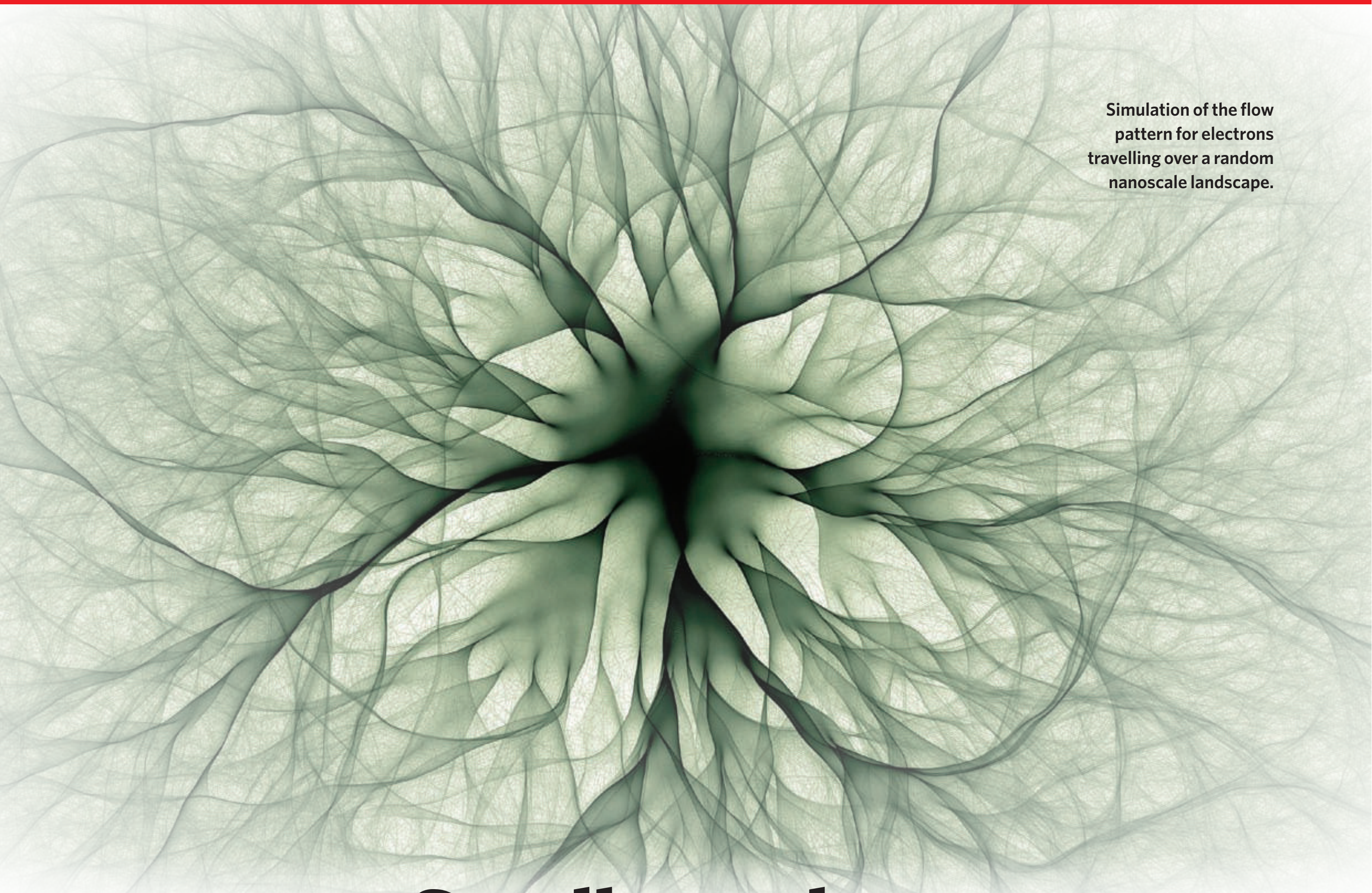


Simulation of the flow pattern for electrons travelling over a random nanoscale landscape.

E. J. HELLER, HARVARD UNIV.

Small wonders

The US National Nanotechnology Initiative has spent billions of dollars on submicroscopic science in its first 10 years. **Corie Lok** finds out where the money went and what the initiative plans to do next.

Richard Smalley's cheeks were gaunt and his hair was nearly gone when he testified before the US House of Representatives in June 1999. The Nobel laureate chemist had been diagnosed with non-Hodgkin's lymphoma a few months earlier, chemotherapy was taking its toll, and the journey from Rice University in Houston, Texas, had been exhausting. But none of that dimmed his obvious passion for a subject that his listeners found both mystifying and enthralling: nanotechnology.

"We are about to be able to build things that work on the smallest possible length scales, atom by atom, with the ultimate level of finesse," said Smalley, whose prizewinning co-discovery of spherical carbon buckminsterfullerene molecules, or 'buckyballs', in 1985 had helped to trigger a frenzy of research into such possibilities. As an example, Smalley told the legislators about his own laboratory's work with carbon nanotubes, which had been discovered in 1991. These hollow cylinders of carbon, only a few nanometres across, not only promised to conduct electricity better than copper, but also had the potential to produce fibres 100 times stronger than steel at one-sixth of the weight. Smalley also predicted that the "very blunt tool" of chemotherapy that had ravaged his own body would be obsolete within 20 years, because scientists would engineer nanoscale drugs that were "essentially cancer-seeking missiles" able to target mutant cells with minimal side effects.

"I may not live to see it," he said, "but, with your help, I am confident it will happen. Cancer, at least the type that I have, will be a thing of the past."

For all these reasons, Smalley concluded, the US government should back a recently proposed National Nanotechnology Initiative (NNI): a multi-agency funding effort that would catalyse these breakthroughs and more by realizing the systematic control of matter down to the scale of atoms.

"As chemists, we were dying to have the community take notice of chemistry and the importance of it."

It was a message that Washington was ready to hear. US President Bill Clinton formally announced the initiative in 2000, with bipartisan support from Congress. The initiative has faced some criticism in the decade since — most notably for its slowness to address environmental, health and safety concerns about nanomaterials. But it has also created more than 70 nano-related academic or government centres across the United States; catalysed new interdisciplinary collaborations between physical, biomedical and social scientists; and fostered a whole system of investors, analysts and start-up companies devoted to commercializing laboratory discoveries. Along the way, the NNI has seen its budget increase steadily (see 'The NNI funding surge'), to the point at which its cumulative funding of more than US$12 billion places it among the largest US civilian technology investments since the

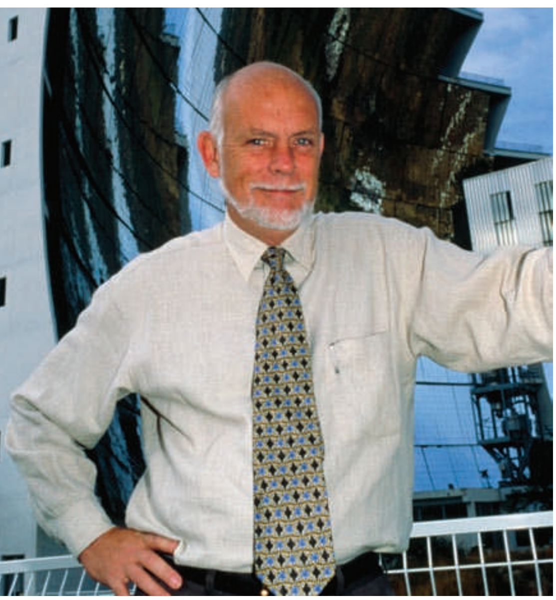
Apollo Moon-landing programme.

As such, the NNI story could provide a useful case study for newer research efforts into fields such as synthetic biology, renewable energy or adaptation to climate change. These are the kinds of areas in which the science, applications, governance and public perception will have to be coordinated across several agencies, points out David Rejeski, director of the Science and Technology Innovation Program at the Woodrow Wilson International Center for Scholars in Washington DC. That is precisely what the NNI was designed to do, he says. "So I would argue that, for emerging areas like this, the concept of the NNI is a good one."

A knack for persuasion

The most obvious lesson of the NNI is that success depends crucially on timing. The initiative happened when it did in part because the science was already moving fast in the late 1990s, thanks to discoveries during the previous decade such as buckyballs, nanotubes and the development of the atomic force microscope, which can image any surface with nanometre-level resolution (see 'The road to the NNI'). A uniquely favourable political climate also helped. The US economy was booming, particularly in the high-tech sector. The government was enjoying a budget surplus. And the Clinton administration, nearing the end of its term in office, was eager to end on a positive note.

But timing alone isn't always enough. Any major initiative also needs its champions: well-placed visionaries with a knack for communication and persuasion. Smalley was one. Sadly, his June 1999 testimony was all too prescient: he did not live to see the targeted nanoparticle-based delivery of cancer drugs (although several are now in development). Given only a limited reprieve by chemotherapy, he died on 28 October 2005. But until then, Smalley was a tireless advocate for nanotechnology in general and the NNI in particular.



Nobel laureate Richard Smalley was a leading advocate of the power of nanotechnology.

P. DUMAS/EURELIOS/SPL

Another champion is Mihail Roco, an engineer who had studied nanoscale particle interactions at the University of Kentucky in Lexington for 10 years before becoming a programme manager at the US National Science Foundation (NSF) in 1990. By 1996, he had come to believe that nanotechnology was not just a collection of individual research projects. He saw it as a new, unified discipline with the potential to revolutionize wide areas of science and industry, from health and agriculture to space, information technology, manufacturing and energy. He was also convinced that a major research investment was needed to give the nascent field momentum.

Roco, an affable man with thick red hair, an even thicker Romanian accent, and an infectious enthusiasm for what he calls 'nano', says people regularly warned him against hyperbole as he tried to get the initiative off the ground. But you have to have the courage to articulate your vision, he says. "You have to promise, then you have to fight to realize it."

He found plenty of others thinking along the same lines: by the end of the decade, Roco and like-minded officials at seven other agencies were hammering out a proposal for the NNI, and bringing in leading scientists to help. It was Roco who recommended Smalley as a panellist for the June 1999 congressional hearing.

Political support was also beginning to build from within the White House. Thomas Kalil, a lead adviser on technology issues for Clinton's National Economic Council, saw the potential of nanotechnology to yield major economic payoffs in many industries, including electronics. In March 1999, he helped to get Roco a 10-minute slot to pitch the NNI idea to key White House officials who were considering what to include in the president's 2001 budget proposal.

Neal Lane, a physicist at Rice who became Clinton's chief science adviser in 1998 after a stint as NSF director, was familiar with Smalley's work and had already given his own testimony to Congress about nanotechnology's potential. In December 1999, Lane encouraged the President's Council of Advisors on Science and Technology, of which he was co-chair, to formally recommend that Clinton include the NNI in his budget.

"Nano was a good story," recalls Lane. "It was real and exciting science, and you had a story that you could sell to a congressman or congresswoman that they could then take to their constituents."

Mihail Roco, a major champion of the National Nanotechnology Initiative for the past decade, is now aiming to reignite the nanoscience field.

NSF

They bought it — and so did Clinton. On 21 January 2000, in a speech at the California Institute of Technology (Caltech) in Pasadena, the president announced that his 2001 budget request would include $500 million for the NNI. "Just imagine," he said, "materials with ten times the strength of steel and only a fraction of the weight; shrinking all the information at the Library of Congress into a device the size of a sugar cube."

Small is effective

James Heath, a Caltech chemist, still remembers his excitement when he first found out about the NNI's creation. "A couple of years earlier, I couldn't even convince people that nano was a real field," says Heath, who had been one of Smalley's students at Rice during the buckyball discovery. "Now it is a big national initiative. Boy, we had better deliver something," Heath recalls thinking.

And they did. Roco, who chaired the NNI's interagency coordinating committee until 2006 and is now the NSF's senior adviser for nanotechnology, notes that the number of US nano-related publications and patent applications increased by an average of 17% and 30%, respectively, every year from 2000 onwards. He can rattle off any number of favourites. In 2006, for example, researchers at Rice tested specially tailored iron nanoparticles for the removal of arsenic from drinking water[1]. In 2008, researchers at the University of California, Berkeley, reported a three-dimensional 'metamaterial' that could bend light in the opposite

THE ROAD TO THE NNI

1959

Richard Feynman, a famed US physicist at the California Institute of Technology, gives a speech envisioning the power of controlling things on a small scale.

1974

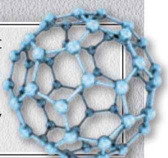
Norio Taniguchi at Tokyo Science University first coins the term 'nanotechnology'.

1981

Gerd Binnig and Heinrich Rohrer at IBM Research in Zurich, Switzerland, invent the scanning tunnelling microscope, allowing researchers to 'see' surfaces at the atomic level.

1985

Richard Smalley and Robert Curl at Rice University in Texas and Harry Kroto at the University of Sussex, UK, discover buckminsterfullerene, popularly known as the buckyball.



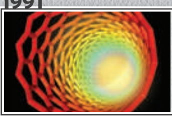
1986

Christoph Gerber at IBM in San Jose, California, and Calvin Quate and Binnig at Stanford University in California invent the atomic force microscope, which not only images surfaces at the atomic level, but can also manipulate individual atoms.

1990

Donald Eigler and Erhard Schweizer at IBM arrange individual xenon atoms to form the letters IBM.

1991



Sumio Iijima at NEC in Japan discovers carbon nanotubes.

1991

The US National Science Foundation launches its first programme devoted to nanotechnology.

1998

A working group of science programme managers from eight US government funding agencies is formed to devise an agenda for nanoscience and technology research.

1999

Discussions of a US national initiative on nanotechnology heat up in the White House and Congress.

2000

The National Nanotechnology Initiative (NNI) is formed.

FROM TOP: J. MUNROE/HULTON ARCHIVE/GETTY IMAGES; LAGUNA DESIGN/SPL; C. DANILOFF; T. SLOAN/AFP/GETTY IMAGES

direction to other natural materials[2,3] — a process known as negative refraction, which could have uses in optical imaging and computing. And last month, a group at Harvard University in Cambridge, Massachusetts, showed that a nanoscale transistor inserted into a living heart cell could measure its electrical activity[4]. The NNI website (www.nano.gov) lists hundreds of other examples, from the creation of nanostructured battery materials for ultra-fast charging and discharging, to the development of nanostructures that aid the regeneration of nerves after spinal-cord injuries.

But many participants argue that counting papers and patents is not the best way to measure the initiative's real impact. By 1999, after all, several science and technology fields were already moving towards the nanoscale, whether in materials research, semiconductor fabrication or the study of molecular machinery inside the cell — much of the ensuing research may have been funded anyway. "What is due to the NNI and what is due to simply maturing of the field? It is very hard to tell," says Phaedon Avouris, manager of the nanoscale science and engineering group at IBM's T. J. Watson Research Center in Yorktown Heights, New York.

> **"What is due to the NNI and what is due to simply maturing of the field?"**

Many observers say that the initiative's most important pay-off has been psychological. Simply by having a name and being recognized as an 'initiative', nanotechnology became a priority programme that has been easier to promote and protect at budget time, says Altaf Carim, a programme manager with the US Department of Energy and a current member of the NNI coordinating committee.

Similarly, the NNI's government stamp of approval legitimized the nanotechnology field and made it look like a less costly and risky investment for venture capitalists. "The NNI was the spark," says Josh Wolfe, managing partner of the venture-capital firm Lux Capital Management in New York City. Industry acceptance of nanotechnology "was faster than we predicted", agrees Roco — to the point at which an industry association, the NanoBusiness Alliance, based in Skokie, Illinois, had formed by late 2001.

That industry interest, in turn, helped the NNI to survive and flourish through the transition from the Democratic Clinton administration to the Republican administration of President George W. Bush. The initiative got $464 million its first year, and its annual budget has steadily expanded to some $1.7 billion today (plus a one-off addition of $500 million in 2009 from the US stimulus bill; see 'The NNI funding surge'). That money is now spread across 25 federal agencies — albeit with the vast majority of it going to just five: the NSF, the National Institutes of Health, the Department of Energy, the Department of Defense and the National Institute of Standards and Technology — and supports the 70-odd nanotechnology research centres that perform much of the NNI's work. Getting all of these agencies to coordinate their nanotech research activities has been one of the NNI's key successes, says Clayton Teague, director of the NNI's coordination office in Arlington, Virginia. "Bringing this huge breadth of expertise from all the different departments together to see how they can move the field of nanotechnology forward is quite powerful."

This involvement from so many different agencies has also helped to boost the awareness of nanotechnology outside the physical-sciences community. The US National Cancer Institute, for example, has funded eight Centres of Cancer Nanotechnology Excellence, which have brought together chemists, materials scientists and biologists to apply nanotechnology to cancer therapeutics and diagnostics. "What the NNI has done really well is expand the view within nano of what it means to be interdisciplinary. It is not just between scientists and engineers, but also social scientists, philosophers and economists," says Kevin Ausman, a chemist at Oklahoma State University in Stillwater. As another example, the NSF is funding two 'nanotechnology in society' centres devoted to issues such as public risk perception and the media's coverage of nanotechnology.

Bottom-up science

Still, the same decentralization that has enabled the NNI to foster interdisciplinary research has also created a management challenge. There are various coordination mechanisms, including Teague's office and the interagency council once chaired by Roco. But there is no central body that controls the NNI budget, which is a compilation of the individual budgetary decisions made by the 25 member agencies. So major decisions for the NNI require the agreement of all 25.

Such 'bottom-up' science initiatives tend to be more successful in fostering collaboration and generating knowledge, says Craig Boardman, a science-policy expert at Ohio State University in Columbus, who has studied the NNI and other initiatives. But Andrew Maynard, director of the Risk Science Center at the University of Michigan in Ann Arbor, points to the obvious drawback: "It is hard to measure the success of the initiative and actually hold someone accountable for what it has or hasn't done."

Nowhere has this been felt more strongly than in what many regard as the NNI's biggest setback: its slow response to considering nanotechnology's environmental, health and safety (EHS) risks. Unfortunately, those risks are potentially serious: not only are many nanoparticles small enough to pass through or puncture cell membranes, but they tend to be far more chemically reactive than the equivalent bulk material — in ways that are not always well understood. From the beginning, says Maynard, "I had a sense that the people driving the process really didn't fully understand how you begin to approach risk and uncertainty with new products. So there was a certain degree of naivety there."

The NNI didn't begin to fund EHS research in a concerted way until 2005. And even then, many of its efforts continued to be poorly coordinated — much to the frustration of EHS researchers such as Ausman. Because nanomaterials span the periodic table and have such a wide range of properties, he says, it is difficult for researchers to prioritize which ones to study. "There needs to be a list of recommended nanomaterials for basic science research on EHS issues," says Ausman, rather than having what he calls the "scattershot" approach to selecting materials.

A watershed came in December 2008, when a National Research Council review committee blasted an EHS research strategy that the initiative had released earlier that year: "The document ... lacks input from a diverse stakeholder group, and it lacks essential elements, such as a vision and a clear set of objectives, a comprehensive assessment of the state of the science."

In response, the NNI has held a series of four workshops to gather outsider input, with the aim of releasing a revamped EHS research strategy by the end of 2010, along with its new overall strategic plan. And the NNI's funding for EHS research has grown to around $92 million this year, roughly 5% of the total.

Overall, says Günter Oberdörster, a toxicologist at the University of Rochester in New York and a member of the 2008 review committee, the NNI now seems to be on the right track with EHS issues. "It is laudable that the NNI has taken them seriously," he says.

Hottest prefix in science

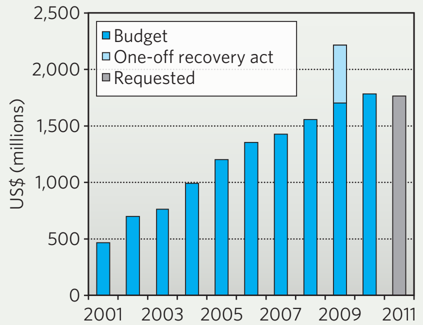
Given all the attention being paid to nanotechnology, a certain amount of hype was inevitable. To the extent that these things can be measured, it began at the birth of the NNI and peaked in the middle of the decade. Researchers who perhaps hadn't previously called their work nanotechnology looked for ways to relabel their research to take advantage of the new funding. The media published optimistic stories. Research-intensive technology companies started up nanotech research and development teams. Students enrolled in specialized university courses and degree programmes. Venture capitalists called up nanotechnology companies begging to invest in them. Nanotechnology journals, websites and conferences proliferated. 'Nano' soon became the hottest prefix in science.

Many scientists found the craze a cause for concern. If promises are made that don't deliver, says Mildred Dresselhaus, a materials scientist who studies carbon nanotubes and bismuth nanowires at the Massachusetts Institute of Technology in Cambridge, "we lose our credibility".

Others saw the hype as a fair price to pay for the much-needed attention the physical sciences were finally receiving because of the NNI. "As chemists, we were dying to have the community take notice of chemistry and the importance of it," says James Tour, a synthetic organic chemist at Rice. After the creation of the NNI, he says, he began receiving e-mails from high-school students wanting to become nanotechnologists. "I would rather have over-promising than underpromising," he says, "because then you get young people excited."

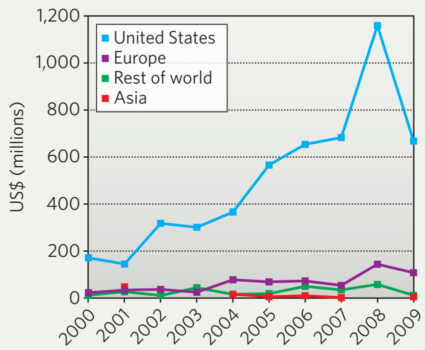
THE NNI FUNDING SURGE...

Support for the initiative continued through Democratic and Republican administrations alike.



...INSPIRED A VENTURE-CAPITAL SURGE

Until the 2009 downturn, government support helped to make nanotech investments more attractive.



SOURCE: NNI (TOP); LUX RESEARCH (BOTTOM)

The applications decade

Just as inevitably, the hype and excitement surrounding nanotechnology have waned as the newness has worn off — which illustrates a final lesson from the NNI: these things take time. If Smalley was right about a 20-year timescale for pay-offs, then the NNI is only halfway there.

That is Roco's view. The initiative's first decade was mostly about basic science and laying the foundations, he says. But he has also seen a definite maturing of the field, as researchers have gone from developing simple nanostructures using trial-and-error methods to the deliberate design of nanosystems that can have more 'active' roles, such as delivering drugs to specific cells in the body. As passionate about 'nano' as ever, Roco expects the next ten years to be the decade of applications.

To flesh out what that could mean, Roco is at it again, tirelessly brainstorming with scientists from around the world to formulate a nanotechnology vision for 2020. He is preparing to present that vision at the NSF later this month.

The NNI's latest annual report also stresses applications. It lays out three 'signature initiatives' for 2011: applications for solar energy, nanoelectronics for 2020 and beyond, and sustainable nanomanufacturing. The need to turn scientific findings into commercialized products is also a key theme in the latest assessment from the President's Council of Advisors on Science and Technology, as well as in legislation pending in the US Senate to continue the NNI's funding.

That need is considerably more urgent than it was in 2000. Although support for nanotechnology is still strong in Washington, the shift in emphasis towards practical applications reflects the changing mood of the country. The optimism of the late 1990s has now been largely replaced by a sense of national self-doubt, fed by challenges in the economy, jobs, energy, climate change, health care and national security. Nanotechnology promises to help in every case, but so far these are still just promises. "Success will depend on the commercialization of nanotechnology," says Avouris. ■

Corie Lok is an editor for *Nature* in Boston, Massachusetts.

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