THE MILITARY–BIOSCIENCE COMPLEX

THE US DEPARTMENT OF DEFENSE IS MAKING A BIG PUSH INTO BIOLOGICAL RESEARCH — BUT SOME SCIENTISTS QUESTION WHETHER ITS HIGH-RISK APPROACH CAN WORK.

BY SARA REARDON

When Geoffrey Ling talks about the future of technology, his ideas go flying around the room like a whirlwind. Ling eagerly describes a world in which people live far beyond their natural lifespans, minds can be downloaded into external 'hard drives' for enhancement by artificial intelligence and robots and aircraft are controlled by human thought.

"It's abso-posi-frickin-lutely going to happen," he declares. "The next 20 years are going to make our heads spin, because we've already crossed over into that realm."

Ling should know: he is doing as much as anyone to make these visions real. A neurologist by training, he is also a US Army colonel and director of the first biology funding office to operate within the Defense Advanced Research Projects Agency (DARPA), the Pentagon's avant-garde research arm. The Biological Technologies Office (BTO), which opened in April 2014, aims to support extremely ambitious — some say fantastical — technologies ranging from powered exoskeletons for soldiers to brain implants that can control mental disorders.

DARPA's plan for tackling such projects is being carried out in the same frenetic style that has defined the agency's research in other fields. Ever since it was created in 1958, a year after the Soviet Union beat the United

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A prosthetic arm developed at Johns Hopkins University and funded by DARPA can be controlled by the wearer's own nerves.

States into space by launching the world's first artificial satellite, Sputnik, the agency's mission has been to prevent any more such surprises by getting there first. So DARPA's programme managers at the BTO are free to pour tens of millions of dollars into ambitious projects without waiting around for niceties such as peer review. And by working closely with its contractors as they develop their technology, the agency aims to drive discoveries across the often-deadly gap between basic research and commercialization.

That aggressive, high-risk strategy has had spectacular pay-offs — most famously with the agency's development of the Internet in the 1970s. And that has happened often enough to inspire imitators such as ARPA-E, a branch of the US Department of Energy that is devoted to high-risk research into alternative energy sources.

But some wonder whether DARPA's full-speed-ahead model will work as well for biology as it has for the physical sciences and hardware. Living systems are much more complex, they argue, with a multitude of variables that are either unknown or difficult to engineer and control. And because so much of the agency's biological research is directly applicable to humans, the work is fraught with ethical concerns — not to mention the possibility that even the most benign-sounding developments could be co-opted for war. Synthetic organisms designed to produce greener biofuels could also make explosives, for example, and brain-stimulation technology intended to heal wounded soldiers could also enhance combat abilities.

Edward Hammond, a biology-policy consultant in Austin, Texas, wonders whether the agency often has ulterior motives when it contracts researchers. "You don't ever really know what DARPA wants," he says. "But they're pretty good at finding people who are resolving questions they're interested in for other reasons."

Still, many biologists are willing to accept money from the Department of Defense (DOD), on the grounds that innovations such as better prosthetics and improved mental-health treatments are needed no matter who is paying for them. And Ling insists that DARPA understands the concerns: every programme in the BTO has a bioethics advisory board. Besides, he says, if visionary biotechnologies are inevitable, then it is DARPA's duty to race ahead and invent them.

"Some people think it's scary," he says, contemplating that future. "But I think it's rather exhilarating."

TIME TO COMBINE

DARPA's embrace of bioscience began in earnest in 2001, when anthrax spores posted to media offices and members of the US Congress brought concerns about bioterrorism to the fore. Then came the wars in Afghanistan and Iraq, which led the agency to invest in fields such as neuroscience, psychology and brain–computer interfaces — all with the intention of helping injured veterans. By 2013, the number of biology-related programmes had grown such that DARPA decided to consolidate them under one roof. The natural choice to head the new office and its US$288-million annual budget was Ling, who was deputy director of DARPA's science division at the time.

The office will certainly speed up research, says George Dyson, an independent science historian in Bellingham, Washington, and not least because of the military's culture of completing missions quickly, without lengthy reflection or debate. Looking at what DARPA has already done in fields such as computing, says Dyson, "it's always the military who move quickly enough to fund the interesting things".

A good example is DARPA's reaction to US President Barack Obama's 2013 announcement of the BRAIN initiative: a high-profile, multi-agency effort to understand the circuitry of the brain. The National Institutes of Health (NIH) spent months designing a ten-year strategic plan for the initiative before distributing its share of the money, and the National Science Foundation (NSF) opened a competition for its spending share to any research project related to brain networks. But DARPA quickly funnelled more than $50 million into just a few five-year programmes.

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These efforts now fall under the remit of the BTO. One, called Restoring Active Memory, is attempting to create a stimulation device that restores soldiers' ability to form memories after brain damage. Another, called SUBNETS (System-Based Neurotechnology for Emerging Therapies), is developing a brain implant that can treat seven mental and neurological disorders. As a first step, both projects are monitoring the brain activity of people with epilepsy who have had temporary electrodes implanted to locate the origin of their seizures. The investigators ask these patients to carry out memory exercises, or to perform tasks that involve neural pathways that might be impaired in addiction or depression, and record the electrical patterns that result.

The pay-offs could still be some way off, however. "There's no question this is a very ambitious goal," says Edward Chang, a neurosurgeon at the University of California, San Francisco, who co-leads one of the SUBNETS teams. "I don't think anyone is naive enough to think they'll be easily solved in the next five years."

As ambitious as DARPA is, however, its funding process can be unsettling for researchers who are accustomed to elaborately peer-reviewed grants from civilian agencies. At DARPA, much of the authority is vested in the programme managers, who rotate in and out from academia, industry and the armed services. They alone design the initiatives, invite researchers to apply for contracts with specific goals and milestones and select the groups they think are most likely to achieve the goals. Then they work closely with the researchers to guide the project as it proceeds.

DARPA calls its grant recipients 'performers' — and if they do not meet their milestones, the axe can fall quickly. In 2007, for example, DARPA started a programme called RealNose: an effort to develop a synthetic dog nose with real olfactory receptors for detecting odorants such as chemical weapons. But the agency killed the programme three years later, after it became clear that the receptor proteins were too unstable at room temperature.

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Researchers who follow DARPA's choreography are almost always free to publish their results, says BTO deputy director Alicia Jackson: very few of the agency's projects are classified as secret. But DARPA grant recipients do give up a certain amount of freedom: if they come across an interesting scientific question as they work, for example, they cannot use DARPA funding to pursue it. "Initially it was a change in culture," says Emad Eskandar, a neurosurgeon at Massachusetts General Hospital in Boston and director of one of the SUBNETS programmes. But Eskandar and his partner, psychiatrist Darin Dougherty, maintain that DARPA's oversight has made the project better. "It's helped us to focus and move ahead," Dougherty says.

Certainly, Ling is determined to prove that DARPA's model can work as well for biologists as for military contractors. One of his favourite successes is a prosthetic arm that DARPA developed in collaboration with the biotechnology firm DEKA in Manchester, New Hampshire. The device works by picking up the electrical signals that travel from the brain's motor cortex into nerves in the stump, then translating those signals into the appropriate motions of the attached prosthetic hand. This allows wearers to perform difficult tasks such as handling soft fruit and even rock climbing. The device won approval from the US Food and Drug Administration last year — the first nerve-controlled prosthetic to do so — and the company says that it is now working on commercialization. Similar arms are being developed for DARPA at

DARPA

An exoskeleton designed through DARPA's Warrior Web programme enhances soldiers' physical abilities.

the Johns Hopkins University in Baltimore, Maryland, and elsewhere; all of them are also being tested in people with paralysis in the hope that brain implants can translate their intentions into electrical signals that drive the hand.

The BTO has also taken over DARPA's health programmes, including one that is seeking to turn bacteria that prey on other bacteria into therapeutic antimicrobial agents. Other programmes have more obvious military applications, such as an exoskeleton that boosts a soldier's strength and speed. A programme called Narrative Networks studies how the brain reacts to different stories and arguments, which could be helpful for planning how to convince a disaster-stricken village to accept US military aid, or to turn terrorists away from their agendas. And several synthetic-biology initiatives are making biological systems that can be programmed to produce any compound a user wants, including some that do not exist in nature. These could include materials for making lightweight body armour, coatings for strengthening equipment, tissues that can be used to repair wounds, and more-efficient biofuels.

Ling and his DARPA colleagues revel in such ideas — the more far out, the better. "We look for ways to say yes, not no," he says.

For all its breakthrough successes, however, there is little evidence that DARPA's fast-track approach is consistently any better than peer review at choosing winners. "They've been successful when they've been successful," says Jonathan Moreno, a bioethicist at the University of Pennsylvania in Philadelphia. A DARPA spokesperson says that the agency cannot determine how often goals are met or contracts are cancelled. One reason is that the goalposts keep moving: if a project starts to seem unfeasible, programme managers often change the criteria for success and salvage what they can rather than cancelling the contract. Another is that unlike civilian agencies such as the NSF and the NIH, DARPA does not make public the grants that it makes. Nor does it conduct internal analyses that could determine whether its programme managers are choosing the best teams and paying for the best science that they possibly could.

"To me, that's a big problem," says Pierre Azoulay, an economist at Massachusetts Institute of Technology in Cambridge. "Pointing to great successes is not enough," he says. The agency's idea of programme evaluation is "very much in the mode of, 'Look, the Internet!'."

But Jackson literally laughs at the idea that the BTO should be more introspective. The office's budget is 1% of the size of the NIH's, she says, with little margin for overhead costs. And besides, she says, "we go with whoever can get the job done" — never mind factors such as experience or lab size. "I think we have a really good track record in our 50-plus-year history," she says. Listing DARPA's successes, she starts with the Internet.

But if DARPA is not slowing down to evaluate its successes, is it evaluating the effect they could have on society? Ling says yes, pointing to the ethicists who provide ongoing guidance on the implications of the BTO's work. That is far beyond the level of scrutiny given to most NIH- and NSF-funded projects, notes James Giordano, a neuroethicist at Georgetown University in Washington DC, and an adviser on SUBNETS. Usually, these undergo ethics evaluation only at their beginning or end. Moreno agrees. "The irony is that people think the national-security world is so far behind the civilian world on these things," he says. "But again and again, DOD has been ahead."

Nevertheless, some researchers continue to be sceptical. At Oregon Health & Science University in Portland, emeritus neuroscientist Curtis Bell worries that technologies such as brain stimulation could be used to subdue people, in a similar way to the prefrontal lobotomies that were used in the mid-twentieth century to deal with some troublesome prisoners. "You could imagine such things being more sophisticated nowadays," he says. "You wouldn't need to damage all the frontal lobes if you could go to a specific nucleus and alter someone's personality."

Dyson points out that there is no guarantee that the Pentagon will actually listen to ethicists' concerns — or to DARPA's. "Some of these technologies are absolutely fascinating and intriguing and hold all this promise for good, but they're very close to being weaponized easily," he says. And, says Moreno, although many people in the military think deeply about the implications of new technologies, the worry is that the political authorities above them may not allow them much freedom to slow down or change direction.

Of particular concern are the BTO's synthetic-biology programmes. The Pentagon has talked about engineering bacteria to clean up sites contaminated by radiation or chemical weapons, stoking fears that these organisms could get out of control when released into the environment. Although there is no reason to think that the United States is creating synthetic biological weapons, some fear even the intimation that microbes are strategically useful. "It's sending a signal that there's a role for synthetic-biology products for use in the field," says Hammond. "I would be concerned about that, and I'm concerned that DARPA doesn't seem to be."

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But other researchers are more supportive of the BTO. Ultimately, says Giordano, it may not matter who funds the research and who accepts the funding, because anyone can use published research for their own ends. "Individuals who look at DOD funding as Darth Vader science don't recognize that any science can be channelled through Darth Vader channels."

That is exactly why Ling feels that DARPA needs to jump into controversial science without hesitation: if the United States does not do it, someone else will. "The only thing we can do is do the work," he says, "but do it in a way where we're thinking about the untold consequences and how to mitigate them."

Ling says that he plans to keep expanding his office over the next year — how far depends on funding — to anticipate surprises coming from any sector. The BTO currently has 11 programme managers specializing in fields from infectious disease to natural ecosystems, and is looking to expand its repertoire to even more-far-flung fields such as palaeontology and astronomy. An expert in exoplanets, Ling says, could develop projects in preparation for the possibility of threats from outer space as well as the more likely scenario that signs of life will be discovered on another planet. "That is without a doubt going to be the most exciting scientific news in the history of mankind," he says. "And I'd love for it to be funded by DARPA." ■

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