more sophisticated in an incremental way as human beings evolved.

Savage-Rumbaugh and Greenfield's conclusions are only now reaching investigators concerned with language and evolution. But even at this early stage it is clear they have some sympathizers. UC Berkeley linguist William S. Wang, an expert in the evolution of language who wasn't a participant in the earlier battles, is keeping an open mind. If the findings with Kanzi are proven true, he says, it would suggest that many of the components we think are crucial to speech and that separate human speech from animal communication are quite old.

At the other extreme is MIT linguist Noam Chomsky, who was a severe critic the first time around and now thinks the issue is settled. Chomsky admits he hasn't seen the new data—and doesn't care to see it—but ridicules the notion that any species would have a capacity highly advantageous to survival but not use it until a researcher taught them to. "It would be a biological miracle if humans had the capacity for flight and never thought of using it," Chomsky says.

Other Round 1 critics, including Terrace coauthors Bever and McGill University psychologist Laura Petitto, aren't as harsh as Chomsky. But they have specific objections to the latest round of Kanzi findings. Those findings are difficult to reproduce, they say, since it is nearly impossible to obtain pygmy chimps (an endangered species) for studies in the United States. Furthermore, they say, the criteria Greenfield and Savage-Rumbaugh used to define grammar are too lenient. Bever and Petitto remain unconvinced that Kanzi is using—much less inventing—grammar.

"Kanzi's behavior differs from children's use of language in systematic ways," Petitto wrote in a review of Savage-Rumbaugh's work with Kanzi on language comprehension in an article in the *Journal of Experimental Psychology, General* (Vol. 116, No. 3, 279). "It is not controversial that many [nonhuman] species communicate," wrote Petitto. "What is controversial is whether any species other than humans possess the capacity to acquire language."

But some of those who are attracted by the new studies don't dismiss the idea that pygmy chimps could comprehend English—and perhaps even use rudimentary grammar. "I think most people would say they're dignifying it to call it grammar—it's protogrammar," says Wang. "But they're headed in the right direction."

One of the directions these studies might take is suggested by work done by paleoanthropologist Nicholas Toth of the University of Indiana. Toth, who is interested in the interrelation between tool use and language in evolution, showed Kanzi how to strike flints from a stone and use them as simple tools. Toth is now interested in finding out whether Kanzi will teach other chimps to make stone tools, yielding an animal "community" of toolmakers that might mirror early hominid toolmakers, further diminishing the putative uniqueness of *Homo sapiens*.

Beyond Toth's work, say many researchers, what is needed are studies of pygmy chimps in other labs to see if the work with Kanzi can be reproduced. Also needed are studies of the same species in the wild to analyze more precisely differences between human and chimp symbolic behavior. One researcher—University of Michigan anthropologist John Mitani—has just begun studies of vocal communication among wild pygmy chimps in Zaire. What he finds may settle the question: Have the chimps really mastered their grammar? ■ ANN GIBBONS

Rising Chemical "Stars" Could Play Many Roles

Enormous polymers that grow from a tiny core might be used in drug delivery, filtering, catalysis—even artificial cells

IF *TIME* MAGAZINE COULD name the computer its "Man of the Year" in 1983, Nature deserves consideration from the Nobel jury for the prize in chemistry. In fact, no chemistry Nobelist has matched Nature's command of the periodic table in turning out enormous polymers—be they hemoglobin or chromosome 12—with precisely identical molecules.

Midland Molecular Institute

Starmaker. *Donald Tomalia of Midland Molecular Institute.*

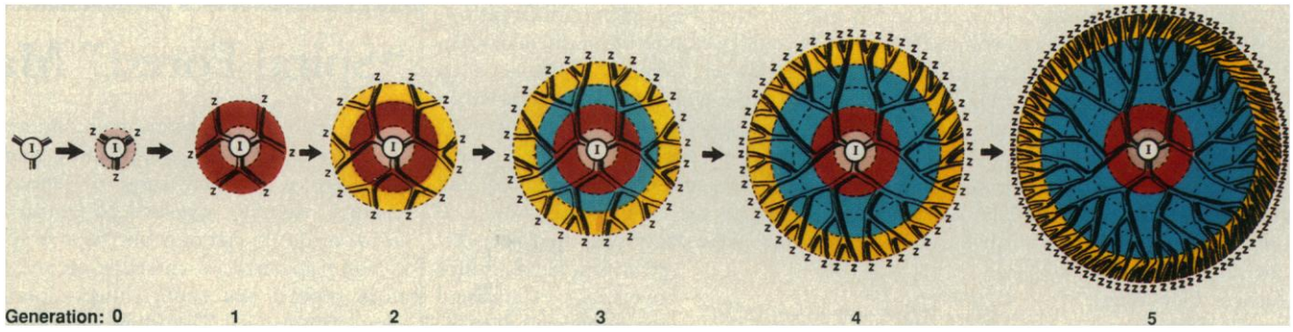
Recently, however, several research teams have begun giving Nature a run for its money. "We have, for the first time, made a large molecule that is precisely defined spatially," says Jean J. M. Fréchet, professor of chemistry at Cornell University, one of those who are at the forefront of this work. "Now, we have the opportunity to design some pretty sophisticated molecules with very useful properties."

Among the useful roles these heavyweights (some have molecular weights of 350,000 and diameters of 100 angstroms) could ultimately play is serving as vehicles for intercellular drug delivery. "Imagine having a molecule that is large enough to carry hundreds of molecules of drug, yet small enough, at 100 angstroms, to pass through a biological membrane," says Fréchet.

Beyond drug delivery, firms such as Kodak, DuPont, IBM, and Allied-Signal are studying how uniform molecules can be used to improve microelectronics processing, selective filtering, catalysis, and advanced materials design. Other companies, afraid of being left behind, are scrambling to get a foot into this new area of polymer research, but the field is so new and small that expertise in making the polymers is in short supply. An indication of just how hot the field has become is the fact that few investigators were willing to disclose details of their work for fear of jeopardizing patent applications.

The new, uniform polymers are called by various names, including hyperbranched dendrimers, starburst dendrimers, arborols, and fractal polymers. Whatever the name, they have the same structure: three or more highly branched polymer chains sprouting from a tiny core. By carefully choosing the conditions under which the chains grow, it is possible to make the chains identical.

The key to obtaining the identical molecules is a sudden change in the growth process. Although the dendrimers begin growing as two-dimensional, fanlike shapes, at a certain point they take on a ball-like form and stop growing, leaving all the molecules with the same shape and mass. "When these molecules reach a certain size, the chains of each molecule undergo a reorganization and pack together to form a tight skin surrounding a largely hollow interior," explains Donald Tomalia, senior scientist at the Midland (Michigan) Molecular Institute (MMI), a state-funded research insti



Donald Tomalia

From generation unto generation. *Two-dimensional schematic projections of a hyperbranched dendrimer growing from an initiator core. At the far right is the fifth generation dendrimer.*

tute affiliated with Michigan State University and Michigan Technological Institute. All the many uses of dendrimers are related to this striking configuration. And those uses, in turn, are due in large part to the Midland researcher's perseverance against long odds.

"Tomalia really created this whole field of research and did most of the initial work of characterizing these molecules" says Cornell's Fréchet. Adds Owen Webster, senior polymer scientist at DuPont: "He's the one who kept promoting these polymers and eventually convinced others that it was an area of polymer chemistry worth exploring."

Hyperbranched polymers were first prepared in the late 1970s, but it wasn't until the mid-1980s that Tomalia, then at Dow Chemical, came up with a way of making batches of them with a uniform molecular weight and size. Given the fact that chemists hadn't been able to do that before, it was quite a feat. But Dow's management remained unimpressed. Says Tomalia: "It was simple, really. They are interested only in bulk, commodity-type chemicals, and starburst dendrimers didn't fit the bill." So Tomalia left Dow, moving to the Midland Institute. There he continued to work out a systematic approach for creating starburst dendrimers of varying sizes and compositions.

Tomalia's basic approach was similar to the "protect-deprotect" strategy that protein and nucleic acid chemists use to make biopolymers. The first dendrimers he made were polyamidoamines (PAMAMs), grown from a three-branched core prepared by reacting ammonia with methyl acrylate, followed by an excess of ethylenediamine. At the end of each branch is a free amino group that can react with two more methyl acrylate monomers—and then two more ethylenediamine molecules—to make a "generation one" dendrimer. This two-step sequence can be repeated to form successive generations, each with twice as many branches as the previous generation. This is called a divergent synthetic scheme: the dendrimer grows by diverging from its small core.

At a certain point this iterative process comes to a grinding halt. "After generation nine the reaction kinetics drop suddenly and significantly," says Tomalia. "That's where we think the chains pack together to form a membrane-like structure, making it very difficult for further reactions to occur." The size of the final, ball-like product (known in chemical terminology as a micelle) varies, depending on the chemistry of the monomers. The ninth generation PAMAM, for example, contains 3069 monomer units, has a molecular weight of 349883, and a diameter of between 98 to 105 angstroms depending on the measurement technique used.

Since creating the first dendrimer—PAMAM—Tomalia and his colleagues have synthesized a number of dendrimer families, all having the same property of forming micelles. Depending on the monomer used to make the penultimate generation, the porosity of the outer membrane can be carefully controlled. "We can make dendrimers that are very tightly sealed and others that are fairly leaky," explains Tomalia. And since control of the porosity of the outer membrane is a central function of living cells, Tomalia has charted his course to go after nothing less than artificial cells. "I think this is the first step towards making artificial cells," he says.

He envisions attaching enzymes within such cells carrying out multistep synthetic sequences in much the same way as biological cells do but without the detritus connected with living systems. Artificial cells could be of great value for studying biological systems, carrying out multistep enzymatic syntheses of drugs, and perhaps also in futuristic therapies where they might act as an artificial liver or kidney, for example.

Then again, most of the uses of dendrimers are rather more down to earth and closer to realization than creating a cell in the laboratory. Although many hyperbranched dendrimers are spherical, by using linear polyethylenimines as the core Tomalia's group has prepared hollow rod-shaped dendrimers about 50 angstroms in diameter and 3000 to 4000 angstroms long. "These might make good molecular wires if we can put the appropriate functional groups on the surface," said Tomalia. Such wires might find use in microelectronic devices made from organic molecules, part of the continuing effort to gain further size reductions in the microelectronics field.

Because of their precise size, dendrimers are ideal for yet another, even more quotidian purpose: calibrating sieves. Polyscience, a supply company in Warrington, Pennsylvania, already sells sizing kits using starburst dendrimers labeled with fluorescent dyes, produced at Midland.

And at Cornell, Fréchet is studying their use in microelectronics processing. "If you can remove one dendrimer molecule at a time from a thin film, you could leave very exact, very tiny holes," says Fréchet. Such an ability would be a boon to those interested in preparing electronics devices operating on the quantum scale.

Many other applications for dendrimers involve using them as carriers of chemicals such as antigens, drugs, imaging agents, or catalysts. Tomalia's group, for example, has prepared PAMAM derivatives containing thousands of gadolinium or manganese ions chelated on the dendrimer's surface. Preliminary tests show them to be several orders of magnitude stronger than conventional contrast agents when used in nuclear magnetic resonance (NMR) imaging. Contrast agents are used to highlight tissues not easily imaged with NMR. And this is of considerable medical value, because the stronger the contrast agent, the less that needs to be injected.

One unusual characteristic of dendrimers is that despite their huge size, they are soluble, some even in water. In addition, lower-generation dendrimers—those large enough to be spherical but not so large as to

form a tightly packed surface—have enormous surface areas in relation to volume: as high as 1000 square meters per gram. That puts them in the same range as carbon black, which forms the standard in high-surface-area materials and is a component of many commercially important heterogeneous catalysts. The combination of high surface area and high solubility could make these polymers useful as catalyst carriers. One thing that makes the prospect appealing is that the dendrimers could be recovered from a reaction mixture by simple extraction or filtration techniques.

Being able to control the architecture of a polymer's surface certainly opens the door to some sophisticated chemistry.

—JEAN FRÉCHET

Alternately, it is possible to make insoluble networks from dendrimers. Webster at DuPont and Tomalia have made thin films of cross-linked dendrimers. Some show potential as catalyst carriers; others might ultimately be used as membranes for separating gases, isotopes, and even biological molecules such as enzymes and other proteins. "Since we can vary the size of the dendrimers and the space between them, we can make filters with very tightly defined pores," says Tomalia.

The main stumbling block to most of these applications is that large-scale synthetic methods remain to be developed. Webster says that current methods of building these molecules from the core produce only small quantities of precisely defined dendrimers. It is possible to make large amounts of starburst dendrimers, but they are less than homogeneous in molecular weight then, since the reactions' conditions are not controlled as carefully, though Tomalia claims that researchers at MMI have just developed a new "kilogram-scale" process that achieves the same homogeneity as previous small-scale techniques.

Even the less-than-homogeneous dendrimer preparations, however, show promise for applications. Fréchet has made dendrimer mixtures that, when added to traditional polymers of similar composition, produce coatings of extraordinary strength and durability. "This, I believe, is where the biggest impact will be in the near future," says Fréchet. Success here, he says, should then produce further advances in more demanding applications, such as drug delivery or membrane separations.

Those demanding applications will require progress in large-scale synthesis, and it is possible that a completely different approach could overcome the problem of scale. Craig J. Hawker, formerly of Fréchet's lab and now at the University of Queensland in Brisbane, Australia, has worked out what those in the field call a "convergent" growth strategy, which starts at the periphery and works back to the core. In this way, it is possible to make dendrimers that have different functional groups covering well-defined regions of the molecule's surface.

Having the ability to make dendrimers with polyfunctional surfaces, says Tomalia, opens up whole new areas for investigation. One application would be to attach tissue-targeting antibodies to one part of the dendrimer and drug molecules to another part. In the same vein, Fréchet believes it should be possible to create artificial catalysts in which the reactants are held on different parts of the molecule and then brought together by a change in pH or solvent.

It might even be feasible to achieve energy storage using a dendrimer that stores opposite charges on different parts of the same molecule. "It's hard to predict what we'll be able to accomplish," says Fréchet, with understandable enthusiasm. He and Tomalia and a handful of researchers around the world are onto a field in its infancy. "We've only just begun making these compounds," Fréchet says enthusiastically, "but being able to control the architecture of a polymer's surface certainly opens the door to some sophisticated chemistry." ■ JOE ALPER

Joe Alper is a free-lance science writer based in St. Paul, Minnesota.

ADDITIONAL READING

"Preparation of Polymers with Controlled Molecular Architecture. A New Convergent Approach to Dendritic Macromolecules." Craig J. Hawker and J.M.J. Fréchet. *J. American Chemical Soc.*, volume 112, 7638-7647, 1990.

"Starburst Dendrimers: Molecular-Level Control of Size, Shape, Surface Chemistry, Topology, and Flexibility from Atoms to Macroscopic Matter." Donald A. Tomalia, Adel M. Naylor, and William A. Goddard III. *Angewandte Chemie*, International Edition in English, vol. 29, 138-175, 1990.

"Photophysical Investigation of Starburst Dendrimers and Their Interactions with Anionic and Cationic Surfactants." Gabriella Caminati, Nicholas J. Turro, and Donald Tomalia. *J. American Chemical Soc.*, vol. 112, 8515-8522, 1990.

"Designer Solids and Surfaces." Thomas E. Mallouk and Haiwon Lee. *J. Chemical Education*, vol. 67, 829-834, 1990.

"Spiral Forest" May

When high-temperature superconductors (HTS) were first discovered more than 4 years ago, a vast new range of superconducting materials appeared to be on the horizon. But in fact only one form of these celebrity materials is currently on the fast track toward real applications: superthin films. The reason: Thin films can carry far more current than bulkier superconducting structures such as wires. That ability may ultimately lead to use of films in faster communications systems, electronic components, sensors for tracking brain activity, and a host of other applications.

But the exact physical properties that enable high-temperature superconductor thin films to carry high currents remain "a bit of a mystery," according to Praveen Chaudhari, a materials scientist at the IBM T. J. Watson Research Center in Yorktown Heights, New York, who was among the first to recognize their enhanced conductivity. Now two teams—one at Los Alamos National Laboratory and one at IBM in Switzerland—may have turned up an important clue to the mystery.

Using scanning tunneling microscopes (STM) and atomic force microscopes (AFM)—tools designed for imaging atomic and molecular landscapes—the teams have discovered unsuspected forests of spiraling grains decorating the films' surfaces. Those tantalizing spiral forests aren't just beautiful artifacts. On the contrary, they may be the defects in the material's crystalline structure that researchers have theorized are at the basis of the current-carrying abilities of thin films, but which have remained undetected. That kind of insight can only hasten the shift of HTS thin films from technology in the works to technology for sale.

Ian Raistrick of the Los Alamos National Laboratory first reported his group's findings on 18 March in Cincinnati at the spring meeting of the American Physical Society (APS). A paper by his group appears on page 1587 of this issue of *Science*. The same evening, during an invited talk, J. Georg Bednorz of IBM Research Division in Zurich, who with K. Alex Müller in 1986 triggered the worldwide research firestorm in HTS materials, briefly described nearly identical observations. His team's work appears in the current issue of *Nature*.

Boths teams focused on thin films of yttrium-barium-copper-oxide, the most widely studied high-temperature superconducting material. Rather than growing layer by layer as many researchers have assumed,