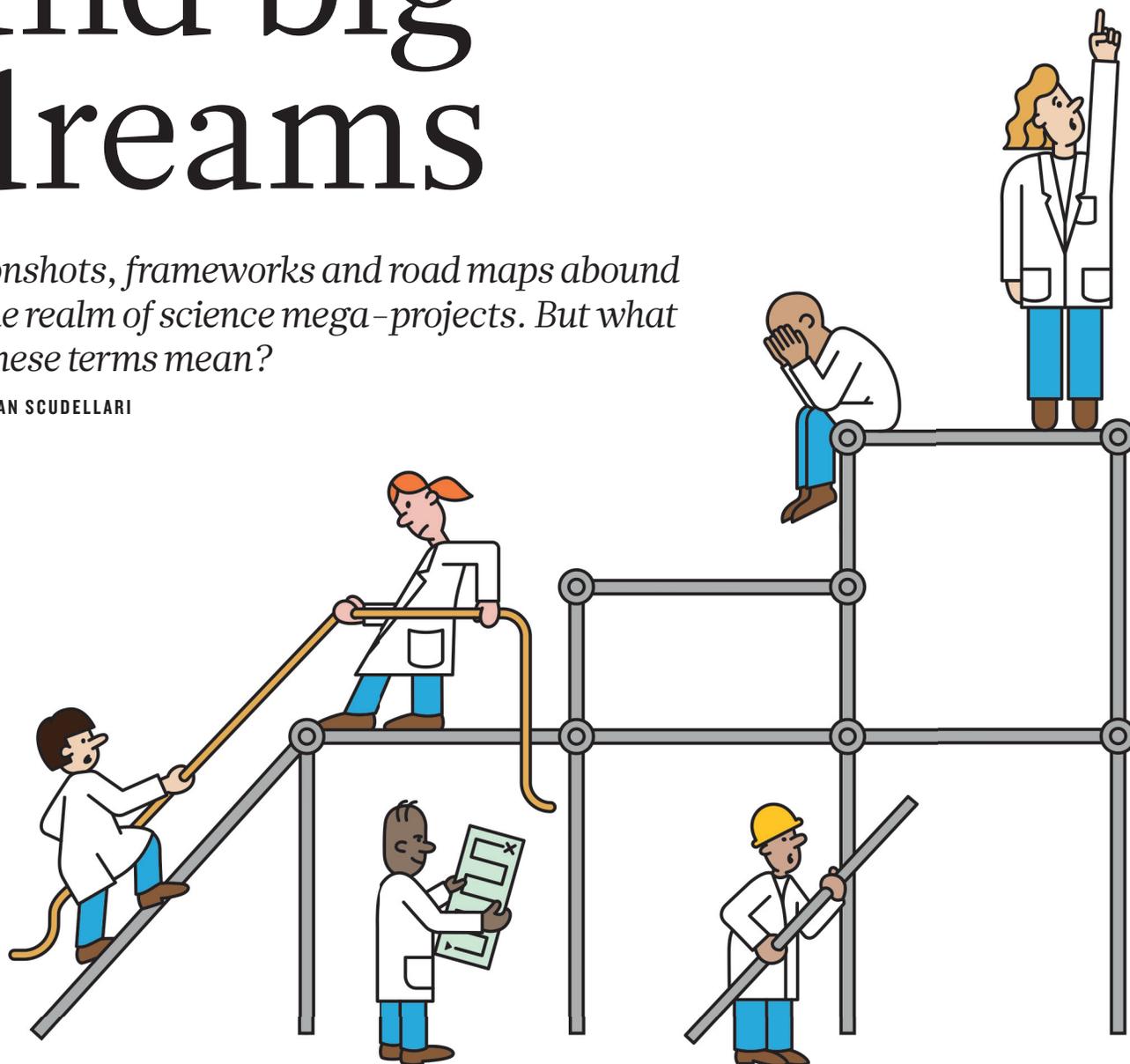


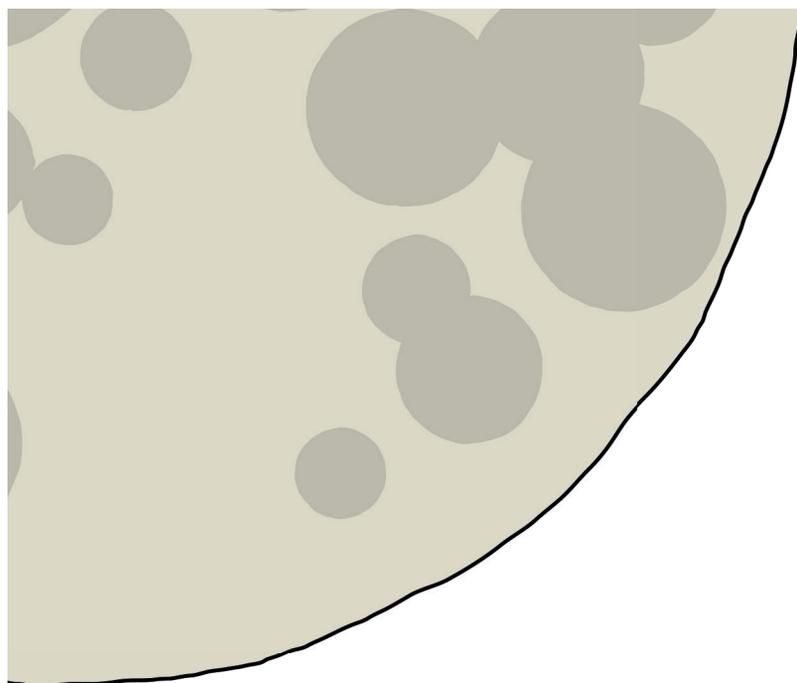
Buzzwords and big dreams

Moonshots, frameworks and road maps abound in the realm of science mega-projects. But what do these terms mean?

BY MEGAN SCUDELLARI



CHRIS RYAN/NATURE



On 12 January 2016, nearly half a century after humans first set foot on the lunar surface, a president and a billionaire each announced a new moonshot. In Washington DC, US President Barack Obama described the establishment of a government-led Cancer Moonshot to accelerate oncology research. Across the country at a press conference in California, billionaire entrepreneur Patrick Soon-Shiong announced Cancer MoonShot 2020, an industry-academia collaboration.

If the name sounded familiar at the time, that might be because the University of Texas's MD Anderson Cancer Center had established its own Moon Shots Program back in September 2012. (It has since filed a lawsuit alleging trademark infringement by Soon-Shiong and his businesses.)

Shooting for the metaphorical moon, it turns out, is a popular pastime in science-planning circles. "I've been in Washington for a very long time, and I feel like every time I turn around, somebody says we need a new moonshot," says Kathy Hudson, who has served as deputy director for science, outreach and policy at the US National Institutes of Health (NIH) in Bethesda, Maryland.

'Moonshot', 'road map', 'initiative' and other science-planning buzzwords have meaning, yet even some of the people who choose these terms have trouble defining them precisely. The terms might seem interchangeable, but close examination reveals a subtle hierarchy in their intentions and goals. Moonshots, for example, focus on achievable, but lofty, engineering problems. Road maps and decadal surveys (see 'Alternate aliases') lay out milestones and timelines or set priorities for a field. That said, many planning projects masquerade as one title while acting as another.

Strategic plans that bear these lofty names often tout big price tags and encourage collaborative undertakings. In the United States, for instance, science-funding agencies are hoping to start or continue many 'big science' efforts in 2017. The National Science Foundation has requested US\$74 million for the Obama administration's BRAIN (Brain Research through Advancing Innovation and Neurotechnologies) Initiative and \$33 million to the National Strategic Computing Initiative. The NIH hopes to continue funding the BRAIN Initiative, as well as the Precision Medicine Initiative and possibly the Cancer Moonshot. And the Department of Energy's Office of Science requested \$818 million for high-energy-physics projects, including the Large Hadron Collider, and \$398 million for continued contribution to the large, international ITER

fusion project. NASA, of course, takes the cake with literal moonshots, including a \$1.5-billion planetary exploration proposal involving a mission to Jupiter's moon Europa and continued missions to Mars.

The value of such projects is continually debated. On one hand, many argue that the coalescence of resources, organization and long-term goals that comes with large programmes is crucial to science advancement in an era of increasing data and complexity. "There are some problems that demand marshalling resources," says Thom Mason, director of the Oak Ridge National Laboratory in Tennessee, which hosts numerous shared research facilities and participates in ITER. "Oftentimes, those big initiatives are really defining for the whole field."

Big thinking and big actions have often led to success. But critics argue that buzzword projects add unnecessary layers of bureaucracy and overhead costs to doing science, reduce creativity and funding stability and often lack the basic science necessary to succeed.

Science, by its nature, needs stability, says Arturo Casadevall, a microbiologist at the Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland, and editor-in-chief of *mBio*. And big projects, especially if they are politically driven, can threaten that. "We all worry that because of need or political expediency, sometimes a lot of money is spent on a specific area, and a field expands disproportionately to what it can handle, and then the money is pulled out."

To help understand the ecology of science-planning efforts, here is a field guide to the various terms that thrive there (see 'What to call your science mega-project').

moonshot

n. /'mu:nʃɒt/ The launching of a spacecraft to the moon

That's the most literal definition according to the *Oxford English Dictionary*, and 'moonshot' is often attributed to NASA's Apollo programme, which first landed people on the Moon in 1969. There is evidence, however, that it was used figuratively to refer to a lofty, but not impossible, goal way back in 1891, when a Minnesota newspaper column referred to keeping within "moon shot" of demand for housing. Others trace the concept of shooting for the Moon to Jules Verne's 1865 science-fiction novel, *From the Earth to the Moon*.

What is clear, however, is that the moonshot has become one of the most inspiring things in US science. Today, scientists use the term to describe ambitious engineering projects. "The Human Genome Project was like the NASA moonshot, because there was a very specific goal — to sequence the genome — and because the technology to do it did not

exist when the project began," says biologist Barbara Wold at the California Institute of Technology in Pasadena, who served as an adviser for the project. The Manhattan Project to develop the first nuclear weapons has also been compared to the NASA moonshot. But, says Wold, the description isn't appropriate "for large-scale efforts that simply apply existing technologies

to programmes with diffuse or unbounded goals".

Apollo 11, the Manhattan Project and the Human Genome Project were successful because they had national interest and politicians supporting them, plus a solid grasp on the basic science needed to achieve those goals, be it Newtonian physics or nuclear fission. But some worry that contemporary cancer moonshot projects tend to lack the basic-science component. "Large research projects succeed once you have done the basic science," says Casadevall. "The question with the cancer moonshot is whether the basic science is there."

Elizabeth Jaffee, director of the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University School of Medicine says that the science is "ripe" for the \$1-billion Cancer Moonshot announced by

"You've got to deliver a benefit to society that's commensurate with that investment."

ALTERNATE ALIASES

Initiatives by other names

Not all science buzzwords pertain to mega-projects led by governments. In many cases, scientific societies, small groups and even individual scientists lead grass-roots efforts to plan a project or bring attention to a field.

DECADAL SURVEY OR STRATEGY A favourite of the US National Academies of Science, Engineering, and Medicine, a ‘decadal survey’ is an exercise to prioritize where a field should invest its money, separate from the influence of funding agencies. The National Academies has outlined scientific priorities for space-based Earth science for 2017–27, and has been producing a decadal survey for astronomy and astrophysics every ten years since 1964.

BLUEPRINT This type of plan or diagram is often visual, but has taken on new meaning as another word for initiative. The 2009 UK Life Sciences Blueprint was designed to speed new medicines to the UK market. In the same year, the US National Institutes of Health (NIH) established a grant programme called the Blueprint Neurotherapeutics Network, part of the larger NIH Blueprint for Neuroscience Research.

PROBLEMS In 1900, German mathematician David Hilbert published a list of 23 unsolved problems, which came to significant

attention and importance in the mathematics community, generating decades of work. In 2000, the Clay Mathematics Institute attempted to create a new version of Hilbert’s problems with a list of seven Millennium Prize Problems. And it’s not the only one to do this. DARPA — the US Defense Advanced Research Projects Agency — published a list of 23 problems in 2008.

RESEARCH STRATEGY A research strategy sets out priorities over a short period of time. In 2014, Cancer Research UK set out a five-year research strategy, and encouraged funding applicants to state how their research relates to the strategy. Not to be outdone, this year the Institute of Cancer Research in London laid out its own five-year research strategy focusing on confronting the ability of cancer to adapt and evolve.

CONSENSUS STATEMENT Often developed immediately after a consensus conference, this statement is typically a summary of non-government, non-advocate expert opinions. Starting in 1977, the NIH hosted a Consensus Development Program that produced more than 160 consensus statements on medical issues. The programme was retired in 2013 when other organizations, such as the Cochrane Collaboration and the Institute of Medicine, took over the task of providing impartial, evidence-based reviews. **M.S.**

Obama in 2016. “We’ve made a lot of progress in the basic sciences and cancer biology and technologies, so now we need to transform these discoveries into rational therapies to not only treat, but intercept, cancer.”

Last September, the Cancer Moonshot’s 28-member Blue Ribbon Panel, which Jaffe co-chaired, identified ten research opportunities that are ready to move forward in the next five years — areas in which a concentrated investment could make a difference. Those opportunities include projects that promote early screening for families at genetic risk of colon cancer, and creating an online network of databases of patient tumour profiles — goals that are well within reach. “It’s not rocket science,” she says.

Nevertheless, the terminology used to describe the project could be misconstrued, says Jarle Breivik, who studies cancer and science communication at the University of Oslo. And that might mislead the public. “I’m concerned about this belief that if we just put enough money into cancer research and chemotherapy, then we will get rid of the problem,” he says.

The public can be forgiven for thinking that the ‘moon’ in the Cancer Moonshot is a cure. In his address last January, Obama said: “Let’s make America the country that cures cancer once and for all.” In reality, the government’s goal is to complete a decade’s worth of progress in five years — not to cure the disease. “In retrospect, ‘moonshot’ was probably not the best name for it,” admits Jaffe. A better, though less sexy, name might have been the Cancer Road Map.

road map

n. /ˈrəʊd ˌmɑːp/ A map that shows the roads of a country or area

Europeans love ‘road maps’. There’s the European Roadmap for Astroparticle Physics — published in 2008 and updated three times since. Then there’s the European Astrobiology Roadmap and the European Hematology Association’s Roadmap for European Hematology Research — a beast of a document that was compiled over 2 years by 300 contributors, and is broken into 9 sections spanning 60 disease groups.

The European Commission, the executive arm of the European Union, has published 384 road maps for various government programmes since 2015 alone.

Road maps are strategic plans or schedules that propose short- and long-term milestones. The 1998 International Technology Roadmap for Semiconductors, for example, transformed Moore’s law from an observation about the speed of development of integrated circuits into an industry-wide research and development plan for how to improve microprocessors.

Road maps came into fashion in Europe in the early 2000s, after they were used widely by the US Department of Energy and by NASA, says Stefano Fontana, who works at the European Institute of Innovation and Technology in Budapest. One of the US efforts that caught attention in Europe was NASA’s 2004 Vision for Space Exploration, which laid out an agenda encompassing returning to the Moon, completing the International Space Station and continuing robotic exploration of Mars.

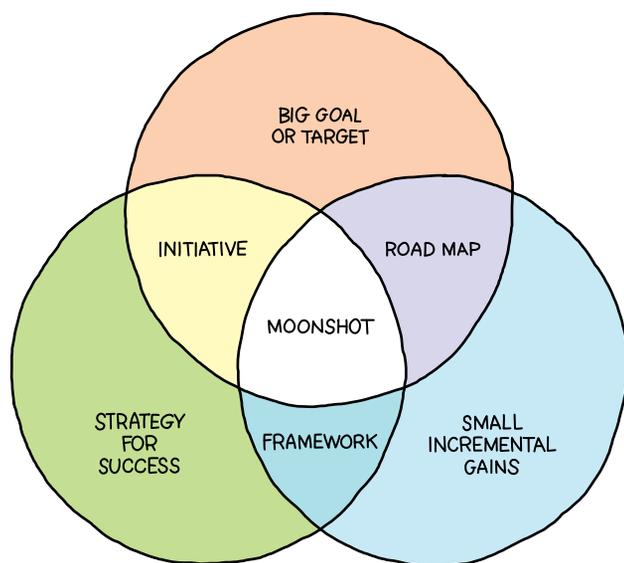
Fontana included NASA’s road map in his 2007 round-up of 16 such efforts — a road map of road maps, if you will, for large-scale research infrastructures¹. The analysis led to a large European report on road maps², which encouraged strategic planning so much that more than 20 countries have started their own road mapping, says Fontana.

Road maps are particularly suited to Europe because they can organize collaborations between the European Union’s 28 member countries and help to avoid overlap. They are “how we deal with complexity”, says Fontana. In his analysis, he uncovered four aspects that are common to successful strategic plans: they are long-term, include funding, have built-in mechanisms for quality assessment and include competition, such as a marketplace where anyone can participate.

The smallest scale at which a road map can be meaningfully implemented is that of a national funding agency, Fontana concluded, such as NASA or the Department of Energy. More commonly, however, road maps are created at the national level. The Cancer Moonshot Blue Ribbon Panel’s plan, for example, is really a road map for the field compiled by representatives from academia, the private sector and government, and funded by four federal agencies. At the larger end of the scale, road maps

WHAT TO CALL YOUR SCIENCE MEGA-PROJECT

Let's say you've got a smart strategy, ambitious goals and a shot at pulling in big money. Try our handy guide to come up with a name.



can span several nations, as is often the case in Europe. Many of them are written as a document to provide pragmatic guidance for — drum roll, please — an initiative.

initiative

n. /ɪˈnɪʃɪətɪv/ That which initiates, begins, or originates; the first step in some process or enterprise

Initiatives are in vogue in the United States right now, with two mega-projects bearing that designation: Obama's 2013 BRAIN Initiative, and his 2015 Precision Medicine Initiative (PMI).

The BRAIN Initiative — a proposed \$4.5-billion, 12-year effort involving almost every research arm in the government — has already awarded \$150 million in neuroscience research grants. The PMI launched with a \$215-million investment, including \$130 million for a centrepiece programme that aims to enrol and collect health data from 1 million Americans over a long period of time.

The PMI is like a large project dressed up as an initiative, but it has also been called a moonshot. Hudson, who co-chairs the PMI's Working Group, says that the two initiatives were named in the same office, but they have more in common than that. Both coordinate large entities — from the National Cancer Institute to the Food and Drug Administration and the Department of Defense — to progress towards a common goal.

Plus, they are creating large, technology-based research platforms to be applied across many types of disease — something that would not otherwise be done, says Hudson. Rather than disease-specific planning towards a single goal, as we've seen in moonshots and road maps, she says, the two initiatives focus on “resources that are going to have a broad, disease-agnostic impact” — resources that require coordination, planning and governance.

But when these kinds of large efforts come to an end, the technology hubs created for them face the challenge of continuing to be useful and can be perceived as a drain on resources. At the conclusion of the Human Genome Project, for example, Francis Collins, then at the National Human Genome Research Institute, proposed a series of grand challenges for genomics researchers, including the creation of the HapMap study to identify the most common genetic variations between people and the ENCODE project to catalogue all of the genome's functional DNA sequences, in an attempt to put the

technology resources developed during the project back to work³.

But gathering data and knowledge is not enough to make a scientific initiative successful, argues policy analyst Daniel Sarewitz of Arizona State University in Tempe (a regular columnist for *Nature*). Last year in an essay for *The New Atlantis*, Sarewitz criticized the BRAIN Initiative and the PMI as being part of a “datageddon”, in which big-data projects try to tackle complex problems with massive data sets, creating an almost infinite number of possible hypotheses to test within that system⁴. Those data sets therefore generate results that look meaningful but have no real application in medicine, Sarewitz says. In a complex system such as the brain, “the science can look like it's making great progress when in fact it's just adding to noise”.

Those concerns remain when people consider big projects today. “There is a real responsibility that comes with resources on this scale,” says Mason. “You've got to deliver a benefit to society that's commensurate with that investment.”

framework

n. /ˈfreɪmwɜːk/ an essential or underlying structure; a provisional design, an outline; a conceptual scheme or system

Frameworks provide a plan for a field or area. As well as helping an organization or nation to plan for the future, they serve as a way to coordinate and communicate ideas about policy and science to the public, says Tracy Merlin, managing director of the Adelaide Health Technology Assessment, a research unit that evaluates health interventions for the Australian Department of Health.

Australia is big on frameworks. In 2009, the government announced a Climate Change Science National Framework to identify “national climate-change science priorities for the coming decade”. It backed up that proposal with a Aus\$31.2-million (US\$23.5-million) funding boost over four years. The country also has government frameworks for safety and quality of health care, chronic diseases, mental-health services, cosmetic medical procedures, postnatal depression and more.

“It's easy if you've got a name for a collection of activities targeting the same thing, so you call it a ‘framework’ and it gains prominence,” says Merlin, who in 2013 co-authored a national framework for reviewing personalized medicines⁵. “It's their way of describing what they're trying to do” plus “a bit of marketing”, she adds.

Used in the right way, a framework or outline not only assists policymakers and the public — it can also help individual scientists to understand and explain how their work fits into a bigger picture, says Mason. “We can think, ‘If I can solve this problem that's keeping me up late tonight, it's another contribution in a larger enterprise that is going to lead to cures for disease or elimination of poverty or the creation of energy for those who need it.’”

This kind of big-picture thinking — whether through frameworks, moonshots or other grand designs — helps to focus attention. There will always be more good ideas than there is enough money, says Mason, so working together as a community to decide on priorities can be crucial to a field's success. “Science partly progresses by serendipity, but it also progresses by the technical capabilities that are developed through going to try to do big, difficult things,” he says. “If you don't have those big problems that you're trying to solve, pushing forward the frontier of what's possible, you're going to miss a lot of scientific opportunity.” ■

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