CASE STUDY: ROBERT LANGER

Introduction

Robert Langer, a pioneer in biomaterials, is one of the most prolific inventors in medicine. His innovations apply to drug delivery systems, vaccines, tissue engineering, diagnostics, novel therapeutics and waste disposal technologies. He is also a dedicated teacher and mentor who has inspired hundreds of students to pursue academic and entrepreneurial careers in inventive medicine. Langer received the Lemelson-MIT Prize in 1998 for his breakthroughs in controlled drug delivery and tissue engineering which have improved millions of lives.


Robert Langer (Photo/Andrew Fingland)

Background and Early Life

Robert Langer was raised in Albany, New York. His parents bought him a variety of Gilbert sets — including Chemistry, Erector and Microscope — which sparked an early proclivity for chemistry, engineering and lab work. Langer even created a lab-like setup in the basement of his childhood home, mixing chemicals and watching their colors change as they reacted with each other.


Langer as a child. (Photo/Robert Langer)

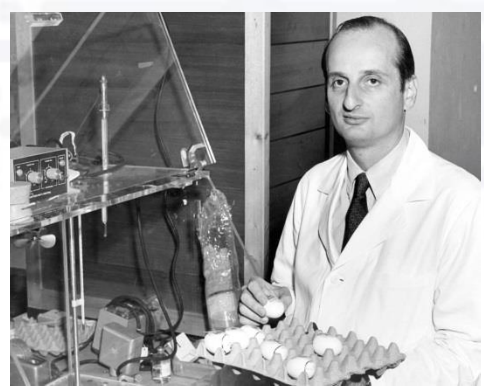
Langer recalls several dedicated, encouraging teachers in grade school, but none he considered truly transformative mentors. He finished high school without knowing what career path he wanted to pursue, but had excelled in math and science. Langer’s father and guidance counselor both encouraged him to become an engineer. Without understanding what the field entailed, Langer matriculated to Cornell University and majored in chemical engineering. He struggled in his classes at first and did not find his major to be particularly interesting, but credits his time at Cornell with sparking another related interest: his love of teaching. Working as a teaching assistant for chemical engineering professor George Scheele in a class on heat and mass transfer, Langer learned that he relished working with students and had a knack for explaining challenging concepts.

Langer had little sense of how he would inhabit his profession when he graduated in 1970. He applied to graduate school and chose to attend the Massachussetts Institute of Technology where he could explore various facets of the engineering field. He began combining his interests with the needs of surrounding communities. At the time, Cambridge maintained the highest high school dropout rate of any city its size nationwide: a staggering 35 percent. Langer started math and science programs at the Group School, an alternative high school for working-class students, and found new and inspiring ways to explain often tedious or intimidating subjects. He created a new chemistry curriculum for the school while simultaneously working on his thesis at MIT, which focused on enzymatic regeneration of adenosine triphosphate. Langer finished his doctorate degree in chemical engineering in 1974.

Process: From Intent to Impact

The early 1970s brought the height of the oil crisis and demand for increased fuel efficiency in the United States. Consequently, chemical engineers commonly sought employment in the oil industry given its many well-paying job opportunities. Langer assumed he would follow that path, but after receiving 20 job offers from oil companies, he began to question whether this was the right direction. His trajectory shifted when he read an advertisement for an assistant professor position at the City College of New York. The job would involve creating a chemistry curriculum, mirroring his work at the high school level during graduate school. He applied for that job and dozens of others like it, but never heard back. Despite some discouragement, Langer found clarity in his drive to land one of these positions. He realized he wanted to devote his career to impacting people's lives for the better — in whatever form that took.

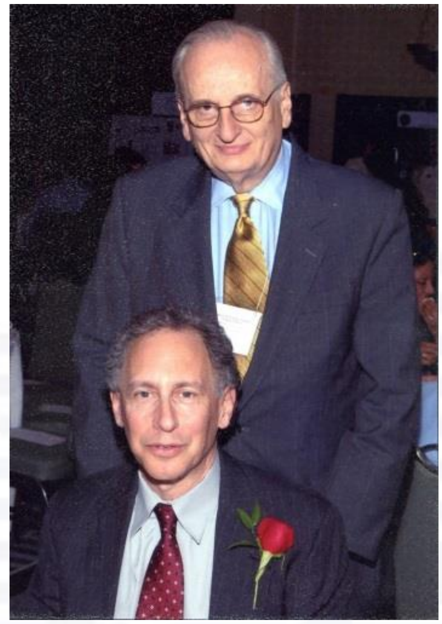
Langer found his calling when a connection at MIT suggested that he contact Judah Folkman, a professor of cell biology and pediatric surgery at Harvard Medical School who would quickly become one of Langer's most profound mentors. Folkman also worked at Boston Children's Hospital and led research on inhibition of tumor angiogenesis (a process through which tumors generate new blood vessels to sustain themselves). Angiogenesis is a normal part of biological growth but, with tumors, also a critical part of their being malignant. Langer began a postdoctoral position in Folkman's lab at Harvard and acclimated to biology, studying ways to isolate and marshal molecules that could inhibit the growth of blood vessels. Many attempts later, he isolated a macromolecule to be used as an angiogenesis inhibitor. Delivery of the inhibitor was quite challenging, however, because the body typically breaks down macromolecules during digestion or obstructs them with body tissues if inhaled or injected. Langer addressed this problem by experimenting with synthetic polymer delivery systems that could resist the body's usual mechanisms for breaking down macromolecules, be implanted next to the tumor, and act as a controlled-release inhibitor of blood vessels.



Folkman in his lab. (Photo/Robert Langer)

By 1976, Langer had completed an unprecedented feat of biology and engineering: he had developed both a technique to plant an angiogenesis inhibitor next to a tumor and, more broadly, a revolutionary method of drug delivery. His controlled-release system, and extensions of it, would be able to safely and effectively deliver not only angiogenesis inhibitors, but also a variety of macromolecules, including DNA, RNA, proteins, peptides and pharmaceuticals through synthetic materials. Many biologists and chemists at the time doubted Langer's methods and objected to his interdisciplinary work. The field of biomedical engineering and the promises it held were just emerging.

Langer pushed forward, crediting Folkman as a foundational role model and his time in Folkman's lab as invaluable to his growth as a scientist and inventor. Folkman provided guidance and inspired persistence. Langer describes him as a visionary who, despite receiving near-constant criticism, remained steadfast in his purpose and believed anything was possible. The sole engineer in Folkman's lab and at the entire hospital, Langer found himself newly exposed to a range of medical conundrums and discovered he could use his background in engineering to solve them.



Folkman, top, with Langer. (Photo/Robert Langer)

Langer's postdoctoral fellowship came to a close, and he began applying to chemical engineering department faculty positions. None accepted his application, often deeming his most recent research in biology as irrelevant to engineering and dismissing the value of his interdisciplinary work. Nevin Scrimshaw, a food scientist and professor at MIT, ultimately hired him to work as a biochemistry professor in the school's nutrition department. In the 1980s, Langer moved to the Departments of Applied Biological Sciences, and also began working in the Harvard-MIT Division of Health Sciences and Technology. In 1998, the Department of Applied Biological Sciences was disbanded and Langer moved to the Department of Chemical Engineering.

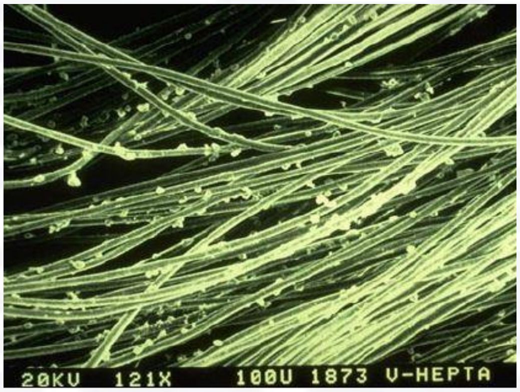
The Gliadel Wafer. (Image/Robert Langer)

Still, in the early years of his career, Langer's work garnered little interest from traditional academic and medical institutions, nor was there any interest from companies either, so Langer began writing patents for his inventions, hoping to bring them to pharmaceutical companies that could fund the development of his discoveries.

Years of difficulty came and went as Langer sought out companies who might commit to investing in his innovations. One of his early patents involved a newer family of degradable polymers that he and his team synthesized, and eventually he found a company that fit the bill. Working closely with neurosurgeon Henry Brem, one of his colleagues in Folkman's lab, Langer developed a polymer wafer to treat brain cancer. This is one of the most lethal types of cancer as its precarious location can make chemotherapy delivery particularly challenging. The wafers they engineered could be stocked with pharmaceuticals and inserted near brain tumors, releasing the treatments they contained in gradual doses. In 1985, Langer partnered with Baltimore-based Nova Pharmaceuticals which licensed one of his patents for delivery of chemotherapy drugs as brain cancer treatment. Twenty years after his first breakthrough in drug delivery, in 1996, the Food and Drug Administration authorized Langer and Brem's Gliadel wafer to treat glioblastoma multiforme which is the deadliest type of brain cancer. It is still used today.

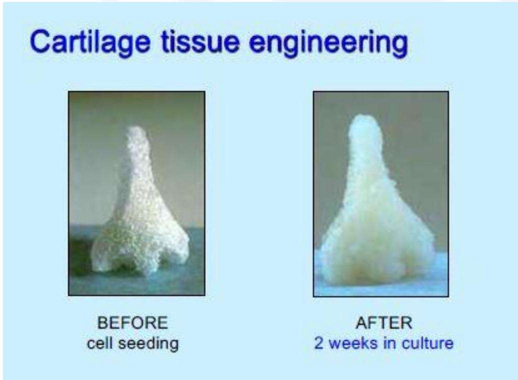
In 1987, Langer founded Enzytech alongside fellow MIT professor Alexander Klibanov. Together, they manufactured a microparticle drug delivery system. This technique has since been applied to ameliorate a range of diseases, from alcoholism to diabetes. The biopharmaceutical company Alkermes acquired Enzytech a few years after its founding and absorbed Langer's drug delivery technologies into therapeutic products to treat schizophrenia, opioid addiction, and other diseases of the central nervous system.

A surgeon and colleague of Langer's at MIT, Jay Vacanti, then inspired him to pursue tissue engineering as another avenue for medical invention capable of enormous impacts. Vacanti, then head of the liver transplant program at Boston Children's Hospital, treated young patients dying of liver failure — but could only save their lives by transplanting livers of deceased organ donors. Langer and Vacanti set out to find a new way to make organs and, accordingly, save lives without relying on organ donations. Collaborating with their students, Langer and Vacanti experimented with creating three-dimensional polymer structures and joining them with cells in order to create a tissue or an organ.



A polymer scaffold. (Image/Robert Langer)

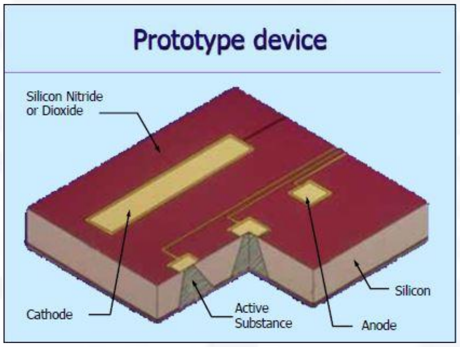
Unable to acquire government funding for this unprecedented work, Langer again looked to commercial sources to support his innovations in regenerative medicine. In 1988, he co-founded Neomorphics, a company that would manufacture biocompatible materials for tissue production. It has since been absorbed into larger companies, and tissue engineering is now applied to a variety of medical contexts to improve lives. Bioengineers can now grow bone, skin, muscle and organs on synthetic polymers, using them to provide artificial skin for burn victims, synthetic organs for those who require transplants, and a range of other medical uses with almost immeasurable impact on quality and duration of



A polymer scaffold before and after cell seeding. (Image/Robert Langer) human life.

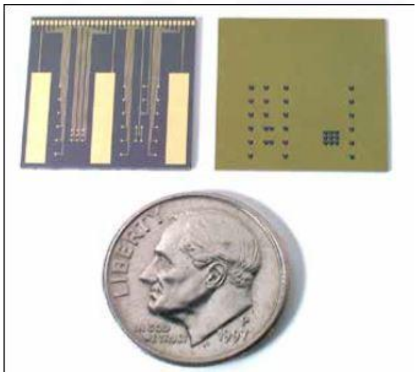
The increasingly clear impacts of Langer's inventions brought more security and broader acceptance to his interdisciplinary approach in both academic and commercial institutions. The 1990s saw the development of a new research and development model for pharmaceuticals, as Langer and his collaborators established a litany of companies to swiftly transform medical discoveries into practical applications for patients in need. He did this, in no small part, by combining his interdisciplinary curiosities with his love of teaching. Langer established his lab at MIT as an invention factory of sorts, encouraging students and postdocs who work there to follow their passions and purpose in order to advance medicine and improve lives. Located in the department of chemical engineering, the Langer Lab has become one of the largest academic biomedical engineering labs in the world. Innovative breakthroughs in his lab often spur startups of their own. Langer not only collaborates with students and postdocs on his own inventions, but also supports their capacity to become innovative scientists and entrepreneurs in their own right.

This style of mentorship, in and of itself, has yielded enormous social and economic impacts. Companies founded by Langer's students have created thousands of jobs, while also generating new treatments for a host of deadly ailments, from cancer to heart disease, as well as COVID-19 vaccines. Hundreds of Langer's former students have followed in his footsteps and continued on in academia, holding professorial positions and training the next generation of inventive scientists around the globe.



Components of a microchip prototype. (Image/Robert Langer)

Langer continues to find new methods for mitigating pressing medical problems. Inspired by microchips used in electronics, in the 1990s he began applying the same fabrication methods to his drug delivery systems. He worked with MIT materials science and engineering professor Michael Cima and then-graduate student John Santini to engineer a microchip with sealable shafts to hold drug treatments. The microchip would be implanted, and the shaft seals removed via remote control to release the pharmaceuticals they contained. Langer and Cima founded MicroCHIPS (now part of Daré Bioscience) to manufacture their invention and, in the decades since, have continued trials to hone in on specific applications. Daré Bioscience, with the support of the Bill and Melinda Gates Foundation, is developing an implantable microchip to deliver a personal fertility control system enabling reversible hormonal contraception.



A dime-sized microchip. (Image/Robert Langer)

Beyond the microchip, Langer and his team have delved into other areas of nanotechnology. They have developed nanoparticle-based therapeutics and diagnostics, nanofiber-based drug deliveries, and technologies centered on synthetic modified messenger RNA. He co-founded ModeRNA Therapeutics, a biotech company that grew into a household name in 2020: Moderna.

A supply of the Moderna COVID-19 vaccine. (Image/Robert Langer)

The COVID-19 pandemic propelled Moderna into vaccine development. Deployed at the end of 2020, the Moderna and Pfizer-BioNTech vaccines were produced in record time, using different technologies than any vaccine in history. Vaccines typically inject a weakened or inactivated virus into the body to trigger an immune response. These COVID-19 vaccines instead provide an mRNA blueprint of the virus that then teaches cells how to make spike proteins, triggering an immune response to protect the body if the live virus invades it. Elements of this revolutionary approach, on track to save millions of lives, trace back to Langer's work with nanoparticles that help to deliver RNA molecules to cells.

These days, Langer is approached with countless potential projects to consider. He remains focused on maximum positive impact on society when deciding which work to take on. Langer consistently maintains a sense of the bigger picture — of what research will eventually help people in transformative, tangible ways, as well as the central role of invention in catalyzing paradigm shifts and profound impacts. Given the depth and reach of his life's work as a pioneer of biomedical engineering, Langer has earned an apt nickname: "The Edison of Medicine."