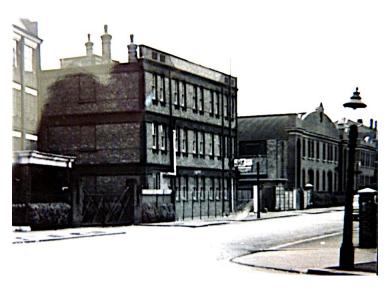
walls and a tiled roof, more a work of art than a shed. Building went well until roof level when the freeholders got wind of it. They sent us a letter demanding that we desist forthwith. Fortunately none of our thirteen neighbours objected to the shed, and the freeholders relented, so we finished the building work. The result was that we had a very small workshop which just provided

space for a lathe, a milling machine and a pillar drill. Vince started working full time on the project while I continued working evenings and weekends. We could now start manufacturing and selling instruments.

#### A factory! - the move to Ace Works

Once instrument sales had started we needed staff and suitable manufacturing premises. In those days factory space was unbelievably difficult to find, any factory was snapped up immediately. To stand any chance of success Vince had to visit the newsagents as it opened, buy a local paper, phone an advertiser, and then drive to see the premises right away.

Eventually he found a night watchman's flat on the top floor of



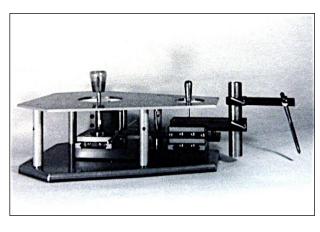
what had been the office block of a printing works in Park Royal, West London. It was 2,000 sq. ft. in size and consisted of seven separate rooms.

It would be difficult to imagine anywhere less suitable for a light engineering factory. Everything had to be carried

up four flights of stairs. Machinery had to be raised up the stairwell by an electric chain hoist, generally at weekends or in the evening when other tenants were not around. One of the heaviest items was a large Reavell air compressor for which we made a wooden anti-vibration base, filled it with sand and mounted it on lorry springs. It was installed in a small room on the flat roof. We never saw our landlords, we just posted the rent to them.

At this stage Vince was full-time Works Director, I was MD and instrument designer working two and a half days a week until 1966 when I became full-time. Ann Lee worked three days a week as Sales Director, and June Grispo three days a week as Finance Director. Mick was a machine operator, it was his first and only job, staying with what became *Research Instruments Limited* (RI). A few months later Roddy, a toolmaker, joined RI and stayed until he retired in the nineties. Alan was taken on as a fitter, and continued with the company for a number of years until his early death. Christine worked on assembly.

#### **Micromanipulators**



RI micromanipulators achieve movement reduction by novel mechanical designs employing lever-reduction. Different types of micro-tool could be attached to the outputs of the micromanipulators according to the application involved.

The prototype in the photo was supplied to Frank whose hobby was collecting marine diatoms and arranging them in patterns on microscope slides. Diatoms are fascinating minute objects needing to be viewed thro**u**gh a high-power microscope. Frank wanted an instrument which would make it easier for him to arrange the diatoms in patterns, and that is where the micromanipulator would be used.

#### Probers

Probers consisted of micromanipulators which position miniature test-prods for making electrical test contacts to integrated circuit lines which were initially 30 microns wide (half the width of a human hair). Line widths decreased as the transistor component density increased. A *micron* is the popular name for a micrometre - a millionth part of a metre.

It was clear fairly early on that probing would be impracticable once line widths became less than a few microns. Moore's Law states that the number of transistors per unit area will double every two years. It follows that line widths would decrease from thirty microns in 1970 to just one micron in 1990. So within twenty years we had to find additional applications for RI micromanipulators, or diversify our product range.

### **First Sales and Incorporation**

After some months we took part in a microelectronics exhibition which generated three very welcome sales of probers. Those sales went a long way towards paying us for a year. We had desperately needed those sales.

### **Incorporation as a Limited Company**

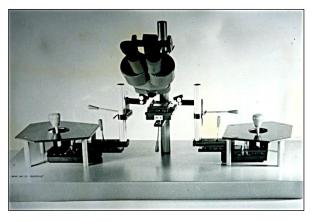
Having started to sell meant that it was a good time to register the company. Getting the name *Research Instruments* accepted by the Registrar of Companies was no easy matter. Their response was that it was unacceptable because of similarity to names already registered. But by this time Bob, who was a Patent Agent, had joined us in his spare time. Bob engaged in a battle with the Registrar. Bob showed that several other registered companies had names with as great, if not a greater, degree of similarity. Bob prevailed, but not without a struggle. The company was duly incorporated as Research Instruments Limited on 28<sup>th</sup> April 1964. Bob was a director from 1969 to 1975; he had a very successful career with a multinational company. Sales for RI in the first year were £4,308, sufficient in those days to buy a semi-detached house. It was a very encouraging start.

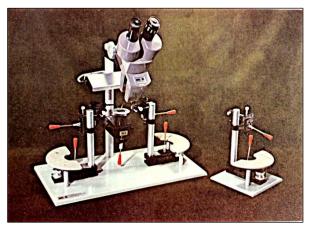
**Our aim:** to meet most applications for micro-movement.

Terminology:

*Micromanipulators*: for movement in three dimensions *Positioners:* for movement in two dimensions

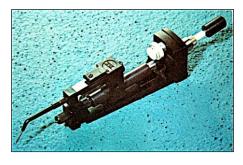
#### Slides: for movement in one dimension.





Micromanipulators for use with the highest optical magnifications. They provide three-dimensional movement from a single control.

Micromanipulators for use with low to medium power microscopes. They have fixed reduction ratios, and provide 3D movement from two levers.



Micromanipulators for multiprobes. Movement in 3D from a single lever. In plan view they are sectors of a circle.



Each carries a probe needle..

Multiprobe for Integrated circuits with bonding pads around their periphery to which simultaneous temporary connections are made

### **Custom design - Ultrastage for Sir Charles Kao**

Charles Kao wanted to measure movement of an optical fibre

with sub-micron accuracy for which the the "Ultrastage" was de-



signed. Charles Kao was a remarkable man. In 1999 the American Asian Week magazine and CNN listed Kao as the 'Asian of the 20<sup>th</sup> Century' in the Science and Technology

category. Kao was considered to be '*The person who contributed most to the betterment of Asia in the past 100 years*'. In 2009 he became a Nobel Laureate, and in 2010 he was knighted. He is considered to be the 'father of optical cables'. He pioneered optical fibre submarine communication cables which are the modern equivalent of the TAT-1 transatlantic telephony cables that incorporated thermionic valves which Vince and I had been making at the Post Office Engineering Research Station.

#### John Gurdon - the design of of the microforge

Another example of custom design was when John Gurdon of Cambridge University required a micromanipulator for an instrument he was building. This led to the design of the microforge.

In 1962, John Gurdon, then at Oxford University, had successfully cloned a frog using somatic cells. Later he became Master of Magdalene College Cambridge. In 2004 the "Wellcome/CRUK Institute for Cell Biology and Cancer Research" was renamed the "Gurdon Institute" in his honour. He was awarded the Nobel Prize for Physiology or Medicine in 2012 for the "discovery that mature cells can be reprogrammed to become pluripotent". Wikipedia states that: at his prep school Gurdon ranked last out of 250 boys, was bottom in biology, and was bottom in every other science subject! A schoolmaster wrote "I believe he has ideas about becoming a scientist, on present showing this is quite ridiculous." Gurdon says that this is the only document he has ever framed.

#### **Shockley-Haynes experiment**

This is one of the classic experiments in semiconductor physics. It shows that minority carriers are involved in transport processes in solids, and allows their properties to be measured. The equipment which we designed consists of a simple prober for making electrical measurements at intervals along a small rectangular bar of the semiconductor germanium.

### Sales promotion and exporting

Experience taught us that the best way to sell instruments was to take part in trade exhibitions organised as part of specialised scientific conferences. In the sixties setting up was a nerve-wracking experience. The man controlling vehicle entry into the exhibition hall needed to be bribed to let us drive in. Then our stand-fittings had to be erected without the use of tools, not even a screwdriver, because the unions considered it to be the preserve of their members. Fortunately these problems eased over the years.

#### **Sales personnel**

Two salesmen were taken on during the sixties. The first performed well, but established his own business with a US firm for whom RI had the "sole" UK agency. The second said he made visits which he had not.

Later, when the UK economy was in recession, customers' budgets for spending on capital items were the first to be cut, this meant reduced sales for RI. No longer being able to afford sales personnel, we had to cope with sales ourselves. Vince visited UK customers. In countries where we lacked a distributor, Ann and I visited customers.

#### **Sales publicity**

Press releases sent to relevant journals proved to be both the most effective and the least expensive way to publicise new instruments. A release consisted of my text and one of Ann's excellent photos. Typically about fifty copies of each release were prepared. They were written in the third person so editors had very little to do if they decided to publish them. The most useful type of periodical had "bingo cards" on which the reader circled numbers corresponding to articles of interest. Although this was time consuming for us, it produced good results in terms of enquiries received.

#### Sales literature

Initially we designed leaflets and photographed instruments ourselves, the printing being carried out professionally. Towards the end of the decade leaflet design including the text was put into the hands of a one-man firm. His designs were excellent, but the text was over-hyped so we reverted to preparing leaflets ourselves.

Overseas distributors were encouraged to participate in a print run by being offered their names and addresses printed on the leaflets instead of ours in return contributing towards the cost. Sometimes even the whole of the text was in the distributor's language. This arrangement worked well.

### Exporting

More often than not potential distributors visited our stand at an exhibition, either in the UK or overseas. Another way we found distributors was through a UK government agency. This agency also provided reports on potential distributors prepared by embassies. Distributors were usually sole traders, except for Japan. The result was that we built up our exports to about 40% of turnover, mostly through distributors. Altogether we must have dealt with about thirty distributors over the years, we only established long-term relationships with six. These distributors all had a principal who showed a keen technical interest in our instruments and spoke fluent English. As RI sold to a niche market, sales of our instruments only constituted a small proportion of each distributor's turnover.

The UK government subsidised *joint ventures* to some more distant markets, including Japan; they would book a group of exhibition stands, arrange travel, accommodation, and in the case of Japan, provide a helpful briefing at the embassy in Tokyo.

In the USA we had several distributors over the years. Sales went reasonably well, but it was difficult for one distributor to cover the whole country, and his distant customers felt they could not obtain effective after-sales support. Although a distributor with a network of branches might appear to be better, this did not turn out to be so because each branch needed to have a set of instruments, and to have at least one salesman who understood our instruments and their applications. This did not happen, the alternative of shipping instruments from one branch to another incurred the risk of damage. The recipient didn't know whether the instruments were working correctly, and were unable to rectify problems. All in all we found that the best solution was a single distributor for all of the USA.

### **Export credit insurance (ECGD)**

An overseas credit insurance policy was arranged with the Export Credit Guarantee Department. It had to cover all RI's exports, and of necessity involved a certain amount of cost and administration.

Later, because IVF sales were mainly made to small private specialised clinics who paid cash with order, no credit insurance was needed.

### Competition

There was little or no competition in the microelectronics market in manual probers. However, there were competitors supplying micrometer slides and stages. Several manufacturers supplied micromanipulators for the biomedical market including one in England, one in Germany, and our principal competitor located in Japan.

As mentioned previously, the market for micromanipulators is essentially a niche market. This has the advantage that it is not a market which would be likely to interest a larger firm who might force us out of business. The disadvantage is the limited market size. This disadvantage was mitigated by starting to develop a range of associated RI products which sold to the same customers, and also by selling resale items such as microscopes.

### **Resale: Microscopes**

There are two fundamentally different types of microscope –

*Stereoscopic Conventio*nal Stereoscopic microscopes have two separate optical trains which converge on the object. Magnification is limited to about x120.

Conventional microscopes can be either the usual upright type, or the inverted type.

#### **Microscopes for micromanipulation**

Stereoscopic microscopes would be best for all types of micromanipulation, but they are limited to a magnification of about x120. This is because there is a physical limit as to how close the two objective lenses can be made. On account of this limitation conventional monoscopic microscopes have to be employed when working at magnifications above x120.

### **Microscopes for viewing probing**

The dimensions of the probe needles mean that stereoscopic microscopes were able to be used when making temporary test connections to semiconductor devices and integrated circuits.

#### **Microscopes for viewing microinsemination**

The choice has to be a high-power inverted microscope so that work can then be carried out in the larger space between the specimen and the illuminator above it. For the specimen to be illuminated it must be translucent, in a transparent liquid, and in a glass dish.

#### **Other resale items**

Microeletrodes and preamplifiers Welding tweezers Vacuum pumps for use with vacuum chuck**s**.

### Production

Company policy was to manufacture as much as possible in our factory so as to minimise the use of sub-contractors because of:-

Variable quality in terms of accuracy and finish

#### Extended delivery times

#### Higher cost

Our work was delayed by sub-contractors if they had a larger and more valuable customer pressing for delivery. We made plastic parts by injection moulding which is very fast, and provides parts with excellent dimensional accuracy which do not need finishing; also minimal scrap. The first injection moulding machine was a hand-operated bench-top machine. Our toolmaker Roddy made injection moulds from my designs. As these mouldings proved very satisfactory, an automatic injection moulding machine was acquired. Later we bought a very large moulding machine as is mentioned under *Groovac* below. Coming back to Ace Works in West London in the sixties, we now had space for more machinery.

#### Machinery

Two lathes were bought at auction, a Boxford centre lathe for accurate and larger capacity turning, and a capstan lathe for a greater production rate. A Reavell air compressor was purchased for airoperated tools, and removal of swarf (small metal cuttings generated by turning, milling, etc.).

An electric chain hoist was obtained for hauling machinery and metal stock up the two floors. Later on larger machines were purchased - a Colchester lathe and a milling machine. Then for toolmaking, a surface grinder and a Hardinge precision lathe.

#### **Sub-contracting**

Metal casting and metal finishing facilities require a considerable outlay and expertise to set up, so these had to be sub-contracted. Metal finishing was mainly anodising and dying black. It was essential to ensure that the black dye did not fade in sunlight. Precision sand casting was necessary for instrument baseplates, and involved the specialist casting firm first making a wooden pattern, and then a metal one. The pattern was pressed down into sand and removed revealing a shape into which molten metal was poured. As the metal solidified it contracted. The pattern had to be made larger than the finished casting to allow for this contraction. The pattern also had to be tapered to allow it to be withdrawn from the sand without disturbing the impression left in the sand. Where a metal pattern was used allowance had to be made in the wooden pattern for double-contraction. It was very satisfying that a wooden pattern I made for the microforge performed very well.

For a small micromanipulator frame (T25) the more accurate investment casting process was used. This resulted in a better surface finish – but was more expensive. The method is also known as lost-wax casting, a process also used for casting artist's sculptures. It was found to have been used in India nearly 5,000 years ago.

### Recruitment

An advertisement was placed in a local paper, and a shortlist of three or four selected for interview. All the directors took part in interviews working from a pro-forma sheet which listed areas of questioning. Each of us asked about a specific area, and we all recorded our opinions of how well the applicant scored on all the areas of questioning. This standardisation proved to be a very effective basis for the comparison of candidates.

### **Intellectual property rights**

UK patents were obtained for a number of products, and international patents for the Groovac described later. Having a patent is a discouragement for anyone considering selling something which would infringe the patent. Expenses involved are for drafting and filing the patent, and then continuing costs for renewal fees on the 4<sup>th</sup> and subsequent anniversaries of filing. Costs relate to a UK patent which protects against someone manufacturing or selling an infringing item in the UK, nowhere else. Taking out a patent abroad involves all the same costs together with translation costs - and this applies to *every* country in which protection is required. A patent can be very useful if an invention is to be sold to another manufacturer, as was nearly the case for the Groovac. If however someone decides to infringe anyway, litigation is likely to be beyond the resources of a small company. An infringer can, for instance, undermine a patent by claiming that *prior art* exists, that at the time of filing a sufficiently similar invention was already known. The degree of similarity may be a matter of opinion. If this fails, the infringer might appeal, this would involve further expense.

### Moving from London to Cornwall

The seven-year lease of our Ace Works factory was due to expire in 1971. By 1970 more space was needed, so we started to look for larger premises. What little factory space was available in West London was very expensive. Fortunately the government provided incentives for moving to the *Development Regions* which included Cornwall:-

A 35% grant towards the cost of building a factory Factory mortgage from the local council Removal grant for machinery, furniture, etc. Grants covering removal costs for "key workers"

Regional Development Grants (RDG) for machinery.

It turned out that most of us wanted to move to Cornwall. For the company, the overriding advantage was the considerably lower cost of premises. Mortgage repayments on a new purpose-built 7,000 sq. ft. factory in Cornwall were the same as the rent on our old 2,000 sq. ft. second-floor factory in London.

Fortunately the majority of our instruments were despatched by parcel post where costs were uniform throughout the UK, it was only for larger instruments that freight costs would be increased.

One particular concern was having to travel further to our customers, which was an unavoidable consequence of moving away from London. But it was anticipated that road travel would become faster over time. So we decided to move to Cornwall. The new factory was finished at the end of the summer of 1970. It was pure luxury compared with the night watchman's secondfloor flat in London!

### A Summary of the Sixties

Instrument design work started early in the sixties, and manufac-

turing commenced in the middle of the sixties. A range of micromanipulators and probers was designed. Manufacturing and sales were going well. Turnover increased tenfold in five years, albeit from a low base. About 40% of sales went overseas. Cumulative inflation for the decade was low at 45%.

The company's overdraft was equivalent to a quarter of the cost of an average house and secured on the directors' properties.

The most important decision taken was the move to Cornwall.

### **THE SEVENTIES**

#### Severe industrial unrest and the economy

In 1971 there was an extremely damaging postal strike. From 1974 to 1975 there was a severe recession caused mainly by OPEC's decision to double the price of oil. This culminated in a *state of emergency* being declared, a 3-day week, petrol coupons, and a ban on Sunday travel using fuel. From 1979 to 1983 there was yet another recession caused by Margaret Thatcher's monetarist policies for the reduction of

inflation which in the seventies began at 9%, increased to 25% and then dropped to 12%. The average inflation over the decade was 13%. The bank rate started at 5% and finished at 16%.

During the seventies there was extreme industrial strife, rising inflation and unemployment. These led to Britain being known as the *sick man of Europe* and built up to the *Winter of Discontent* of 1978-1979.

### The 1971 postal strike – near disaster

Postal workers walked out on 20 January 1971. They stayed out for seven whole weeks. During the entirety of the strike we did not receive a single purchase order, nor did we receive a single payment – it almost finished us.

In those days there was no email, fax machines did not arrive until the Eighties. Purchasing departments insisted on placing orders in writing, so with no post we very soon ran out of orders. Our order book was usually only about a month long - more extended delivery times would have been unacceptable to our customers. At the end of the postal strike we found, to our dismay, that there were no undelivered orders. We suffered seven weeks total loss of income which very nearly bankrupted the company.

### **1972 Miner's strike & three-day week**:

In early January 1972 the miners came out on strike demanding a pay rise of 43%. They sent *flying pickets* to power stations and other major coal users, and then they tried to stop the movement of all fuel supplies. On the 9th February a *state of emergency* was again declared. Two days later a three-day working week was introduced to save electricity. The strike continued for ten more days, making seven weeks in all.

To continue production we bought a 24kW diesel-electric generator to make our own electricity. Unfortunately an oil price crisis was soon to make it uneconomic to continue generating our own electricity.

### 1974 Miner's strike & stock market crash

On the 10<sup>th</sup> of February 1974, the miners once more came out on strike for a pay rise. The prime minister, Edward Heath, declared a further *state of emergency* and introduced a three-day week. On 28<sup>th</sup> of February there was a general election after which the new Labour government reached an agreement with the miners who ended their strike on 11th March after accepting a 35% pay rise.

Even worse than the strikes was the 1974 stock market crash. The FT30 (now the Footsie 100) lost three quarters of its value. Inflation rose to 25% by 1975, and interest rates were 15%. The new Labour Chancellor promised to squeeze the rich "until the pips squeak". He raised the standard rate of income tax to 33%, the top rate to 83%, plus 15% on investment income giving a marginal rate of 98%.

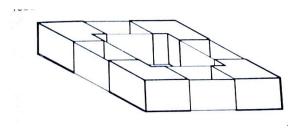
### **1978-9 Winter of discontent & recession**

The Callaghan government set a ceiling on pay rises of 5%, but the ceiling was broken by strikes. Further crippling strikes in the autumn of 1978 seriously disrupted everyday life, causing widespread and frequent power cuts. This period became known as The Winter of Discontent, and led to the election of Margaret Thatcher. Inflation had reached 27%.

The phrase 'Winter of Discontent' is from the opening line of Shakespeare's Richard III: "Now is the Winter of our Discontent / Made glorious summer by this son of York...". Margaret Thatcher used monetarist policies to reduce inflation, and reduced public spending - these deflationary measures resulted in the 1979-1983 recession.

#### **Retailing Hi-Fi**

Following the postal strike RI urgently needed more turnover, so it was decided to try diversifying into retail hi-fi. Permission for partial *change of use* for premises was granted in October 1971. Binoculars and microscopes were also sold. It was not very successful because our factory was not situated in a retail shopping area. It was a sad fact that half the UK-made hi-fi products delivered to us needed repairing before they were saleable. After a few



years the shop was closed.

## Instrument design in the seventies

### **The Cloister Stage**

A novel xy-stage was designed which considerably improved

our high-accuracy micromanipulator. It consisted of four double flexural hinges joined together to form a hollow square, it was named a *cloister stage*. These stages have the great advantage of being inherently free from lost motion – which is invaluable for high accuracy micromanipulators. The cloister stage was patented. These stages transformed the precision and reliability of our high-accuracy micromanipulators.

#### **Microscope positioner**

This solved the problem which arose when probing had to be carried out simultaneously on widely separated points on an integrated circuit. It consisted of a gantry which supported most of the weight of the microscope and a lever-operated x-y positioner.

#### Lever stages

A series of lever-operated stages was designed which provided greater horizontal movement. One version also gave vertical movement via a lever-and-cam mechanism in the large base on which micromanipulators were mounted, this facilitated the rapid exchange of specimens.

#### Other instruments and accessories

The following were designed, and included in the product range:

Programmed stage which followed a pattern in a guide-plate Direct-drive manually-operated stage Measuring microscope using an x-y micrometer stage Micrometer syringe

Vacuum tweezers

### **Biological and medical applications**

As mentioned earlier, previous attempts to sell to this market had met with limited success, but fortunately one interesting sale was made to a very enthusiastic biologist who was working on Legionnaires disease. *Legionella* bacteria grow and reproduce in amoebae in water. When this infected water is made into an aerosol by, for example, a large air-conditioning system, the water in the aerosol droplets evaporates enabling the bacteria to be inhaled. The first recognised outbreak occurred in 1976 at a meeting of an American military veterans association. Within two days veterans began falling ill with what was then an unidentified pneumonia.

### **Diversification - the Groovac**

The foray into retailing hi-fi in the early seventies was at a time when vinyl gramophone records were in their heyday. They were much better quality than magnetic-tape cassettes. CDs (compact discs for audio) were not to become available until 1983-5. In fact CDs did not replace vinyl in popularity until the late 1980s, and it was not until 1988 that CDs started to outsell vinyl. One major limitation of vinyl records was due to audible clicks caused by dust. Dust also contributed to wear of the stylus tip and the record grooves.

It occurred to me in 1973 that here was an opportunity to design a sophisticated gramophone record cleaner. The idea was to vacuum-clean records while they were being played. The *Groovac* was mounted onto a gramophone, and its arm with suction nozzle tracked inwards like a miniature pick-up arm. There were already several types of record cleaner available, but none that provided suction cleaning, they just employed a brush that pushed the dust along without removing it. The Groovac was like a miniature version of a vacuum-cleaner, and like the domestic version it did actually remove dust and collect it.

Our existing production facilities were suitable for making the suction nozzle, arm and base. The suction pump was bought-in, as was the pump housing which came flat with three grooves to allow it to be folded to become a rectangular box. Subsequently we made the housing by injection moulding. This necessitated the purchase of an extremely large Russian injection moulding machine some 6 metres long and weighing 15 tons. It also involved the design and construction of suitable moulds. The result was a pleasing moulding with a matt black finish.

Later a small brush was included in order to discharge the static electricity which would otherwise have attracted dust onto the surface of the record. The brush had hairs made of carbon fibres that were electrically connected to earth. It was attached to the suction nozzle, which it preceded.

A number of assemblers were recruited to construct the Groovac, and it was at this time that the total workforce approached 30 - the highest ever.

Patents were taken out in a number of countries, and Bob was very helpful because he knew reliable Patent Agents abroad. Although it was expensive we considered it to be necessary because of the overseas sales potential.

We were very excited when a popular TV show offered to use the

Groovac live on its nationwide show. We watched the TV without any idea of what to expect, but feeling excruciatingly embarrassed. It was their custom to "test" products as they saw fit, which in our case was to pour cigarette ash over a vinyl record and to expect the Groovac to pick it up. The Groovac was designed to pick up very fine dust, not to empty ashtrays.

A potential distributor expressed an interest in selling into the USA. He explained that if he decided to sell the Groovac he would place an initial order of "one to show and one to go" for each of his 2,500 retail outlets. That initial order would have equalled the total number that we ever made! It was out of the question to ramp up production fast enough.

It became clear that the Groovac needed to be made by a firm which had production facilities that could be switched onto making the Groovac, then onto making another fairly large volume product as soon as the Groovac reached the end of its life-cycle.

Sales for the Groovac had seen an increase and then a steady decline. In 1983 it was decided to discontinue production, and to try to sell the know-how and IP rights. A number companies took an interest, including Philips, Sony, Decca and several other overseas and UK firms. Eventually Decca agreed on £20,000 (which was about 20% of annual turnover at the time). Unfortunately Decca was taken over, and negotiations ceased.

### Money, accounts and board meetings

### **Overdrafts, Bank loans and Credit**

In London RI had banked with Lloyds, and when we moved to Cornwall they recommended their Camborne branch because it handled business accounts and was experienced in overseas transactions. This proved to be a good choice. The manager used to visit us each year, he appreciated a small box of metal odds and ends for his hobby of model engineering.

An overdraft facility was arranged against the security of our two houses. In general we were averse to borrowing, and we tried to keep the overdraft as small as possible. This was to prove difficult later in the decade. Our overdraft as a percentage of turnover started at about 5% and remained there until the mid-seventies, (except for 1972, the year of the postal strike). Subsequently it rose briefly to 15% before dropping to 10% where it remained until it reached zero in 1988. From then on the bank owed us money – a very agreeable situation.

To finance building the factory, a twenty-year mortgage loan of  $\pounds 21,750$  was obtained from Penryn Borough Council at 10.5% fixed - a reasonable interest rate at the time. The mortgage loan covered most of the balance of the cost of the factory after allowing for the 35% grant.

Invoices stated, as was customary, payment within 30 days. Customers almost invariably interpreted this as payment at the end of the month following receipt of invoice; that is, about six weeks credit. In reality they took two months, and sometimes as long as three months. In those days it was not possible to take action to recover the debt through the County Court until three months had elapsed from the invoice date, and some customers deliberately delayed payment for three months for this reason. One case in point was Marconi, so a letter of complaint was written to Lord Weinstock – Marconi being part of GEC. To our very considerable surprise a reply was received from Weinstock himself, literally typed by him in capital letters as was apparently his custom. After that we received a flurry of letters, and no further late payments from Marconi. Unfortunately this was the exception rather than the rule amongst our customers.

#### **Company taxation rates**

Corporation tax on company profits started at 40% in 1965, rising to 45% by the end of the sixties. It was to decrease gradually to 19% by 2000.

#### **Board Meetings**

These were held monthly, and were kept short (less than two hours). Most of the time was devoted to discussing what had to be done, rather than just reporting what had been done. A single A4 sheet was drawn up with boxes to be entered in advance with details of sales and production in the previous month, and the usual accounting data. Discussion almost always centred on how to obtain more sales.

### **Bookkeeping and Auditing**

### Bookkeeping

Up to 1972 June had looked after bookkeeping, then Linden was recruited as our accountant and Company Secretary. He had accounting qualifications and had previously worked for a larger local firm which made bras and went bust. He always took a keen interest in RI's progress, and was soon appointed a director. He was able and conscientious. Unfortunately he died young, he was greatly missed. He had been with RI for 15 years.

### **Invoicing programme**

Initially a multi-part set of forms had been devised which only needed to be typed once to give a Customs declaration (acceptable to the Post Office), a works order, a delivery note, an invoice and a statement. As soon as computers became available for office work, this set of forms was turned into a computer program by young man called Ian who was the son of a friend of mine. Ian worked for RI in his school holidays for several years, and by the time he started his university studies he had written an excellent computer invoicing program. We always knew him as 'Planet' after Marvin the Paranoid Android, a character in '*The Hitch-hiker's Guide to the Galaxy'* by Douglas Adams. Marvin was afflicted with severe boredom because he had a 'brain the size of a planet' - no task he was given occupied even the tiniest fraction of his vast intellect.

### **Annual accounts and Auditing**

In London a small firm of accountants had prepared our annual accounts and acted as auditors. On moving to Cornwall, the local branch of a large national firm was recommended. Their fees were high and they were unhelpful - in one instance we had to find the money to pay a substantial tax bill 6 months earlier than they had told us. Their thinking was that not only did their firm prosper when clients were doing well, but also when clients failed because they derived income from dealing with the insolvency. After that we had a smaller firm. Eventually we engaged a one-

man firm who was very good. When he retired we had another one-man firm who turned out to be even better.

#### A new smaller factory

Staffing levels were allowed to fall after discontinuing the Groovac, and it soon became apparent that less factory space was needed. Less space would reduce our local authority rates bill, which was costing as much as a man's pay, and it would also reduce other overheads. There was space available on site, so we applied for planning consent to build an additional smaller factory little more than half the size of the original factory, and very well thermally insulated. The design was for an easily-built low-cost structure. We had little money, but we did have time. So, apart from bricklaying, we carried out most of the building work ourselves. This provided very useful work during the recession. In addition to reducing overheads, we derived rental income from the original factory which we had vacated.

### A Summary of the Seventies

First and foremost we were very thankful to still be in business. The decade had been exceedingly difficult for RI and everyone else. By the end of the decade it had been necessary to let the payroll fall to eight. However turnover more than doubled, although in real terms it decreased slightly due to extremely high inflation - 240% over the decade. Our overdraft increased from  $\pounds 4.700$  to  $\pounds 10.800$ , although this was only a tenth of turnover.

We successfully moved the factory to Cornwall, having had a new factory built to our own design. All but one of those employed in London moved to Cornwall. 1970, the year of our move, turned out to have been one of the very best years for buying property – both for the factory site and for our houses - because it was just before the early seventies property boom.

Diversification was achieved in 1973 by the design and manufacture of Groovac record cleaners. Sales of consumer products made a very useful contribution to turnover for ten years.

A start was made on writing a 36-page catalogue of RI instruments. This was designed to provide customers with a much clearer and more convenient description of the RI range of instruments than individual leaflets

We could look forward to the next decade, the eighties, with the prospect of considerable savings on overheads in the new smaller factory, on lower council rates, and to receiving rental income from tenants on a 21-year lease in the larger factory we had vacated (they stayed 20 years).

### **THE EIGHTIES**

#### The economy: more industrial unrest

For much of the eighties the UK, and the the rest of the world, experienced a period of boom. But unfortunately the UK also experienced continued industrial strife. When Margaret Thatcher came to power in 1979 inflation was 27%. Powerful trade unions caused wage inflation and time lost from strikes. However, inflation dropped to 4.5% by the end of the decade..

The bank rate which had started at 15%, fell to 10%, and then climbed back to 15% by the end of the eighties. Higher taxes and reduced government spending led to lower economic growth and resulted in a full scale recession by the middle of the 1980s

Sterling became a petro-currency in the early eighties due to North Sea oil. The pound rose rapidly from being equal to \$1.5 to \$2.5 which adversely affected Britain's exports and manufacturing sector.

### The 1984 miner's strike

When Margaret Thatcher became Prime Minister in 1979, her first priority was to reduce the power of the unions and their ability to paralyse the economy, a battle which culminated in the miner's strike of 1984. It lasted one complete year!

#### A new self-built factory

Having received planning permission, building work on the new smaller factory commenced in the summer of 1980. Excavation, levelling and laying hardcore were carried out by a hired digger driver. We laid reinforced concrete-raft foundations, and a mason carried out the blockwork. RI manufactured and installed the aluminium window frames, the timber roof trusses, and installed the roof cladding. Using experience gained from the original 1970 factory, a much improved internal layout was achieved. The result was an efficient factory with very considerably reduced outgoings.

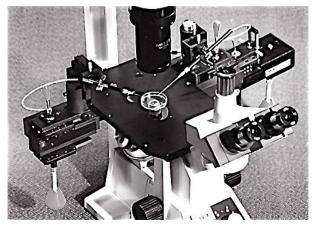
### More self-built factories

On the proposition that if one is good then more will be even better, it was decided to apply for planning permission for an additional industrial building (B2) that was to be half as large again as the first factory that we had built (B1), and attached to it. This building was divided into three individual factories.

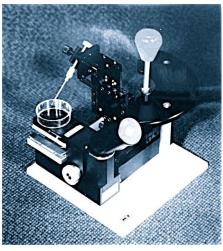
Unfortunately being larger meant the factory would exceed a bureaucratic threshold, so structural calculations had to be submitted relating to wind and snow loadings. It was scarcely credible that there was a regulation requiring roofs to be be designed to withstand a snow loading in Cornwall (where it seldom snows) which was the same as that required in the highlands of Scotland – where there are ski resorts! However, my calculations were accepted and planning permission was received in August 1981. These three factories were again largely built by ourselves, and provided a further useful source of rental income.

### **Micromanipulation in cattle breeding**

In 1979 pioneering work by Steen Willadsen produced monozygotic twins (identical twins) in cattle by dividing fertilised oocytes (eggs). Initially the technique was developed in laboratories using high-precision micromanipulators.



Micromanipulation equipments used in the laboratory for producing monozygotic twins in cattle.



This equipment was used in the field. It incorporates the very compact McArthur microscope.

As the technique developed, lower preci-

sion micromanipulators proved satisfactory for use by veterinary surgeons on farms. This was a very welcome new market at a time when microelectronics sales were falling due to microcircuit line widths becoming lower than the limit for probe testing.

Monozygotic twin work was new to us and very interesting. The procedure was to select a very good quality cow, inseminate her with high-quality semen and then remove the fertilised eggs. Each of the eggs was divided into two, and each half placed in an ordinary cow to carry to term. In this way it was possible to expedite the breeding of a very high-quality herd.

We generally visited customers to install instruments and provide training in their use. One such visit was rather unusual, it was made to behind the Iron Curtain in Romania under the communist dictator Ceausescu. On the flight out we met Ray, an English vet who provided training in the specialised new techniques involved. Romania was in a bad way. In Bucharest only townspeople could obtain petrol and then only a gallon a month, and after queuing for eight hours. Electricity was available for only a few hours a day. Russia was still exacting war reparations from Romania.

After visiting a customer in Bucharest we flew to a State farm in Turgu Mures in the Transylvanian Alps. This internal flight was in an old piston-engined plane of the national airline TAROM. On the flight our group was accompanied by a burly and taciturn Commissar who, on being asked what TAROM stood for, said "Take Another Route Or Miss it".

Meeting Ray led to participation in micromanipulation courses

which he organised at his farm near Nayland in Suffolk. Our contribution was training in micromanipulation and in micropipette preparation. Courses and workshops were a valuable way of contacting potential customers.

### **Micromanipulation in human IVF**

Human conception by In Vitro Fertilisation (IVF) was first achieved in 1977 by Robert Edwards and Patrick Steptoe in Manchester.. This pioneering work resulted in the birth of Louise Brown on 25 July 1978. Edwards was awarded the 2010 Nobel prize in *physiology or medicine* for the achievement. Their *test tube* technique consisted of mixing sperm and eggs together in a *test-tube* or culture dish. The fertilised eggs were left to grow, and then transferred back into the mother's uterus.

Developments in assisted conception led to work being carried out under the microscope on individual eggs and sperm using micromanipulators. This was the start of a new and expanding application for micromanipulators, an application which was to grow into the best ever market for RI instruments. To enter this market RI started to participate in IVF-related exhibitions. It was at an exhibition in Italy that Vince met Dr Simon Fishel. This was fortunate because Simon Fishel was very interested in micromanipulators for new IVF techniques he was developing. He encouraged RI to participate in commercial exhibitions which took place alongside the annual meetings of the European Society of Human Reproduction and Embryology (ESHRE). Simon Fishel is one of the world's foremost specialists in the field of fertility treatment. He was a member of the team that produced the world's first IVF baby, Louise Brown, in 1978.

### **Oocytes and sperm**

Human oocytes (unfertilised eggs) are approximately 120 microns in diameter (twice the diameter of a human hair). Sperm are extremely small, the head of a sperm is three microns in diameter by about six microns long (its head is only one twentieth of the diameter of a human hair). They have an overall length of about 40 microns including the tail. Sperm use their thin tails to provide propulsion. A high power microscope has to be used to

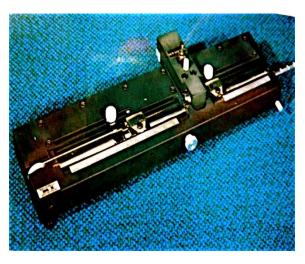
see sperm, and a high-accuracy micromanipulator is essential for chasing a sperm so that it can be drawn up into a micropipette.

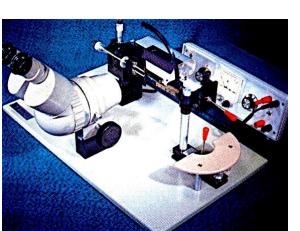
### Partial zona dissection (PZD)

This was the first micromanipulation technique to achieve a pregnancy, (reported 1988). PZD involves making a small incision in the zona of an oocyte to facilitate the entry of a sperm. Unfortunately PZD was associated with a high proportion of oocytes being fertilised with more than one sperm (polyspermy) – these oocytes were abnormal and not viable.

### Subzonal insemination (SUZI)

The first subzonal microinsemination (SUZI) birth was obtained in 1990 by S Fishel et al <sup>[1]</sup> in Rome. In the SUZI technique sperm are injected into the perivitelline space between the zona and the oolemma.





# Micromanipulators for PZD and SUZI

In both techniques the egg is held by suction onto a glass pipette controlled by a micromanipulator. For PZD an incision is made by a microneedle held by a second micromanipulator. For SUZI the second micromanipulator holds a very fine micropipette for sperm injection.

### Instruments for making micropipettes

Micropipette Puller

A glass pipette is clamped onto fixed and moving carriages. A hot coil melts the glass, the spring pulls the moving carriage, reducing the glass diameter by a factor of about 10. A second pull reduces the glass to a very small diameter.

### Microforge

An electrically-heated wire "cuts" square ends on micropipettes. Used to melt and smooth tips of micropipettes so they can hold oocytes without damaging them. Can also bend micropipettes.

#### **Production - CNC machines**

In the early eighties, computer-numerically-controlled (CNC) machine tools were becoming available at reasonable prices, and fortunately a government grant was available towards their cost. A Fanuc machining centre was purchased which is basically a CNC milling machine. It was useful, but only able to handle small work-pieces, and proved to be unreliable. The next CNC acquisition was a very accurate Traminer CNC lathe. It was a "single-spindle sliding-head Swiss auto" with a magazine of five tools, and automatic bar feed. It could work unattended for several hours.

Finally the unreliable Fanuc was replaced by a much larger and more substantial Haas CNC machining centre which could handle large work, and when machining flat-out was positively awesome. It had a carousel of twenty-four tools. A batch of twenty parts could be mounted on the Haas and machined without the necessity for any further attention.

Writing programmes for these CNC machines involved Vince in a great deal of work. However, once written no further programming was called for until existing parts were modified or new parts designed. CNC machines initially appealed because of their much faster work rate, said to be eight times faster than manual machines. However, the excellent dimensional accuracy combined with the absence of errors were considerable advantages. The necessity for individual inspection of machined parts was eliminated because every part was made with high dimensional accuracy.

### **Exhibitions & lectures - microelectronics**

RI participated in exhibitions held annually in Tokyo for which the UK government provided financial support. It also provided the opportunity to liaise with our Japanese distributor. At one of these exhibitions I gave a lecture on high-*accuracy probing of LSI circuits (large-scale integrated circuits)*. In general lectures were not particularly effective for the microelectronics market. However this did not apply later on in the IVF market where giving lectures, and especially arranging workshops, proved to be very effective in promoting sales.

#### **Catalogue of RI instruments**

Product literature had been increasing, and we had a number of individual leaflets and data sheets, so it was decided that a catalogue was needed. This would make it easier for customers to choose the instruments they required. The catalogue was 36 A4 pages. It had coloured headings and diagrams, and full-colour for four pages. Ann again took the excellent photographs with our old Sanderson plate camera.

#### "Single European Act" – free movement of goods

Prior to this Act coming into force a *carnet* had been necessary for taking instruments across national borders. This *carnet* needed a bank guarantee covering 40% of the value of the instruments. RI's overdraft facility was reduced for 12 months by the amount guaranteed. The *carnet* had to list every country to be passed through in the correct sequence. Every instrument and its value had to be listed. Customs at every border meticulously checked every item, and stamped a counterfoil. On one occasion we arrived at a French border on a Friday afternoon only to be told that they were just finishing and we would have to wait until Monday – we fumed, and had to sleep in the camper-van. Once the Single European Act came into force in 1992 *carnets* were no longer necessary which made travelling through Europe very much more convenient. Ann and I used to travel with a set of instruments in a small second-hand VW camper-van to exhibitions and workshops in the UK and continental Europe, this worked very well.

### Hiving off the trading

Towards the end of the eighties our accountant Clive made the very helpful suggestion that ownership of the land and of the the factories should be separated from ownership of the trading company. To do this a new limited company called 'R. I. Estates Limited' was formed with the same directors and shareholdings as RI. The trading was then transferred to R. I. Estates Limited. Finally the names of the two companies were exchanged. The advantage of this *hiving-off* was that no transfer of a valuable asset was involved, and so no tax liability was incurred. The result of this was that if in future it was decided to sell the trading company (RI), then ownership of the land and factories would remain with the directors of R. I. Estates Limited. Liability to tax would only arise on any future sale of assets by R. I. Estates Limited.

### A Summary of the Eighties

The eighties was a decade of consolidation, with turnover almost doubling, as it had done in the previous decade. However with cumulative inflation for the eighties at about 95% the net result was that turnover only increased slightly in real terms. Nevertheless, the mortgage of £21,750 from Penryn Borough Council was paid off two years early. At the same time our bank overdraft was reduced to zero, so that the bank owed *us* money.

Overheads were considerably reduced by moving into the new smaller factory which we had largely built ourselves. We built an additional factory, part of which housed the new large Haas CNC Machining Centre. The other part of this additional factory provided more rental income.

A range of instruments had been developed for the biomedical market, and the high-accuracy micromanipulator had been greatly improved by the novel cloister stage. A 36-page catalogue was printed in 1982, a valuable marketing asset.

It was decided to discontinue the manufacture of the Groovac vacuum record cleaner on account of falling sales. However, the sales revenue generated by the Groovac had been very useful at a time when the use of probe-testing in the microelectronics market was diminishing. Fortunately, two new markets emerged. One in cattle breeding in the middle of the decade, and the other in human IVF at the end of the decade. Human IVF was to develop into the largest market in the company's history.

### THE NINETIES

### **Economic and industrial landscape**

In 1990 John Major was elected Prime Minister. The pound was tied to the Exchange Rate Mechanism (ERM). Restrictions imposed by the ERM caused a run on the pound, and disaster for Britain. Black Wednesday in 1992 ended ERM membership for Britain.

For the first three years of the decade the UK was in a recession caused by the collapse of US savings-and-loan associations. Shareholder panic and. falling consumer spending led to a fall in demand for manufactured goods.

There were long-running localised strikes and disputes at the Liverpool Docks in the middle of the decade, but fortunately nothing like the damaging nationwide strikes of the seventies and the eighties.

Tony Blair's Labour Party swept to power in 1997, and continued with the former government's spending plans. The power to set interest rates was given to the Bank of England. During the nine-ties interest rates fell from 15% to 5%, and inflation fell from 4.5% to 3%.

Luckily for RI, the new human IVF market was not closely linked to the fortunes of the UK economy. Up to the nineties, RI sales had been largely to industrial and government laboratories whose capital spending budgets generally varied according to the state of the UK economy. In the nineties our sales increased rapidly as more IVF clinics were set up to meet demand, and new clinics needed new equipment.

Novel IVF techniques were being developed so that treatment could be offered for an increasing number of different fertility problems. One related technique was a screening procedure for genetically transmitted conditions called preimplantation genetic diagnosis (PGD). These new techniques contributed to a rapid expansion of of the market.

### The future of Research Instruments

In 1998 I reached the retiring age of sixty-five, for Vince it was two years later. What should happen to the company?

- 1. *Sell the company as a going concern* unlikely, the products are very specialised, only a few companies worldwide might show an interest; the jobs of RI employees would be at risk.
- 2. *Wind-up the company and auction its assets* straightforward, but little return, all employees out of work.
- 3. *Recruit new management* young people had to be found.

After a great deal of thought the third option was selected.

### **Recruiting graduates**

While attending the *British Association for the Advancement of Science* meeting at Plymouth University in 1991 we met Professor Burns from Plymouth University. By a lucky chance he happened to mention a government initiative called *Teaching Company Schemes*. Each scheme consisted of an industrial company, a university and a graduate. The graduate was called a *Teaching Company Associate* (TCA) and was employed by the Teaching Company for a three-year period, partially funded by the government. TCAs worked on R&D projects spending part of their time with the Company and part with the University.

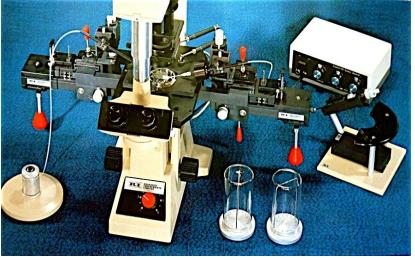
A Teaching Company Scheme was set up and a number of young graduates interviewed, from whom Bill was selected. He had an MBA with distinction in marketing and had a keen interest in joining and helping develop a small enterprise, he also showed a keen interest in RI instruments and their applications. Provided he proved to be suitable, the objective was that Bill would after a few years become a director, and if all continued well after that he would take over from me as managing director.

Subsequently three talented local graduates were recruited (not under the TCS scheme) with the objective that, if they lived up to expectations, they also would become directors. Justin (who was *victor ludorum* at his school) was to take over sales and marketing from Ann, David (who was *head boy* at his school) to take over R&D from me, and Harvey to take over production from Vince. Option three had been been a good choice.

### New micromanipulation techniques for IVF Intracytoplasmic sperm injection (ICSI)

In 1991 Fishel's SUZI technique was developed by Palermo into a procedure in which a single sperm was injected through the oolemma and directly into the cytoplasm at the centre of the oocyte. This procedure was called intracytoplasmic sperm injection (ICSI), it became the most widely used micromanipulation technique for assisted fertilisation.

Pre-implantation genetic diagnosis (PGD)



This procedure avoids couple a transmitting a genetic disease to their children. It was first carried out in 1989 by Alan Handyside and collaborators. Using micromanipulation a cell is removed

from an 8-cell fertilised egg, this cell is replicated using the PCR (polymerase chain reaction) process and genetic diagnosis carried out. If the cell is healthy the egg is transferred to the uterus, if not further eggs are diagnosed until a healthy one is found,

### **Micromanipulators for ICSI and PGD**

The photo shows two high-accuracy micromanipulators with the instrumentation needed for a complete microinsemination setup.

At the top right is a temperature controller for the microscope stage which surrounds a petri dish containing the sperm. On the right is a liquid-filled micrometer syringe for aspirating and injecting sperm. On the left is an air-filled syringe which provides suction for holding the egg into which a sperm will be injected.

### Workshops and lectures (ICSI)

Workshops had been found to be very effective in selling to the animal breeding and IVF markets. Participants first attended lectures explaining the techniques and the instrumentation involved, followed by practical sessions. RI provided and set up the instruments, and I generally gave a lecture on the practical aspects. An embryologist gave a lecture on the biological aspects involved. Then participants would be ready to perform micromanipulation themselves using RI instruments under instruction from experts. Participants became familiar with RI's instruments, and came to realise that they were made by a company which was very well acquainted with the techniques involved. Some of the workshops and exhibitions in which RI participated are described below.

#### **Bourn Hall Clinic**

The world's first test-tube baby clinic was established in 1980 by the IVF pioneers Steptoe and Edwards at Bourn Hall near Cambridge. This followed their breakthrough with the conception of Louise Brown - the world's first test-tube baby, born in 1978.

RI contributed to the running of many workshops at Bourn Hall in the nineties. Ann and I used to instruct participants in the use of RI instruments using live sperm and discarded oocytes, preceded by my lectures on micromanipulation and on the making of micropipettes.

### **QMC Nottingham and Belgium**

RI cooperated with Dr Fishel from the Nurture Clinic, Nottingham and with Professor Goertz of Loeuven, Belgium using a similar format to that established at Bourn Hall.

### The RI Workshop in Hong Kong 1995

This was an altogether more enterprising undertaking. RI organised the workshop, took the financial risk, and arranged the biological materials. An embryologist experienced in IVF micromanipulation techniques was invited to cooperate in running the event. Participants paid a fee which they could more than recover in one cycle of IVF treatment. Approximately fifteen took part in each workshop. Our overseas distributors encouraged participation in these RI Workshops because those attending were potential customers. Ann and I, Bill and Justin took part.

### The RI Workshop in Bali 1995

Held after the Asian and Oceanic Congress on Obstetrics and Gynaecology Congress. Attendees could stay stay on to participate in the RI Workshop.

### **Exhibitions at Symposia**

**AZ-VUB annual symposia in Belgium at** the *Vrije Universiteit Brussel* where the ICSI technique was developed.

### ESHRE annual symposia in Europe

The European Society of Human Reproduction & Embryology (ESHRE) symposia were very relevant meetings for RI. They were held annually in a different European city.

### **Overseas Distributors' 1995 in RI's factory**

It was well attended, and provided an excellent opportunity to demonstrate our new instruments and IVF techniques.

### **Exporting and payments**

Sales in Europe were almost entirely made to small independent clinics, and as mentioned previously, payment was made with or-

der, so there was no need for credit insurance.

Another advantage of selling to small clinics was the absence of the bureaucratic procedure involving budgets etc. For IVF clinics it was a virtuous circle – the clinic paid



RI who then supplied the equipment - the clinic had the equipment it needed for microinsemination – patients were delighted by a pregnancy and paid the clinic. Everyone was happy.

### SMART Award 1991 - for the Sonic Sword

At an exhibition a man from the DTI (Department of Trade and Industry) asked if we would be interested in applying for a SMART Award (Small Firms Merit Award for Research and Technology). It was competitive, with only one in ten applications being successful. As it was a quiet time at the exhibition, we filled in the application forms. Fortune smiled on us, and we won a SMART award. The DTI arranged an award ceremony at the *Exploratory* in Bristol where RI, along with a dozen others, were to receive an award from the hands of none other than the Secretary of State for Trade and Industry himself, Peter Lilley. He gave a short speech ending with his experience of a prize-giving at a girl's school in his constituency. He said a few words to each prize-winner. When he asked one girl what she intended to do after school, she fluttered her eyelashes and said "that's up to you". (It seemed very amusing at the time).

A prototype sonic sword showed that application of an alternating voltage to a piezoelectric device in order to provide axial movement to the micropipette was unsuitable because of parasitic transverse movement of the tip. However applying a voltage as a rapid step function gave a good axial stabbing movement.

In 1992 an application was made for a Stage 2 SMART award which had a one-in-three chance of success. Again the application succeeded, and a grant was awarded to contribute to the cost of manufacturing the sonic sword.

#### EU Fourth Framework grant: 1994-1998

A telephone call was received enquiring if RI was interested in a substantial EU grant for a research project. Apparently the EU had €13 billion available for four-year research projects. The caller knew RI had received a SMART award, which made him appear genuine. He said he and a colleague ran an Agency which

would deal with the EU and look after the application for 10% of the grant. This was a *Fourth Framework* programme designed to foster collaborative research projects across national borders within the EU. He explained that they would find partners, and that RI would manage the project. All this would be subject to our being successful, only one in ten applications was successful. It seemed too good an opportunity to miss. We gave the project the title "The Sonic Sword for pharmaceutical neurophysiological research". The main application was patch-clamp work and the role of the cell membrane in the regulation of physiology, growth and development are investigated. Patch clamping makes it possible for this to be done without experimentation on animals. Another important area of research was the cell biology of phytoplankton which are microscopic sea creatures that play a major role in regulating the transfer of the greenhouse gas carbon dioxide between the atmosphere and the oceans, and in regulating atmospheric carbon dioxide.

The project consisted of two phases, an initial evaluation phase and a longer development phase. It turned out that the Agency would receive 90% of the grant money for the first phase. The 10% that the Agency had originally mentioned only referred to the second phase - the first surprise! The other members of the consortium were the Marine Biological Association in Plymouth, a large European microscope manufacturer and a German electronics firm. The project was a revelation. The microscope manufacturer provided two microscopes on loan, nothing else. RI even had to carry out the design and construction of a modified microscope stage. This microscope stage design work was carried out by David using a computer-aided-design program. The electronics firm had no interest, or expertise, in the type of amplifiers involved; so again RI was obliged to carry out the work, but at least we arranged to receive their grant money.

The sonic sword was part of a *patch-clamp workstation* that consisted of two micromanipulators mounted onto a microscope together with amplifiers, a temperature control and a perfusion system for the specimen. A modified micropipette puller was also associated with the workstation. During the first phase it became clear that the Agency was not carrying out its part of the bargain, so RI was obliged to carry out their work. Bill even had to rush with a report to Directorate General XIII of the European Commission in Luxembourg before a deadline, this the Agency should have made. Later one of the Agency's principals of was convicted of video piracy and given a non-custodial sentence.

The project involved a fair amount of report writing which was carried out mainly by David, but the grant was quite a considerable amount of money.

Long after the project had been completed we were contacted by a firm of economic development consultants on behalf of Directorate General XIII. To our surprise and delight they told us that our project had been assessed as being among the top fifteen out of 150 projects. Apparently an important criterion they used for assessment was that the project paperwork should occupy as little of their shelf space as possible.

### Dr Ian Willmut and Dolly the sheep

We supplied micromanipulation equipment to the Roslin Institute and an associated Scottish laboratory where they were working on breeding sheep, led by Dr Ian Willmut. In 1996 they succeeded in producing "Dolly the sheep", the first ever cloned mammal.

### Micropipette manufacture

Bill believed that it would be a good idea for RI to manufacture micropipettes. Consequently a clean-room was constructed and the necessary manufacturing equipment set up. There were manufacturing problems, including one that was particularly intractable, but Bill persevered and micropipettes became a new and successful product line.

### **Transfer to the new directors in March 2000**

A management consultant recommended treating the transfer as a *Management Buyout*, the assets of Research Instruments Limited being transferred to a new limited company owned by the new directors. The name Research Instruments was then transferred

to the new company.

Bill, Justin and David had been with the company for most of the nineties, and they had become capable of running the company. The "new RI" rented premises from R I Estates Ltd (us) for three years and then moved to their own factory a couple of miles away

### A Summary of the Nineties

Cumulative inflation for the decade was 40%, the lowest since the sixties. In 1991 RI won a SMART award stage 1, then a stage 2 award the following year. In 1994 RI won an EU Fourth Framework Programme award.

RI developed a complete set of instruments for microinsemination, and towards the end of the nineties manufactured readymade micropipettes.

Well-qualified and able graduates had been recruited to take over the company when we retired at the end of the decade.

The emergence of the expanding IVF market proved to be extremely good for RI, with turnover doubling in real terms. It was the first expanding market for the company. For RI the nineties was an interesting, successful and profitable decade.

\*\*\*\*\* END \*\*\*\*\*

#### Notes for Printers:

- a. use Times New Roman throughout
- b Page 16 line 12: spacing of words should be the same as the rest of the text page 27 line 12, ditto