GABRIELA HASBUN FOR *NATURE*

**Thomas Insel left Verily, a health-science spin-off formed by Google's parent company, to co-found a start-up called Mindstrong Health this year.**

# Join the disruptors of health science

**Thomas R. Insel**'s biggest lesson from his shift from NIMH director to Silicon Valley entrepreneur: academic and technology company researchers should partner up.

In early 2015, I testified with several other National Institutes of Health (NIH) directors at an annual hearing held by the US Senate. It was my 13th and final year as director of the US National Institute of Mental Health (NIMH) in Bethesda, Maryland. What struck me most was how the harsh fiscal reality tempered the passionate bipartisan support for the NIH. As one senator noted, with a federal deficit of nearly US$500 billion, there was little hope of any significant increase in funding.

Six months after that hearing, I left the NIH for Silicon Valley, first working at Verily in South San Francisco, California, a health-science spin-off formed by Google's parent company Alphabet. Since May, I've been president and co-founder of a start-up called Mindstrong Health in Palo Alto, California. I've witnessed the tremendous possibilities that immense resources, massive computing power and the application of data science can bring to biomedical research. I've watched some of today's best junior ▶

faculty members and postdocs launch their careers in Silicon Valley instead of in academic departments. And I've wondered how technology giants and start-ups will change biomedical and health-care research.

These companies have transformed the worlds of information, entertainment and commerce. But by moving into health care, they face some formidable challenges. In my view, solving them will require deep partnerships between technology companies, clinical experts, patient advocates and academic scientists.

## A FINANCIAL FRONTIER

In the United States, public funding for science has not kept up with inflation over the past decade. The proposed 2018 budget from the White House recommends funding cuts for the NIH and the National Science Foundation of more than 10% each. Appropriations may ultimately be more generous, but no one is expecting Congress to repair a decade's loss of purchasing power.

Meanwhile, private-sector investment has become a bigger piece of the research-funding pie — increasing from 46% in 1994 to 58% in 2012 for biomedical research[1]. Tech companies, in particular, have been ploughing more funds into research, and moving into areas such as health and life sciences that have typically been the domain of the NIH, pharmaceutical and biotechnology companies. By any measure, tech companies have enormous sums to spend. The collective cash reserves of Apple, Microsoft, Alphabet and Facebook — roughly $500 billion — exceed by tenfold the annual federal investment in biomedical research.

So what does this changing ecosystem mean for US biomedical science? Has the locus of innovation shifted from academia to Google and Facebook?

In some areas, such as artificial intelligence (AI), tech companies already dominate. According to a 2017 report, the tech giants invested between $20 billion and $30 billion in AI in 2016, with 90% of this going towards research and development. Some, such as Google and the Chinese web-services company Baidu, are rebranding themselves as AI or deep-learning companies, with a focus on both expanding the science of machine learning and applying the approach to big-data problems[2].

In health research, the landscape is still evolving. Three years ago, IBM began selling a software suite called Watson for Oncology to cancer-treatment centres around the world. The program is built around what IBM call cognitive computing and is designed to help clinicians to select the best treatment. The company claimed that by using its cloud-based data on cancer, Watson could recommend interventions for individual patients, although some say the effort was premature and oversold[3].

Over the past 12 months, Fitbit, the developer of several fitness trackers, has expanded into a health-care and health-research company. With more than 50 million registered users, it is involved in 400 research projects, including studies of diabetes and heart disease. In fact, Fitbit has just been listed as one of nine digital health companies to be considered by the US Food and Drug Administration (FDA) in its precertification pilot programme — a new, supposedly more agile, approach to regulation that will focus on the software developer rather than on individual products.

> *"Health tech has become one of the hottest areas for venture investment in the United States."*

Since March 2015, Apple's ResearchKit has made it easier for developers to create health apps for the iPhone or Apple Watch. It has also provided a platform for enrolling thousands of participants remotely in clinical projects, for instance in diabetes, cancer and diseases of the central nervous system. A study at Johns Hopkins University in Baltimore, Maryland, for instance, has used ResearchKit to capture data just before and throughout seizures in nearly 1,000 people with epilepsy[4].

Also in 2015, Alphabet launched Verily — a company focused on creating software and hardware to transform health care. After growing to more than 500 employees in just over 2 years, Verily seeks to address diabetes, heart disease, cancer and diseases of the central nervous system using miniaturized sensors in smart devices — such as a contact lens that estimates blood sugar levels.

Just six months ago, Facebook revealed the existence of Building 8, a division focused on delivering consumer "hardware products that are social first", including brain–computer interfaces designed to aid people with disabilities.

Meanwhile, health tech has become one of the hottest areas for venture investment in the United States: more than 1,000 new digital-health companies have started up since 2012. A report from Rock Health, a US venture-capital fund headquartered in San Francisco that invests in digital-health start-ups, estimates[5] that $15 billion has poured in to the sector over the past 5 years, up from $1.5 billion in 2012 and $1.1 billion in 2011 (see 'Betting on health').

Like pharma and biotech, big and small tech companies are product-focused and team-based. This contrasts with academia, where scientists are rewarded for publishing papers and incentives are built around individual promotion within a departmental structure.

But what struck me most on moving from the Beltway to the Bay Area was that, unlike pharma and biotech, tech companies enter biomedical and health research with a pedigree of software research and development, and a confident, even cocky, spirit of disruption and innovation. They have grown by learning how to move quickly from concept to execution. Software development may generate a minimally viable product within weeks. That product can be refined through 'dogfooding' (testing it on a few hundred employees, families or friends) in a month, then released to thousands of users for rapid iterative improvement.

During my first month working at Verily, I returned to Bethesda for the winter holidays; when I went back to work in early January, I found that a group of engineers had developed an entirely new product between Christmas and New Year's Day.

KIYOSHI OTA/BLOOMBERG/GETTY

**Fitbit, the developer of these sleep-monitoring wristbands, is currently involved in 400 research projects.**

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**At its California office, Mindstrong Health is developing digital phenotyping as a diagnostic tool.**

Contrast that with the NIH-funded world of research, where it usually takes at least 18 months to go from proposing an idea to getting a project funded, or the years it can take to transform the discovery of a molecule into a marketable drug.

This intense focus on the rapid development of consumer products is very different from the pursuit of fundamental knowledge that has been a hallmark of academic research. And as a newcomer (what Google calls a noogler), I found the language of product development and the drive towards 'quarterly OKRs' (objectives and key results) a bit off-putting. But the truly disruptive impact of tech companies is not the rapid-fire push for consumer products or their deep pockets; it's their focus on AI and data resources.

## MINING DATA

It is not surprising that companies that are dependent on information processing for their main revenue would be at the vanguard of developing the tools for collecting, storing and analysing data. A by-product of this is that tech companies are transforming data science — much as pharma and biotech transformed medicinal chemistry and molecular biology in the last decades of the twentieth century. In an era when biology is increasingly an information science, the tools being created by tech companies can provide insights that will almost certainly be translated into advances for health.

The potential is awesome — for discovery as well as for product development.

Three examples illustrate what can be achieved through having extraordinary access to population data as well as massive data-storage and data-processing capacity. Importantly, none connects in an obvious way to a primary business of the company.

First, in 2016 a team at Google used a version of machine learning called convolutional neural nets to create an algorithm to detect diabetic retinopathy[6]. The researchers started by having 54 ophthalmologists rate 128,175 retinal images. Once the algorithm had been trained on this data set, the team used two new sets of retinal images to test against eight board-certified ophthalmologists. The results were striking: depending on how the researchers set its parameters, the algorithm performed better than seven of the eight clinical experts, in terms of sensitivity and specificity. This approach is not markedly different from previous efforts to identify cats and faces with machine learning, but the potential impact on diagnostics and clinical care is profound.

Second, a team in Facebook's Building 8 is seeking to develop new brain–computer interfaces that (with the use of non-invasive optical sensors) will enable people to type simply by thinking — what is now called 'silent speech'. Although several universities have teams working on brain–computer interactions, the number of engineers and the computational resources that Facebook can muster would be difficult for any academic investigator to fund using federal grants. Importantly, Facebook is supporting some of these academic scientists (as well as recruiting many) to expedite this project.

Third, a team at Microsoft has used anonymous Bing search histories from 9.2 million users to predict cases of pancreatic cancer several months before people are usually diagnosed with the disease[7]. The team identified characteristic patterns of historical symptom searches in more than 3,000 anonymous users who subsequently indicated a probable diagnosis of pancreatic cancer — indicated by searches such as 'just diagnosed with pancreatic cancer'. This approach lacks the corroboration of a pathological diagnosis and the sensitivity is poor (only 5–15% of cases can be identified). But false-positive rates are extremely low (less than 0.0001).

In short, tech companies have scale and speed: an experiment can involve millions of people and be completed in months. But scale and speed aren't everything.

## STICKING POINTS

In moving from software or hardware development to biomedical research and health care, tech companies large and small face formidable challenges. They usually do not have the regulatory expertise needed to develop medical products, they rarely have access to clinical samples and they often lack a deep understanding of the clinical problem to be solved.

Various moves are being made to try to address these issues. In May, Verily hired Robert Califf, former chief of the FDA, to help with its personalized-medicine effort called Project Baseline. In 2015, 23andMe, a personal-genomics company based in Mountain View, California, recruited Richard Scheller, former head of research at the biotech company Genentech in San Francisco, to lead its research programme. And in 2016, Apple brought Stephen Friend, an open-science advocate from the non-profit research organization Sage Bionetworks in Seattle, Washington, to assist with its health projects.

How a culture built around engineers and designers will incorporate people from different sectors remains to be seen, and whether companies that build consumer products will be able to work with health-care payers and providers is unclear. But the willingness of tech companies to hire national experts on health, regulation and health data to aid in discoveries that will have clinical utility is a hopeful sign.

Yet there are at least four further major areas of uncertainty.

Open science increasingly drives innovation in the public sector. It is unclear to what degree the drive for intellectual property and profits will limit the transparency of research in the tech sector[8]. The stereotype is that for-profit companies will focus only on commercial end points. But there are notable counter-examples from AI research, in addition to the biomedical examples above. In 2015, Google made its machine-learning software library, TensorFlow, open source, and AI researchers across the board quickly adopted this powerful tool. Likewise, the *Apple Machine Learning Journal* launched in July to provide more transparency about the company's current projects (see go.nature.com/2yckpi9).

It's too early to say whether big or small tech companies will favour open source for their biomedical scientific initiatives. The success of ResearchKit gives some indication of what could be accomplished if they do.

Another uncertainty is whether the business model in tech, which is often based on advertising revenue or the sales of devices, will limit the rigour, generalizability and validity of the science carried out. Especially in start-ups that are dependent on rapid returns for their investors, the financial runway may be too short for lengthy or large clinical trials.

And then there's the issue of trust. It has become the norm for tech companies to use personal shopping or geolocation data for commerce. It's unclear whether the public will be as accepting about the use of personal health data, especially by behemoths such as Google or Facebook.

The recent commitments of big and small tech companies to discovery and clinical research are exciting. But during an economic downturn, these projects could be the first to be axed to protect the company's bottom line.

Science needs commitment. Bell Labs — at its peak, the premier research and development company of the United States — is an example of extraordinary scientific success in a for-profit organization. But as author Jon Gertner pointed out[9] in *The New York Times* in 2012: "Mark Zuckerberg noted that one of his firm's mottoes was 'move fast and break things'; that of Bell Labs' might just as well have been 'move deliberately and build things'."

## PARTNERS, IN TIME

The practical questions are these. What will each of the sectors in the evolving ecosystem do best? What can be done across sectors? How can bridges be built between companies with unprecedented access to data and massive computational resources, and academic scientists who may have a deep understanding of a clinical problem or access to unique clinical populations?

It seems likely that the academic sector will continue to lead on those aspects of fundamental biology and clinical research that do not require big data or machine learning — the purification of an enzyme, perhaps, or the development of a mouse model for a rare disease. Pharma and biotech will continue to be the source of new medicines. The domain of the tech industry will be research that is data-intensive, and product development that requires a legion of software engineers working with designers.

Transformative medical products that require clinical testing, regulatory standards and insights about the health-care marketplace, including the practical constraints faced by providers in the clinic, will almost certainly require partnerships between public research entities and private companies. These must include precompetitive partnerships across tech, pharma–biotech, academia and patient-advocacy groups. Developing these partnerships will not be easy, given the different stakeholders, cultures and incentives.

Yet there are successful public–private partnerships to learn from.

Since 2006, the Biomarkers Consortium, managed by the US charitable organization the Foundation for the NIH, has brought academics and private companies together to develop biomarkers across a range of diseases. The Alzheimer's Disease Neuroimaging Initiative, which since 2004 has worked to establish standards for imaging biomarkers in dementia, is among the studies it has supported. As is I-SPY2, which since 2010 has created treatment pathways based on biomarkers for breast cancer. Another Foundation for the NIH initiative is the Accelerating Medicines Partnership. This has paired the NIH and the FDA with 10 pharma and biotech companies as well as 12 non-profit patient-advocacy foundations to define new targets for drug development for rheumatoid arthritis, type 2 diabetes and Alzheimer's disease.

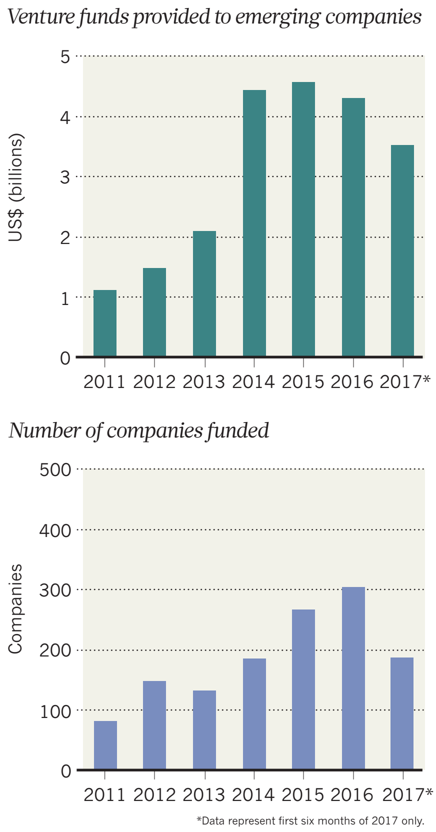
A new sector in the research ecosystem means that health problems, even those that do not present an obvious commercial opportunity, can be approached from a fresh angle. Data science could integrate the full stack of patient information, from genomics to socio-economic factors, to guide clinical care. Sensors and big data could transform our description of phenomics — each person's set of behavioural, physical and biochemical traits. For example, digital phenotyping through the use of smartphone sensors, keyboard performance and voice or speech features can provide, for the first time, an objective, continuous, passive measure of behaviour and cognition at the global scale. Mindstrong Health is using this approach to detect the earliest phases of dementia, mental illness and possibly a range of medical disorders[10].

As just one example of an urgent opportunity, attempts to prevent suicide worldwide have been remarkably ineffective — including public-health measures to reduce stigma, raise awareness and reduce access to guns. Social media, just-in-time interventions and new analytical tools for prediction could change our understanding of risk and yield new strategies for prevention[11]. Tech companies, paired with other players, could start to solve this and many other historically intractable problems.

There is an old African proverb: "To go fast, go alone; to go far, go together." Science to improve health has proved frustratingly slow. Perhaps, with a new fast partner, all of us in research can go farther. ■

## BETTING ON HEALTH

Private investment in health technology has soared in recent years in the United States.




SOURCE: ROCK HEALTH

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*Nature*'s Editor-in-chief, Philip Campbell, serves on an unpaid basis as a member of the science advisory board for Mindstrong

## CORRECTION

The Comment article 'Join the disruptors of health science' (*Nature* **551,** 23–26; 2017) should have disclosed that *Nature*'s Editor-in-chief, Philip Campbell, serves on an unpaid basis as a member of the science advisory board for the start-up firm Mindstrong Health.