PROFILE
VIKTOR HAMBURGER

A Lifelong Fascination With the Chick Embryo

Since the early days of developmental biology, Viktor Hamburger has inspired scientists. And at age 100, he isn't done yet

Breakfast is always at 8 a.m. A short walk, 11:30. At 4 p.m., a book—Thomas Mann, perhaps, or Goethe. Such is the carefully choreographed day of Viktor Hamburger. Inside his St. Louis home, Hamburger divides up the hours. Blue eyes dart to his watch again and again, instinctively. There is time for biographies, news, visitors. Yet there are few hours to waste. Hamburger is 100.

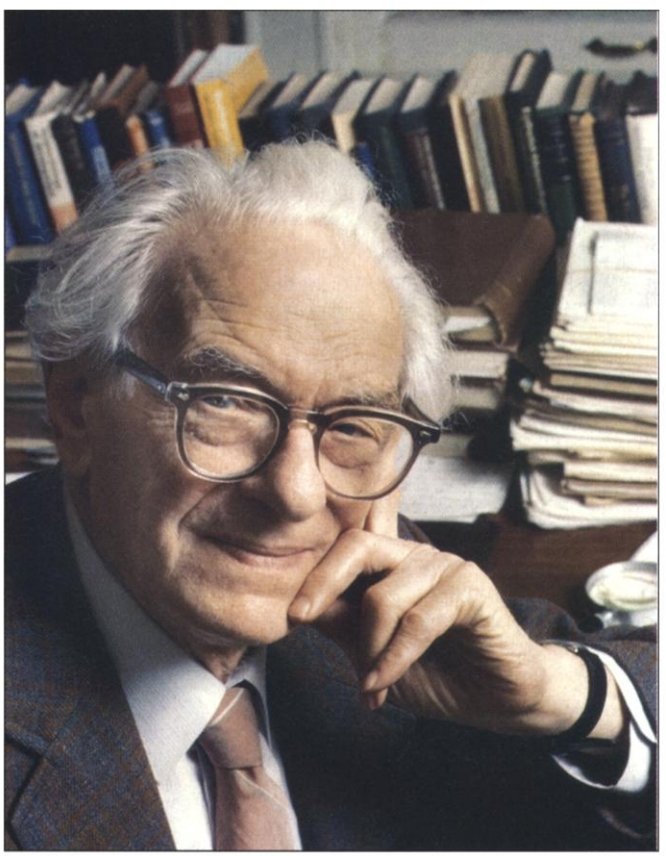
For a lifetime, Hamburger (pronounced "Hawmburger"), an embryologist, has made the moment count. Working with the simplest of tools—small glass needles, a basic microscope, a camera—he has asked, and helped to answer, some of biology's biggest questions. What do nerve cells gain from their targets? Do neurons die naturally? What causes an embryo's earliest movements? Hamburger did not have genomics or the polymerase chain reaction to help him tackle those mysteries. What he had was curiosity, discipline, and a sharp eye. At least three times—at ages 34, 50, and 66—Hamburger turned developmental biology on its head. He also weathered some storms, including rejection by his native country and, at least once, his peers.

In this, Hamburger's 100th year, accolades fall like rain. At the Society for Neuroscience meeting in New Orleans last week, colleagues honored his accomplishments. In October, Washington University in St. Louis hosted the "Viktor Hamburger Centenary Symposium." And just a few months earlier, the Society for Developmental Biology gave him its first lifetime achievement award.

Gerald Fischbach, director of the National Institute of Neurological Disorders and Stroke, calls Hamburger "a true intellect, always wry and warm." Dale Purves, a neuroscientist at Duke University, adds: "Viktor is one of the most influential scientists in neurobiology and development."

Hamburger was a biologist from the beginning. He grew up comfortably in the quiet German town of Landeshut, now part of Poland. His parents, who owned a textile factory, collected art and entertained often. Meanwhile, Hamburger and his two brothers spent plenty of time outdoors, scrambling over rocky hills and wading in ponds. By age 10, Hamburger was scooping up the spring eggs of frogs and salamanders so he could watch the eggs develop in an aquarium.

Still, it was partly luck that he landed in developmental biology. In 1920, Hamburger enrolled in zoology at the University of Freiburg. At the time, renowned embryologist Hans Spemann headed the department. "And so, I had no choice," jokes Hamburger. "I became an embryologist."



Father figure. As head of zoology at Washington University for 25 years, Hamburger cared for generations of chick embryos—and scientists.

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In 1932, Hamburger, then an instructor at Freiburg, met his lifelong lab partner: the chick embryo. He accepted a Rockefeller Fellowship to join Frank Lillie's lab at the University of Chicago, leaving the familiar German hills for the "powerful, impressive, but somewhat scary new scenery" of the United States. At Chicago, Hamburger learned to saw a window in a chick shell and, with glass microneedles, cut and transplant budding limbs on the embryonic chick inside. He had a basic question: In the embryo, how do developing limbs influence the nerve centers that stimulate them?

Answers soon began to emerge. When Hamburger removed a chick embryo's limb bud, the adjacent part of the spinal cord seemed to shrink. But wherever he transplanted an extra limb bud, the nearby spinal tissue appeared to swell. Some growth factor, Hamburger reasoned, must flow from developing peripheral organs, like limbs, back to the nerve cells that innervate them. That insight would eventually lead to two of his major contributions.

But his Chicago adventure was rudely interrupted. In April 1933, a letter arrived from the chancellor at Freiburg informing Hamburger that he was out of a job. Adolf Hitler had come to power—and banned Jews from teaching at universities. Hamburger hurried to Germany to collect his wife and young daughter. His professional fate was secure—he soon accepted one of several offers and moved to Washington University. But the exile took a personal toll. Hamburger lost contact with many family members, including his brothers, for years.

He found solace at the lab bench. "I spent morning and evening—and sometimes hours after dinner—on my research," Hamburger recalls. He also forged an extended family of faculty members. As head of the zoology (later called biology) department for 25 years, he organized weekend outings in the Missouri hills. Researchers would often bring their children along, gathering salamander eggs for embryology classes or identifying flowers in the meadows. "Viktor had a genuine regard for the people he worked with, and we were all a big family," remembers Doris Sloan, one of Hamburger's two daughters and a geologist at the University of California, Berkeley.

Embryonic art

The academic family grew in 1947, when Hamburger invited Italian neurobiologist Rita Levi-Montalcini of the University of Turin to spend a year in his lab. Working together,

they repeated his earlier limb bud experiment—and soon reached a conclusion. Developing limbs, they suggested, pump some trophic factor back to the spinal cord that prevents the nerve cells inside from dying.

Along the way, they noticed something striking: lots of nerve cells dying normally. At the time, researchers assumed that decaying neurons reflected biology gone awry. But Hamburger and Levi-Montalcini discovered that in most areas of the nervous system, many more neurons are born than will ever be needed. Regulated cell death then shapes the nervous system, matching innervation centers to targets, like limbs. That discovery paved the way for today's studies of neurodegenerative disease.

Buoyed by their discovery, the researchers kept on with their original task: finding the trophic factor, or growth protein, that developing tissues must send back to nerve cells. They might have labored for decades. But at just that time, Hamburger says, "a rare gift from Heaven" arrived: a reprint from Elmer Bueker, one of Hamburger's former Washington University students. Bueker had discovered that implanted tumor tissue, like developing tissue, sends some maintenance protein back to neurons—quickly doubling the size of some neural regions in experimental chick embryos.

This easy-to-measure effect was just what the team needed. Within months, Hamburger and Levi-Montalcini had planted mouse tumors in their chick embryos and confirmed that the tumors secreted a molecule boosting nerve cell growth. Soon after, they recruited biochemist Stanley Cohen. In the 1950s, Cohen and Levi-Montalcini finally isolated and identified the mystery molecule: nerve growth factor (NGF). Levi-Montalcini devoted the rest of her career to characterizing NGF, spending more than 2 decades at Washington University.

But Hamburger had little interest in the biochemical minutiae of NGF. Instead, he turned his gaze back to the chick embryo, charting its stages of development like a parent sketching day-by-day portraits of a newborn. His description of normal chick development became one of the most widely cited papers in biology.

Looking back, researchers say Hamburger was uniquely equipped for the job, with a sharp visual sense that came from art as much as science. As a child, he was surrounded by the art—and artistic friends—collected by his parents. And as an adult, Hamburger befriended his own circle of artists and dancers, filling his home with original paintings. "If you confine yourself too much to science, you lose a lot," Hamburger says now. "A lot of scientists become very abstract and forget about the visual world in which they live. The eyes are important." Indeed, it was Hamburger's keen eyes that led to another landmark discovery in the 1960s. He had long noticed the herky-jerky movements of embryonic chicks in their earliest days. A chick's right wing, say, or left foot would randomly quiver in uncoordinated fashion. This early, awkward movement, Hamburger reasoned, must be spontaneous, without any urging from sensory stimuli. But that idea was theoretical heresy: Behavioral psychologists were convinced that, from the beginning, movement is simply a response to sensory stimulation.

A biologist from the beginning. As a child in Germany, Hamburger carted home jars full of salamander eggs *(below)*. Later, as a young scientist, he pried secrets from the shells of chick embryos.

To set the record straight, Hamburger spent the decade of his 60s tracking the chick embryo's movements, from its first bend of the head at 3.5 days. Working with both chicks and rats, he and his colleagues also removed key sensory neurons that normally stimulate the embryos—and found that the embryos still twitched and quivered as before. "In characteristic fashion," says Washington University developmental biologist David Kirk, "Viktor turned this field on its head in just a few years." The research ultimately showed that in vertebrates, at least, adaptive motor behavior is preprogrammed and develops in the growing embryo without any sensory feedback.

Like clockwork

Kirk arrived at Washington University in 1969, when Hamburger had reached retirement age. "He told me he was going to have one more 3-year grant cycle and then be done," Kirk says. "But every time that grant came close to expiring, he'd say, 'I can't quit now.' It just never occurred to him to slow down, as long as there was another question." And there was always another question.

In the 1980s, Hamburger finally left the lab bench—but not the university. He lunched with colleagues at the medical school every Tuesday for almost a decade; when he could no longer drive, he came by cab. "Viktor was like clockwork," recalls Fischbach, who was at Washington University at the time. "He would arrive at the same time every week to eat the same kind of sandwich, wrapped precisely the same way." Hamburger came to talk about science: how it should be done, and why it should be remembered. "He had a wonderful sense of humor," adds Fischbach, "and you never knew when he'd burst out in a guffaw."

That sense of humor was put to the test in 1986, when the Nobel Prize committee stunned biologists by awarding the Nobel Prize in physiology or medicine to the discovery of growth factors, including NGF—but not to Hamburger. Instead, the prize went to Levi-Montalcini and Cohen alone (*Science*, 31 October 1986, p. 543). "This research could not have been done without Viktor," comments Jean Lauder, a developmental biologist at the University of North Carolina, Chapel Hill. His omission from the prize, adds Purves of Duke, was "extremely unfortunate." But Hamburger took the slight in stride. When Lauder phoned him following the announcement, he told her: "That's all right—I don't have time to go to Stockholm right now. I need to finish proofreading the bibliography for my Spe-

mann book."

By that time, Hamburger had launched the last major effort of his career: a series of books and articles reviewing embryology's history, including an English translation of papers by his German mentor, Spemann. Hamburger wrote it all by hand, reliving a century's worth of science in even, steady pen strokes. "I never did own a typewriter," he reflects. "I guess I trusted myself more than a machine." Recounting his achievements in print, he understood all that he had accomplished. "I know what I've contributed," Hamburger says.

And so do his colleagues. Visiting Hamburger last month, Fischbach expected to find him frail or fatigued. Had life finally caught up with the man who helped define it? Yes, Hamburger had lost some hair and some hearing. He moved slowly. And yet there he sat, grinning in his chair, telling stories, gesturing past stacks of books yet to read. This, perhaps, is Hamburger's most personal contribution. "Viktor," says Fischbach, "has taught us how to overcome life's challenges." **–KATHRYN BROWN**

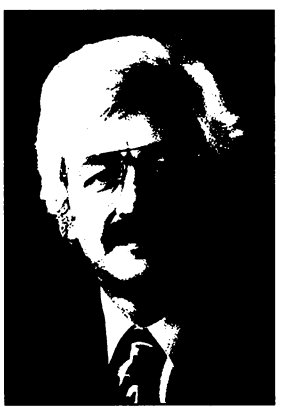
Kathryn Brown is a writer in Alexandria, Virginia.

EUROPEAN SPACE AGENCY

New Science Chief Must Juggle Missions and Politics

Space scientists hope David Southwood can balance ESA's research with its widening interests

Early in his career, David Southwood says, he had to choose whether to apply his training in plasma physics to fusion research or to space. "I didn't have any doubt which way I wanted to go," he says. "I particularly find the solar system fascinating, because I'm interested in why the place we live is the way it is—why the Earth is like it is, why the planets are like they are." That career choice, Southwood says, has landed him "one of the most interesting jobs in Europe, and equally so in space science": Next May, he will take over as the European Space Agency's (ESA's) science director.



Can do. David Southwood says Europe "must be successful" in space.

Southwood, 55—who has spent most of his career at Imperial College in London, where he headed the physics department from 1994 to 1997—will take on a clutch of ambitious projects that ESA hopes to pull together in the coming decade. Two bright stars are European participation in the Next Generation Space Telescope—the Hubble's replacement, which is scheduled for launch in 2008—followed the next year by a half-billion-dollar mission to Mercury called Bepi-Colombo. Others to fill out the constellation include an orbiting gravity wave detector, a satellite for monitoring storms in Earth's magnetosphere, and a mission to determine the positions of stars with high precision (*Science*, 22 September, p. 2019).

But perhaps the most daunting task Southwood faces is to walk a political tightrope: He must balance the aspirations of scientists from ESA's 15 member states with calls to tie the agency more closely to the business and security sectors (see sidebar). "The scientific challenges are great, but I also like the political challenges of getting a European program together," says Southwood. Experts say he's up to the task. Southwood "has a good background of relevant experience," says Britain's Astronomer Royal, Martin Rees. Adds Stamatios Krimigis of the Johns Hopkins University Applied Physics Laboratory, "You know he is a leader when you meet him."

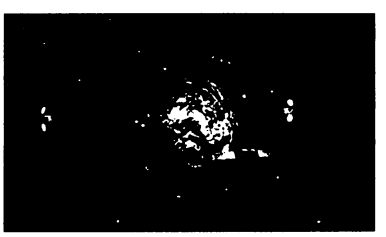
Southwood is no stranger to ESA politics. He has contributed to several ESA projects, including the Cluster mission to explore the interplay of the solar wind and Earth's magnetic field, and the SOHO mission to study solar storms. And he led the team that built a magnetometer for NASA's Cassini mission, now on its way to Saturn. "I became a theorist and then realized it was more fun working with experiments as well," he says, "and ultimately I became an experimentalist by leading the building of instruments."

Perhaps crucial to Southwood's appointment was the time he spent earning his management stripes in ESA's Earth Sciences Division from 1997 until last April. South-

Getting More Out of Space

Space is too important to Europe to be left to scientists alone, according to a report on the future of the European Space Agency (ESA) released last week. The report (available at www.esa.int) concludes that better coordination between ESA and the business and defense sectors is essential to Europe's development. "We see the need to integrate space efforts, or space activities, with European political and other activities much more clearly than has been the case in the past," says former Swedish Prime Minister Carl Bildt, who led the study.

The report refers to the $2.5 billion Galileo project (image, right)—a satellite navigation system intended to rival the U.S.'s Global Positioning System (GPS) and Russia's GLONASS system—as a case in point. The first of Galileo's 30 satellites is slated for launch in 2004. For Europe, Galileo offers self-sufficiency in global navigation and a break from foreign military hegemony. Telecommunications and other commercial opportunities seeded by this joint ESA–European Union project are expected to be huge. Galileo "will give strategic autonomy to Europe in a sector which is vital for the evolution of the European economy," says ESA Director-General Antonio Rodotà. But the report points out that at present there is no mechanism to decide how to limit access to Galileo in times of conflict. Other unsettled questions that ESA should get involved in include how to guarantee a return on private-sector investments and how to organize a single public entity for operating it.



The report from the "Three Wise Men"—the other two are Jean Peyrelevade, president of the Paris-based Credit Lyonnais bank, and Lothar Späth, CEO of JENOPTIK AG, an optoelectronics firm in Jena, Germany—offers few surprises, says ESA science director–designate David Southwood. "The aim, I am sure, is to try to wake European policy-makers and politicians up to the fact that space capability and space-derived information provide part of a modern developed society's infrastructure," he says. His only reservation is that in broadening ESA's horizons, science could lose out. "Space science cannot be ignored or downgraded," he says, "as one broadens the perception of space's use." **–A.W.**

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