

## News Analysis

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### A bio lab on a chip

Micro-arrays and integrated electronics and photonics on a sliver of silicon let researchers probe for individual genes responsible for a disease

The semiconductor technology company STMicroelectronics has produced a silicon chip with micro arrays that support on-chip DNA analysis at the genetic level. When DNA from diseased and healthy sources is added to the silicon, it becomes a platform for genetic research into the cause of diseases. The monolithic (one-chip) array includes the sensing and supporting electronics.

A media group taken to Catania, Sicily in South Italy in September was shown a machine placing droplets containing DNA onto silicon; through a scanner, computer and software. We then saw the array of color dots representing healthy gene pairs and those that were likely candidates for specific diseases.

The array of tiny dots on a silicon surface allow genetic researchers to accurately place a single polynucleotide strand of the twin-strand, double-helix DNA from individuals with specific diseases (the target DNA) along with a strand of healthy DNA as reference (the probe). The objective is to find out the precise difference between the two DNA strands, thus identifying the genes that could be responsible for the disease.

Like a lock and key, the two strands will come together completely if the specific deoxyribose and phosphate groups are

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complementary, forming strong covalent (chemical) bonds. If there is a difference, that pair will not form the bond, showing a different color characteristic. One end of the DNA strand itself forms a covalent bond with the silicon, anchoring it firmly in place.

The chromatically marked DNA fluoresces when excited by electrons and this can be detected by photo-sensors. Different colors indicate whether the gene pairs have paired correctly or not, and therefore whether they are identical or different.

Such a micro-array silicon platform for DNA allows the monitoring of expressions of 10,000 or more genes at a time. And the single piece of silicon contains the active electronics, and even the micro-channels carrying the DNA fluid, all integrated into one piece of silicon, increasing the speed of analysis and reducing its cost. The solution with the DNA can even be transported by capillary forces in the micro-channels.

The silicon chip integrates even the photo-sensors. This is an achievement, as silicon's optical properties are not suited to either photoreceptor or light source use, which is why devices like LEDs tend to use gallium arsenide and other "III-V" compounds, so called because they belong to groups III and V of the periodic table of elements. But this would mean that adding an LED or photoreceptor to a silicon device would involve multiple stages and devices. To integrate the whole device out of a single piece of silicon, STMicroelectronics engineers "doped" the silicon with specific "impurities" to change its optical properties, in this case to create a photoreceptor element on a silicon chip, which can detect the fluorescence and color of the DNA just above it.

Thus, adding optical functions to silicon helps allow active DNA analysis within a silicon chip, and the integrated electronics in the same silicon senses and communicates the color changes in the DNA pairs in the array. Using silicon for the base substrate for the DNA analysis also has other advantages—mainly, a great benefit in signal to noise ratio. Glass itself would fluoresce, so such background noise from glass would have to be "subtracted" from the results of such an experiment.

Parallel with the silicon biosensor array development is ongoing research into DNA strands to explore genetic pairs as alternative memories, including research on organisms that change state or color after absorbing a photon, making them candidates for future "optical storage".

While yet at the research and testing stage, ST officials say they expect to manufacture the "gene platform" biosensors in a year for "simple stuff" and in three years for "more complex stuff".

The \$6.3 billion STMicroelectronics is the fourth-largest semiconductor company in the world. It is particularly strong in "system-on-chip" technology.

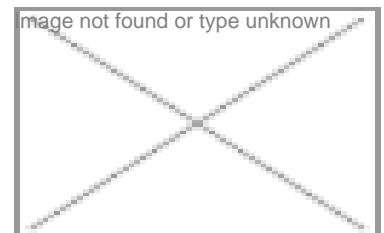
The ST group was formed in 1987 after the merger of SGS of Italy with Thomson of France. In May 1998, the company changed its name from SGS-Thomson Microelectronics to STMicroelectronics. Today, it has 43,000 employees (including over 1,000 in its India development center in Noida, UP), 16 R&D units and 39 design and application centers. The company is NYSE-listed ("STM") since 1995.

*Prasanto K Roy traveled to Catania, Sicily in South Italy  
at the hospitality of STMicroelectronics*

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## **AP leaves no stone unturned**

The state is moving at a rapid pace to promote biotechnology in the state.



With every state concentrating on promoting biotech, the big question that arises is which is the biotech capital of India? Is there a clear trend? Our recent survey points out that the South has the largest representation of biotech companies. The companies from South accounted for 39 percent market share of the total biotech industry with revenue generation of Rs 899 crore. Out of this figure of Rs 899 crore, Karnataka accounts for close to Rs 500 crore, while AP for over Rs 200 crore. So is Karnataka the capital? "It is the Biocon group that comes in the way of Hyderabad being crowned the biotech capital of the country," remarked a senior official from the industry. How true! The biggest player in Karnataka is the Biocon Group with total revenues in excess of Rs 285 crore and accounts for greater than 55 percent of total contribution of companies in Karnataka.

Statistics apart, is Andhra Pradesh really inching towards being the biocapital? Looking at the flurry of activity in the state, one cannot ignore it. It is leaving nothing to chance. Wooing the investors, building the infrastructure, spreading the awareness and increasing quality education. Chandrababu Naidu, the state chief minister, in the recently concluded Biotec International conference said, "For the phase-II of the Biotech Park, 162 acres of land has already been allotted. We have now decided to go for Phase-III and Phase-IV of the ICICI Knowledge Park, which is adjacent to Genome Valley. This will help to provide plug and play R&D facilities to biotech and pharma companies. A marine biotech park and Pharma city near Visakhapatnam will come up soon." A biotech incubator with assistance from DBT has been launched. Further an agribiotech park and incubator has been started on the ICRISAT campus jointly by the state government and ICRISAT. These are just some of the initiatives on the infrastructure front.

On another front, the state is also forging several alliances globally. It signed a MoU with Thailand to mutually promote biotech through collaboration in research and exchange of scientists and teaching professionals. This MoU would pave the way for collaboration, particularly in marine biotechnology and biotech applications for aquaculture and tropical medicine. With Iowa State of USA, it would collaborate on research and business in agribiotech and bio-medical research. With Saskatchewan of Canada, it will jointly promote technology transfer, research collaboration, regulatory approvals, educational exchanges etc. While these are some of the latest developments, the State had entered into an agreement for collaboration with Research Triangle Park of North Carolina last February. These are now producing results. CiVentiChem, an US-based contract research and drug discovery support company announced the formation of a subsidiary, Indus BioSciences, in Hyderabad. Similarly, Kard Scientific Inc. of Cambridge, USA is setting up its unit for drug development in SP Biotech Park. Several other pharma and biotech companies, such as Astra Zeneca, Pfizer and Chemical Diversity, Genoexpression, Transzyme have agreed to start their Biochemical R&D operations and contract research in ICICI Knowledge Park and SP Biotech park. The deals are expected to be finalized. Indian firms like Ranbaxy too have announced to set shop.

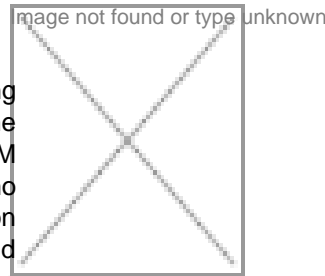
What separates it from the rest? The state has a large number of pioneers, the biotech initiative started as early as 1997 with the setting up of an advisory committee, a chief minister who is a favorite of the scientific community, great institutes like IICT, CCMB, National Institute for Nutrition, and the Centre for DNA Finger Printing and Diagnostics. The list can continue. But the differentiation is AP has set itself an ambitious vision. Naidu's vision statement explains, "By 2020, the state will achieve a level of development that will provide its people varied and realizable opportunities to achieve prosperity. We, therefore, propose to give a thrust to knowledge-based industries such as IT, biotechnology and pharmaceuticals. Biotech is a frontier technology, which has the potential to provide substantial benefits to the society in a wide range of sectors, such as agriculture, medical and health, forestry, and animal husbandry."

This intention is the biggest facilitator. The state has a biotechnology policy, APIDC Venture Capital Ltd, a joint venture between the AP Industrial Development Corporation and Dynam Venture East of USA, which has been providing venture capital to biotech start-ups. It has also an integrated IPR facilitating cell at ICICI Knowledge Park established in association with CII. This is to cater to the growing demands of the industries in AP for patent search and analysis, patentability advisory services, IPR awareness and training.

With the basics in the right place, so what should be the next step? Dr D Balasubramanian, director of research, LV Prasad Eye Institute, Hyderabad, who is also the advisor to the state government, has a few suggestions. "AP should discover, manufacture, and distribute vaccines. It should be the global vaccines supplier. It should attract a few world leaders in the biotech sector to set up operations in the parks. Put up an animal research and testing in the park. The International Institute of Life Sciences should be set up soon." With such visionaries around, entrepreneurs taking the risk, and a supportive facilitator, it is only natural for Andhra Pradesh to be "a neighbor's envy, owner's pride".

Ch. Srinivas Rao

The biotechnology policy is yet to be declared, but the state steps up the tempo.



It was like any other conference of the industry and public were interested in knowing what is happening in biotechnology. The auditorium was packed. Everyone at the auditorium was eager to listen to the words of the speakers like Ajay Piramal, Habil Khorakiwala, Dr Rashmi Barbhaya, Utkarsh Palnitkar, M Vidhyasagar, Dr Sudhir Parekh, Dr Harish Padh, Dr Urmish Chudgar, Alok Gupta, Prof. BB Chattoo, who are attached to biotechnology sector in one or the other way. The speakers made presentations on varied topics from global trends shaping the health sciences industry to biotechnology and pharmaceutical sciences to the dawn of a new era on the Indian horizon. The conference was on "Pharma Biotechnology Development in Gujarat". You may ask what was so special about this conference and why are we referring it? It was a first conference on pharma biotechnology in Gujarat. And more over it was a part of the three-day "Vibrant Gujarat - Global Investors' Summit" organized by the government of Gujarat. Looking at the presence of the audience and speakers, it was difficult to say the conference was a global one.

This being the first conference in pharma biotechnology, it was able to get the attention of the industrialists and also the attention of the investors, who announced an investment of about Rs 350 crore in different projectsâ€”from setting up of BT park, green house technology plant, International Pharma and Biotechnology Park to plasma fractionation centerâ€”in the state.

Expressing satisfaction in organizing the conference, Rajesh Kishore, secretary, department of science and technology, government of Gujarat, who was instrumental in organizing this conference said, " The critical thing is not in organizing the event but to keep the momentum going. That will take lot more efforts. We will put in that kind of efforts and organize four more events in different sectors of biotechnology such as agribio-technology, industrial biotechnology, marine biotechnology and bioinformatics before the end of this fiscal."

Replying to the queries on the participation of investors at the meet, Kishore said, "I didn't believe in numbers. The key objective of this event is to provide a platform to discuss a lot about the happenings in the industry. This will give a little bit push. Champions are here. They want some support to venture into this new knowledge-based industry." He even said that things were being carefully planned for the sector and success should not be judged by the announcements made at the summit.

### **Industry's concern**

The industry still has its concern on the issue. The industry captains, who made their presence felt at the conference, said that they can't go with the speculations and hype. They want some concrete measures from the government in the form of policy on biotechnology. The state government is already working on it and is also in the process of setting up a biotechnology mission to draw up strategies.

BioSpectrum brought this to the notice of the chief minister of Gujarat, Narendra Modi, who made a brief visit to the NID complex, the venue of the conference, who had earlier in February this year assured the industrialists of providing all the necessary support at Biotech India 2003 event. Commenting on the delay in announcing the Biotechnology policy, Modi informed us, "No government will run without a policy. Biotechnology policy is there but not yet declared." The government signed a MoU with Ganesh Housing Corporation Ltd, which is setting up International Pharma & Biotechnology Park at Ahmedabad. This measure shows that the government has kept up its assurances of providing the necessary facilities to the industrialists, who are looking at Gujarat for their biotechnology ventures.

Though Gujarat's pharmaceutical sector accounts for around 45 per cent of the total pharmaceutical output of the country with players like Zydus Cadila, Alembic, Sun Pharmaceuticals, Torrent Pharmaceuticals, Cadila Pharmaceuticals, Ambalal Sarabhai Enterprises and Intas Pharmaceuticals to name a few, the local pharma industry was not upfront at the conference. Pankaj Patel of Cadila Healthcare and Dr Urmish Chudgar of Intas Pharmaceuticals made presentations.

But the enthusiasm among the scientific community, students, public and government officials about the upcoming biotechnology industry will definitely help biotechnology to take shape in the state. The participation of chief minister Narendra Modi and his ministerial colleagues at the conference shows the state's interest in developing biotechnology. Besides pharma, the state has already identified healthcare, agricultural biotechnology, industrial enzymes, bioinformatics, contract research and marine and environmental biotechnology as thrust areas and is planning to organize events in agri and industrial biotechnology next month. A beginning has been made. The thing is to keep the momentum in place.

