Taking his chances with molecules

BY CHEONG SUK-WAI
SENIOR WRITER

INDIAN chemist Gautam Desiraju would be the first to tell you that all scientists have huge egos. So how many rising stars among them are more equal than their average peers? Dr Desiraju, 58, recalls a recent lunch at which he debated this point with five German professors. Then a sixth came over to their table and said: "There's only one way to do this: mention a name and ask everyone here to answer from the pits of their stomachs as to whether he is a good chemist or not."

"If six German dons say someone is a good chemist, I bet you he is," he says wryly, underscoring just how rigorous and reluctant scientists are in acknowledging their fellow eggheads' achievements.

Happily for him, other chemists invariably call him the father of crystal engineering, a relatively new science which susses out how molecules of a drug should be structured to, say, deliver it faster into one's bloodstream.

This Chennai-born alumnus of the University of Illinois and St Xavier's College, Mumbai is one of India's most widely cited scientists. He founded his field after his mentor, Professor David Curtin, told him: "Don't do things that look like my work."

Except for two summers at Cambridge University and a stint each in New York and Wilmington in the United States, he has worked in India all his life. Even so, the kindly don avers, "if I were 27 today and had the qualifications I had when I actually was 27, I wouldn't get a job in India today".

The married man was in town to attend the first powwow between Indian and Chinese chemists earlier this month, many of whom were meeting one another in person for the first time. He is trying to get his peers in both countries to set aside their age-old misperceptions about one another and think in Asia's collective interest, especially since both are forerunners of crystal engineering.

■ *What do you do, exactly, and how will it change lives?*

I study complexities and complex systems, and complexity is a very important theme today. Complex systems are those in which cause and effect are not easily related. Organic crystals, such as those of snowflakes, salt and sugar, are built up from molecules and I'm dealing with crystals used in drugs and explosives... and discovering new molecules.

■ *Why do molecules have to be discovered?*

It's because the nature of diseases is becoming more complicated. Fifty years ago, we didn't have so many anti-depressants; now it's a major area of study. Life itself has changed. So what I'm doing is to first discover a molecule and then make different crystal structures, or polymorphs, of it in the hope that they have better (curative) properties.

■ *What about your work has kept you keen for 30 years?*

That crystals are a complex system in which you cannot predict the outcome of things.

■ *That's very human.*

Absolutely. It's molecular sociology. We don't yet understand fully how molecules come together; we understand them a little, which is why it is a science and not pure speculation or drama.

For the past 15 years, the big drug companies such as Pfizer and GlaxoSmithKline have driven research, especially in organic chemistry... Ninety per cent of drugs are sold as tablets, not as injections, syrups or emulsions, because tablets dissolve and go quicker into the bloodstream.

The molecule of a tablet can have two different polymorphs, which affect solubility – swallow one and it might go into your bloodstream in half an hour; another might take three hours to do so. The thing is, we still don't know how to control the process of making polymorphs, or how many there are to a molecule.

Amid all this, in the mid-1990s, a judge in Chicago decided that each polymorph could be patented.

■ *Hasn't that restricted research a great deal?*

Yes, if you were the guy who discovered the molecule, but not if you were the guy who made the polymorph.

What's very important to note is that discovering a new molecule is very expensive – it can cost up to US$1.5 billion (S$2 billion) a molecule – and can be done basically only in the US and such other big countries. But you can make polymorphs anywhere, especially in India and China – what we call generic pharmaceuticals. And Asian generics have become so innovative that Pfizer and other big drug companies have had to (invest in) their own generics, because the only way to beat these polymorph innovators is to join them.

■ *Isn't all this great news for the poor who are ill?*

That's the point. The judge in Chicago was a very wise man. He said he (made his ruling) to prevent monopolistic tendencies among drug companies. Otherwise, those guys would be too rough for us to handle. Today, the big drug companies are asking me: "This is our molecule – how many polymorphs does it have? Can you control how they behave?" And they want the answer yesterday, so they can file their patents quickly.

■ *Why did you bother to study organic crystals at all?*

That's a very nice question, and one relevant to Singapore. When I started out, nobody thought that organic crystals were even part of organic chemistry. I didn't realise it at that time, but studying something with no clearly defined field – not even a name – was an advantage. Of course, the risk you had to take was that there might be nothing to it in the end.

Now, the question for Singapore is: Do you invest in that which gives you safe returns or that from which you can gain a lot but also lose everything?

The whole question of research is where do you pitch it? Many people claim they're doing something outstanding that will change the world but most of them are crazy... The vast majority of researchers play it safe... The essence of success is decentralisation and lack of micro-management; you've got to let people grow and do their own thing.

■ *But wouldn't a lack of competition lead to slackened study?*

You don't need competition at the beginning of research. You need mental space... Singapore's speedy route to research disturbs me.

■ *Why so?*

You need to have manual overwrites, that is, people who are sufficiently honest to say what is right. For example, a candidate for research (might not meet certain qualifying criteria). This is very common in India. But in 5 to 10 per cent of such cases, you need someone on the selection panel to say: "This guy is good and, if necessary, we should bend the rules to get things going."

It cannot always be done; otherwise there would be anarchy. But someone must be empowered to say that in special cases so that you get the best of both worlds.

■ *Why do you want Singapore to keep bringing India and China together?*

Historically, Singapore has had very long and good connections with India and China, which otherwise have had very little contact with one another. India is not doing well in many research areas globally, but the country and China are doing very well in crystal engineering... Indians are very good at seeing patterns in seemingly unrelated facts while the Chinese have team spirit and a sense of discipline in putting a large amount of effort into a narrowly focused field.

I didn't have the maturity or data to say this 10 years ago, but today, I believe that Asian countries are overwhelmingly the same in their attitudes and priorities.

■ *So how best can Singapore distinguish itself in science?*

Singapore is not going to make it by importing areas of research that are already at their peak. You cannot be successful that way because whoever has done it first in the milieu of his country will give you only something extra or on the side. You might bring in, say, a professor from Stanford University and tell him to run a laboratory of 20 people for two weeks here every two years. He will do that because the conditions are quite nice for him. But what does Singapore get out of it? Practically nothing. Why don't you create a Nobel laureate instead, by bringing in someone from India, China or XYZ country and getting him into an area which might not have peaked yet but might do so tomorrow? Take a chance on that.

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Dr Desiraju is regarded by his peers as the father of crystal engineering, and is one of India's most widely cited scientists.
PHOTO: COURTESY OF JAGADESE J VITTAL

Straight from the shoulder

CHEMISTRY don Gautam Desiraju trusts his intuition when it comes to milestone decisions – such as choosing for his life career a science so obscure that only two other people were initially interested in it. Here he is on:

Being the father of crystal engineering
"I never thought it would have impact and outreach. I just did it because it was interesting to me."

Humility
"You have to read a thousand books to quote from two of them. So most of what you know, you shouldn't show that you know."

How egotistical scientists can be
"Each one of us thinks he is the best in the world; if we didn't think so, we'd be dead. We couldn't function."

Citing the works of other scientists
"A scientist is actually surrendering his ego when he does that, as it's the highest praise he can give someone else."

Chemists
"They're very good at dividing themselves into little groups, which are finally so small that everyone in them becomes an expert on anything."

Information overload
"In the old days, marks were given for what you had in your head. Today, marks are given for how you can keep things from getting into your head."

Why Asia is the next superpower
"Asia has 2.5 billion people and a little money has come into the region – and Asians know better than anybody else how to make a little money go a long way."

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