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HARDWARE AND SOFTWARE ARE DEVELOPING SO FAST IT'S HARD TO KEEP UP!  
MORE THAN FIFTY EMPLOYEES BY THE END OF 2000  
EINDHOVEN UNIVERSITY OF TECHNOLOGY TO DEVELOP GENETIC ALGORITHMS

*Universities invest in Avantium stock*

## **The most advanced lab in the world**

### **INNOVATIVE**

**The three Universities of Technology in the Netherlands, in association with Shell, SmithKline Beecham, Alpinvest and Generics, have set up a new chemical research business. The company, Avantium, will be using robots and later even lab-on-a-chip technology to screen and optimize catalysts and chemical processes. Avantium's president, Dr Ian Maxwell, says 'The new technologies can transform the traditionally conservative chemical industry into an innovative sector'.**

*By Martine Segers\**

A chemical process lab in 2005. The computer hums. It is running a simulation program that optimizes the experimentation. Elsewhere in the lab, a robot is simultaneously filling hundreds of mini test tubes with chemicals. There is a different catalyst in each tube. Once the chemical reactions have been initiated, an infrared camera picks out the best catalyst by seeing which tube is developing the most heat of reaction. The liquid and the gases being given off are analyzed for undesirable by-products. These data let the computer calculate the selectivity of each catalyst. Once all the reaction parameters have been automatically measured under all sorts of different process conditions, the computer simulates the way the catalyst will perform under slightly different process conditions in order to establish just how robust the process is.

This approach makes it possible to get new chemical products to market much faster, explains Dr Ian Maxwell, president of Avantium and former research manager at Shell International Chemicals. With catalysts, it is difficult to predict the effect of the structure on their eventual performance. This is why catalysts are constantly 'improved', synthesized and tested after the original design phase. Robots can dramatically speed up this process by making numerous, slightly different catalysts and then testing them all simultaneously.

### **Fine chemicals**

Maxwell had been working on the high throughput screening of catalysts at Shell International Chemicals since 1994. 'We kept quiet about what we were doing for a very long time. But when we saw that an American high-tech company, Symyx, was investing more and more in the new technology we were faced with a choice—either invest more ourselves to stay in the race or start up a new company of our own that could attract venture capitalists.' Shell opted for the latter course, and Maxwell resigned to set up Avantium. 'It went just as we'd hoped. We were actually approached by all sorts of companies much sooner than I'd expected.'

In addition to the three Dutch universities of technology and founder Shell, stockholders in Avantium, which was officially incorporated on 24 February, now include major international corporations like pharmaceuticals giant SmithKline Beecham, simulation software house GSE Systems and fine chemicals company W.R. Grace & Co. Discussions are ongoing with Akzo Nobel, and Avantium has turned down a number of smaller companies.

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\* The author is a freelance journalist.

It costs a lot of money to develop robot units and simulation programs. What's more, they require a range of specific skills which are seldom if ever all found in a single company or a single university. And this is what makes the alliance in Avantium of such interest to all the partners. 'Hardware and software are developing so fast it's hard to keep up. Avantium can afford to invest in robots that carry out experiments fast *and* in software that can process data fast. By keeping these investments in balance, we can save a great deal of time,' explains Maxwell.

### **Exclusive**

For a fee, Avantium's shareholders get exclusive access to the new technology that the company develops. 'However, in a few years' time, when we've developed another new generation of technology, we will market the current technology commercially,' says Maxwell.

The stockholders, with the exception of the universities, also undertake to outsource contract research to Avantium.

The new company has raised 64 million guilders in start-up capital. The three Dutch universities of technology are each investing 3.3 million guilders in stock. The bulk of the money comes from venture capitalists like S.R. One, Alpinvest and The Generics Group, and from SmithKline Beecham itself.

The Dutch Ministry of Economic Affairs also appears willing to invest substantial sums in the research company. Avantium and the three universities of technology have mapped out projects costing ten million guilders. The application for a grant from the Economics Ministry for these projects is now in the final phase.

When it was set up, Avantium also had an estimated 15 million guilders' worth of technology and patents to its name. Shell is contributing all its know-how in the field of robot units and will probably also second some eight people to Avantium. GSE Systems already has simulation tools for chemical plants. 'We will be combining the GSE Systems models with the results of high speed experimentation.'

### **Pharmaceuticals**

Robots have been used in the development of new drugs for some time now, and the technology is also standard in DNA screening. Chemical engineers have been slow to pick up on these new technologies. According to Ian Maxwell, this is because 'major chemical corporations are used to doing everything themselves, whereas the biotech and pharmaceuticals industries have a history of working with small, innovative research companies. The chemical industry has traditionally been much more conservative, but this is about to change. In the States people are already forecasting that chemical companies' stock prices will rise before long as a result of the introduction of new technology.'

But, says Maxwell, there are still a lot of gains that can be made by pharmaceuticals companies, particularly on the process side. 'There are still numerous opportunities for using new catalysts.'

In April, Maxwell was working with a dozen or so people in a temporary office in Hoofddorp, setting up Avantium. Working in a small company came as a complete revelation. 'You can take decisions very quickly. It's also very exciting working with people of all nationalities from a range of disciplines to set up something new that we all believe could have a massive impact.'

Maxwell hopes to have around fifty people on the payroll by the end of the year. 'At the outset our investors were concerned as to whether we would be able to find enough suitably qualified people. However, we haven't run a single job ad yet, but we're already getting lots of letters from young research scientists who've heard about us on the grapevine. People are evidently very attracted by a high-tech business. We will probably only have to search actively for senior managers in the finance and human resources departments.'

### **Contract research**

Avantium will be setting up two laboratories. Since the start of this month the company has leased 2500 m<sup>2</sup> in a business park near Amsterdam Sloterdijk for its commercial laboratory for confidential contract research. Avantium's creative and innovative lab will be housed in a building belonging to Delft University of Technology. The science faculty is freeing up around 500 m<sup>2</sup> by converting a number of teaching laboratories.

Through Avantium, the universities of technology in Delft, Eindhoven and Twente will have access to the most advanced lab of any universities anywhere in the world, believes Delft professor Dr Thomas Maschmeyer. 'It keeps us on the scientific map and makes us more attractive to students, funding agencies like NWO, and companies.'

A university investing in stock in a new company is an unusual set-up. Why was this structure chosen? 'We wanted a strategic relationship with the universities of technology,' explains Ian Maxwell. 'Because they are stockholders they will make a greater contribution to the thinking about the company's technology strategy.' And it's no bad thing in terms of finding staff. 'Our close contacts with the Dutch universities put us right at the source of new talent.'

Each of the three universities has its own reasons for getting involved in Avantium. They are each investing 3.3 million guilders and will get a guaranteed minimum of two millions worth of research assignments in return. Patent rights will be negotiated on a contract by contract basis.

Eindhoven is not interested in developing robot technology itself. 'Operating robots is not the first thing you want to teach a chemical engineer. The approach is highly empirical, whereas in the first instance we want to teach our students to gather knowledge systematically,' says Dr Rutger van Santen, Professor of Chemical Engineering at Eindhoven University of Technology. 'What's more, building robots is really a matter of mechanical engineering. It would consequently be too great an effort for us to develop these technologies completely on our own. The advantage of holding stock in Avantium is that we can get access to this equipment through the lab in Delft.'

When other institutions develop robots it raises a number of interesting research questions for Eindhoven. 'We are going to be working on smarter algorithms for Avantium—genetic algorithms, for example, to recognize patterns in the huge volume of data that you generate with robots. We are also modeling catalytic reactions on the basis of chemical insights. These models will make it possible to identify and select catalysts that are worthwhile testing with a view to speeding up a particular reaction.'

Whereas in Eindhoven the emphasis is on information technology, the people in Delft want to get involved in the development of robot units. 'We were planning to develop minireactors anyway,' says Dr Jacob Moulijn, Professor of Chemical Process Catalysis. 'Our association with Avantium means that we will be able to get started much sooner and gives us the opportunity to take the lead in a new field. Robotization leaves more scope for intelligent work, because it gives you more time to think about things. We can be more creative and do more adventurous experiments. This advanced technology does away with the need for a lot of laborious experimentation and that makes it much more enjoyable for the students.'

### **Microreactors**

Researchers in Twente are already working on even more far-reaching miniaturization—not mini but microreactors. The advantage of microchips is that, in tiny channels as fine as a human hair, things can be mixed fast, rapid temperature variation can be induced and it is easy to generate very high pressure.

The University of Twente also had another motive for wanting to get in on Avantium. 'We've been researching ways of carrying out microanalyses using chips for five years and now, for the first time, we're going to start doing real chemistry with our chips. Until recently the applications for these lab-on-a-chip technologies were essentially confined to medical diagnostics and chemical analysis,' says Professor Albert van den Berg. 'So we're delighted that Avantium wants to use our technology and

will be taking it to the chemical industry. The fact that we're investing in their stock demonstrates our confidence in the company and means that we want to enter into a strategic relationship.'

Dr van den Berg is currently involved in negotiations about the sale of licenses for a number of flow control technologies that have been developed in Twente. 'For example we can make liquids flow by applying an electric field to the wall of a capillary tube. We are also working on microfilters, microvalves and flow sensors. We can already achieve flow rates of milliliters per minute using a voltage of no more than 50 V. This means that it is no longer always necessary to scale up the production of fine chemicals. In the future it will be possible to produce the substance you want quickly by getting a large number of chips to perform the same reaction simultaneously, which will mean that new products can be brought to market faster.'