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How Big is Nano?

MU's renowned cancer researcher knows the next big thing in medicine comes from thinking small.

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Story by Alan Bavely
Photos by Rob Hill

Fred Hawthorne has plenty of experience in big science. He worked on the rocket fuel that launched the U.S. into space. He pioneered a whole new branch of chemistry.

Now, six decades into his career, he has landed at the University of Missouri–

Columbia to explore a new scientific field that's incredibly small.

Hawthorne is the recently appointed director of Mizzou's new International Institute for Nano and Molecular Medicine.

Don't feel insecure if you're scratching your head wondering what a "nano" could possibly be. Nano refers to things that are extremely small, a billionth of a meter long, to be precise. Consider the width of a human hair. A nanometer is 10,000 times smaller.

Nanotechnology is a burgeoning new field that is based on things that tiny. These customized materials have applications in computing, medicine and technologies for the military. Nanotechnology already is at work in such diverse products as computer hard drives, car parts, sunscreens, antibacterial bandages and stain–resistant fabrics.

"I've been doing the same thing for years," says Hawthorne, who is 77, "and now I find out it is nanotechnology. It's chemistry that I do."

Hawthorne is studying innovative cancer–destroying drugs that can be packaged in nano–size molecular shells that slip into malignant cells and detonate like microscopic bombs.

MU recruited Hawthorne from the University of California, Los Angeles (UCLA), to give Mizzou a head start on this new technology. His appointment here is considered quite an academic coup. He took retirement at UCLA and came to MU the next day.

Hawthorne's résumé is filled with professional awards and honors. At UCLA, he held the rare position of University Professor and had a cadre of young researchers working in his lab. Many of them have joined him in Columbia.

"Fred is bringing unique technology and a lot of expertise in molecular medicine," says Kattesh Katti, a professor of radiology and biomedical physics and the deputy director of Mizzou's nanotechnology institute. "He'll give us something we didn't have, and we are doing things he wasn't. The combination makes us more powerful almost instantly."

Hawthorne is excited by the research opportunities at Mizzou, opportunities that were surprisingly hard to come by in California.

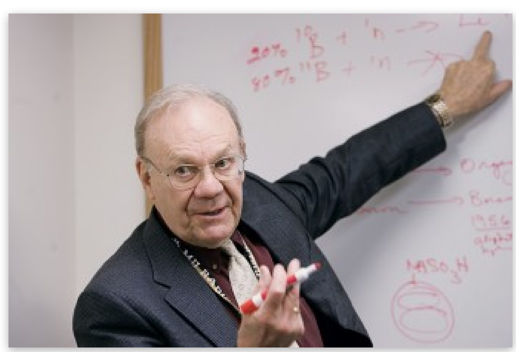
"I've told everybody Mizzou is exactly what I was looking for," Hawthorne says. "I had a large backlog of materials and ideas for medical applications I couldn't develop at UCLA."

Hawthorne says he had been frustrated by the lack of collaboration between UCLA's science faculty and its renowned medical school. Facilities and equipment were often unavailable. He had to search for collaborators at other universities and government laboratories.

Willing to Work Together

At Mizzou, Hawthorne is finding researchers who are more willing to work together rather than guard their academic territories. "I've found people who are still ambitious and energetic and want to improve their institution," he says. "These people have different professional interests and talk to each other. It's great."

And by having medical, veterinary, agricultural and engineering schools all on the same campus, Mizzou researchers can accomplish things that would typically take



The formula is simple for researcher Fred Hawthorne:

collaboration among two or three universities, Hawthorne says.

Mizzou's discipline-crossing researchers plus a powerful research reactor equal a potential nanotechnology treatment for cancer.

"The scope of research done here is unbeatable," he says. "I don't think the average Missourian realizes that."

Hawthorne and MU began their courtship in April of last year when Katti invited him to give a speech at a dinner inaugurating a new journal that Katti is editing.

Hawthorne says he was "treated royally."

MU Chancellor Brady Deaton suggested to him that he collaborate with Mizzou researchers. "I assumed he meant something like trading samples, but Brady asked me to relocate to Columbia," Hawthorne says. "Wow. This was a thought that had never occurred to me. It would be like going home."

How so?

Even after spending most of his adult life in California, Hawthorne is a Midwestern boy at heart. He still has strong emotional ties to the area.

Hawthorne was born in Fort Scott, Kan. His father was a civil engineer who supervised federal construction projects throughout Kansas during the Dust Bowl days of the 1930s. Wherever he would go, his family would come along. By the time Hawthorne had reached high school, he had attended 22 schools throughout the state.

"I know Kansas pretty intimately," he says.

From the beginning, Hawthorne was a science prodigy. He started taking summer classes at the Missouri School of Mines (MSM), now the University of Missouri–Rolla, when he was 15. A year later, he dropped out of high school to study chemical engineering at Rolla full time.

After three years at Rolla, Hawthorne left Missouri to follow one of his MSM chemistry instructors to Pomona College near Los Angeles, where he majored in chemistry. He did graduate work at UCLA under Donald Cram, who later won a Nobel Prize for the invention of a new type of molecular bonding based upon organic chemistry.

In 1954, with his doctorate in hand, he got a job at the Redstone Arsenal in Huntsville, Ala. He worked on rocket propellants for the federal government.

Those were heady days. The Soviet Union launched its Sputnik satellite in 1957, kicking the space race into high gear. The once sleepy cotton town of Huntsville became a booming science city.

“The city grew. It mushroomed. Amazing,” Hawthorne says.

Hawthorne became acquainted with Werner Von Braun and his crew of rocket scientists. He saw, and heard, the mighty engines of the Saturn rocket’s main booster being tested.

“It was a pretty impressive noise,” he says.

By the early 1960s, Hawthorne returned to academia, first at the University of California, Riverside, and then back at UCLA, where he stayed until his retirement.

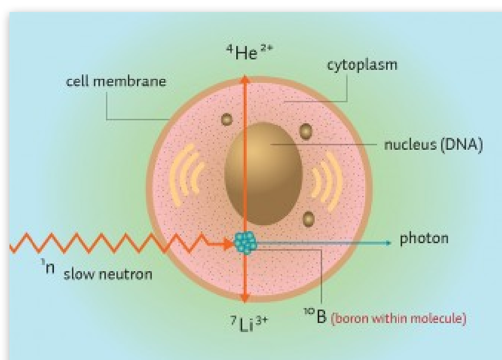
While working at the Redstone Arsenal, Hawthorne was introduced to the newly developing field of boron chemistry. To most people, boron is probably better known as part of the chemical compound, borax, used in that old–fashion laundry detergent with the team of 20 mules on the box.

Boron is a light element that sits right next to carbon on the periodic table. And like carbon, scientists have found that boron is incredibly versatile.

Carbon combines readily with other elements to form countless compounds, including proteins and other basic building blocks of life. The uses of carbon are so rich and varied they form an entire scientific discipline: organic chemistry.

Beginning in the 1930s and accelerating in the 1950s, scientists discovered that boron has many of the same properties as carbon. Boron–hydrogen molecules, called boranes, in principal could be used to make plastics, fuels, dyes and medicines, just as carbon compounds had been used.

"You can begin a whole rerun of organic chemistry with boranes, and to make it even more interesting, you can add in carbon," Hawthorne says.



Graphic by Dory Colbert

At the Redstone Arsenal, scientists used boron to make extremely volatile compounds for rocket fuel. Hawthorne made a major contribution to the field by discovering highly stable compounds called aromatic boranes, which can be used as components for drugs that don't degrade in the body as organic compounds do.

Potential to Destroy Tumors

Scientists seeking new cancer therapies have long eyed one form of boron, called boron–10, which has the potential to destroy tumors. Bombarding this otherwise stable boron–10 isotope with neutrons leads to the capture of a neutron by the boron nucleus, which leads to a miniature nuclear reaction that releases lethal amounts of radiation and energetic fission products (helium and lithium nuclei) at the cellular level. If enough of this isotope could be inserted into a cancer cell and then irradiated with a low–energy neutron beam, it would tear up the DNA of the cell's nucleus.

"You destroy it in one event. Bingo," Hawthorne says.

Even more attractive, the neutron beam would cause relatively little damage to healthy tissue. And the nuclear reaction

How Boron Nuclear Capture Therapy Works

Atoms of an element can contain different numbers of neutrons in their nucleus. Each of these versions is called an isotope. A common, naturally occurring isotope of boron is boron-10.

Each atom of this isotope has five neutrons instead of the usual six.

When bombarded with neutron radiation, normally stable boron-10 undergoes a nuclear reaction. The atoms disintegrate, leaving behind byproducts — helium ions and lithium ions. Boron nuclear capture therapy attempts to use this nuclear within the cancer cells would be so small, it wouldn't harm neighboring cells.

Scientists recognized the potential for using this approach to treat cancer as far back as 70 years ago. But research on the therapy had to wait until the early 1950s, when nuclear reactors that could supply the necessary neutron radiation were built.

So far, clinical trials using this boron nuclear capture therapy have concentrated on a rare and deadly brain cancer called glioblastoma multiforme. Conventional treatment includes repeated doses of radiation. Although this therapy often prolongs life, the cancer is invariably terminal.

Boron nuclear capture therapy is intended as a one–time treatment that would save the patient from multiple bouts of radiation. Experimental results in the United States, Europe and Japan have been promising but limited.

Hawthorne is certain there's room for improvement.

reaction to destroy cancer cells.

Scientists attach boron-10 to chemicals that selectively seek out cancer cells in the body. To ensure that enough boron-10 reaches the cells, Fred Hawthorne is packaging the chemicals in microscopic pouches called liposomes that can slip inside tumors.

When tumors loaded with boron-10 are irradiated by a neutron beam (slow neutron in the image above), the charged particles of the disintegrating isotope destroy just the cancer cells. During this nuclear reaction, the resulting helium ion and lithium ion shoot in opposite directions. In the

"I think this stuff is as good as hot bread, but it's been abused," he says. "They all did the same thing over and over again with the same boron compounds, same radiation and same tumor. The only difference was that the patients spoke in different languages."

example shown above, the helium shoots through the nucleus of the cancer cell and destroys its DNA. Adjacent healthy cells are largely unharmed.

Therapies for Common Cancers

Hawthorne is eager to expand this therapy to more common cancers.

"What gives me great heartburn is that people never had the means or the encouragement to look at the cancers that kill John and Jane Doe by the hundreds of thousands — breast cancers, prostate cancers, lung cancers and so on."

Hawthorne's first step is to find the right boron compounds that will selectively favor uptake by different kinds of cancer cells. The next step is to deliver those compounds to the cancer cells.

That's why nanotechnology is critical.

A lethal nuclear reaction requires a billion boron atoms per cell. That's a thousand to a million times the concentration required for most drugs to be effective. Selective delivery of that big a dose to cancer cells isn't practical in a simple pill or shot.

Instead, Hawthorne plans to use nanostructures called liposomes. These spherical pouches are made of the same membrane material as natural cell walls. They resemble an orange, with the outer membrane — like the peel — holding a water solution of the boron-10 agent.

Kattesh Katti, a professor and force in nanotechnology, says recruiting Hawthorne will help the University solidify a spot atop this burgeoning field of medical research.

Liposomes packed with boron could be administered intravenously to cancer patients. The liposomes are small enough to pass through the leaky blood vessels of tumors to carry boron directly to the cancer cells.

"They're like supertankers of boron," Hawthorne says.

Hawthorne looks forward to potential collaborations with professors in MU's veterinary college to conduct animal experiments and to the medical school for the eventual clinical trials with patients.

Hawthorne also will tap the University's research reactor, one of just a handful nationwide capable of supplying the neutron radiation crucial to the new therapy. The reactor is undergoing modifications for his work and is expected to be ready next year. After those modifications, Hawthorne says, it will be an even more precious commodity — one of just two of its type. The other one is at MIT.

"I think MU is just a gold mine that hasn't been discovered yet," Hawthorne says. "We have a shot to do some new things. We can really become international leaders by creating medical advances in Columbia."

Cancer therapy is just one of a half-dozen or more projects Hawthorne has on his list. He is eager to pursue a molecular motor, a nanotechnology device that can work like a switch to turn the chemical reactions of enzymes on and off.

The excitement that will be coming out of his lab suits Hawthorne far better, it would seem, than daydreams of retirement.

"I like what I do," he says. "If I didn't do this, I don't know what I'd do. I like to fish, but I'd get tired of fishing.

"Right now, I'm in pretty good shape, and I'm certainly motivated. The University of Missouri was nice enough to take a chance on me, and I'm going to pay them back as best I can."

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