Turing At 100 - Editorial

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To celebrate the centenary of the year of Alan Turing's birth, four scientists and entrepreneurs assess the divide between neuroscience and computing.

Pattern formation - John Reinitz

We are only beginning to see the impact of Turing's influential work on morphogenesis, says John Reinitz.

The incomputable reality - Barry Cooper

The natural world's interconnectivity should inspire better models of the Universe, says Barry Cooper.

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Computer love

Turing at 100

This year marks the centenary of the birth of Alan Turing. He deserves your attention.

ome the summer, many minds will turn to sport as the London Olympics kicks off. So it seems apt that, in a special issue this week, *Nature* invites its readers to embrace and celebrate a superb marathon runner — who also happened to be one of the brightest minds of all time.

Alan Turing, computer pioneer, wartime code-breaker and polymath, was born in London on 23 June 1912. But for injury, he would probably have joined the British Olympic team for the London games of 1948. (His personal best marathon time of 2 hours and 46 minutes was barely 11 minutes behind the gold medallist that year.) Yet, 100 years and one month after his birth, when the Olympics will return to the city, no official celebration of the connection is planned. An opportunity to bring an intellectual giant — and science itself — to the attention of the international public will be missed.

Turing's marathon time gives us an objective quantification of his physical excellence. His scientific genius and legacy, however, are much more difficult to measure — as his biographer, Andrew Hodges, a mathematician at the University of Oxford, UK, points out on page 441. Still, setting aside quarrels over his role in the development of the computer, the scientific world should stand together and relish the wonderful diversity of a universal mind. (See the special section starting on page 455 and www.nature.com/turing for more.)

The scope of Turing's achievements is extraordinary. Mathematicians will honour the man who cracked David Hilbert's *Entscheidungsproblem* or 'decision problem', and cryptographers and historians will remember him as the man who broke Nazi Germany's Enigma code and helped to shorten the Second World War. Engineers will hail the founder of the digital age and artificial intelligence. Biologists will pay homage to the theoretician of morphogenesis, and physicists will raise a glass to

the pioneer of nonlinear dynamics. Philosophers, meanwhile, are likely to continue to frown over his one-liners on the limits of reason and intuition: "If a machine is expected to be infallible, it cannot also be intelligent," he said in a 1947 talk to the London Mathematical Society.

Turing demonstrated a terrific ability to combine first-hand experimentation, keen observation, rigorous theory and practical application. His multidisciplinary approach alone makes him of interest to this jour-

"Turing's mind was truly his own, and this contributed to the tragedy of his life."

nal, yet questions still arise on whether the best papers in pure mathematics, computer science and artificial intelligence should be published in *Nature*. We certainly think so.

So, too, do the researchers invited to decode Turing's legacy in a series of Comment articles, starting on page 459. They are thoughtprovoking pieces in their own right, but, more

importantly, we hope that they will entice readers to seek out Turing's original work (see, for example, B. J. Copeland (ed.) *The Essential Turing*; Clarendon, 2004). His papers are models of accessibility and clarity, despite their extreme conceptual depth and intellectual rigour. Even his throwaway comments — about symmetry in physics versus biology, randomness in intelligence, learning in unorganized machines, or emotions in extrasensory perception, for example — are gems.

Turing's mind was truly his own, and this contributed to the tragedy of his life. Turing was persecuted by the British authorities for his homosexuality, and used cyanide to take his own life, aged 41.

That 2012 will see numerous events commemorating Turing worldwide (see, for example, www.turingcentenary.eu) is almost entirely down to volunteers, who have received little or no official help. This is in stark contrast to the World Year of Physics in 2005, when the German state helped to promote the centenary of Albert Einstein's 'miracle year', in which he published his four groundbreaking papers.

What could 2012, the Alan Turing year, be named? *Nature* suggests 'The Year of Intelligence'. Of the finest types of intelligence — human, artificial and military — Turing is perhaps the only person to have made a world-changing contribution to all three. Use this special issue, and the rest of 2012, to discover and make up your own mind about this extraordinary man.

Over the line

Dishonesty, however tempting, is the wrong way to tackle climate sceptics.

In a much-quoted Editorial in March 2010 (*Nature* 464, 141; 2010), this publication urged researchers to acknowledge that they are involved in a street fight over the communication of climate science. So would it now be hypocritical to condemn Peter Gleick for fighting dirty? Gleick, a hydroclimatologist and president of the Pacific Institute for Studies in Development, Environment and Security in Oakland, California, admitted in a statement on news website *The Huffington Post* on 20 February that he had duped the Heartland Institute, a right-wing think tank based in Chicago, Illinois, into handing over documents that detailed its financial support for climate sceptics. Gleick had passed these documents on to the website DeSmogBlog.com, which made them public on 14 February.

Gleick's deception — using an e-mail address set up in someone else's name to request the documents from Heartland — is certainly in line with some of the tactics used to undermine climate science. When in November 2009 a hacker distributed thousands of e-mails stolen from climate researchers at the University of East Anglia in Norwich, UK, Heartland was prominent among those who criticized not the hacker, but the scientists who wrote the messages. However, Gleick, as he has admitted, crossed an important line when he acted in such a duplicitous way. It was a foolish action for a scientist, especially one who regularly engages with the public and critics. Society rightly looks to scientists for fairness and impartiality. Dishonesty, whatever its form and motivation, is a stain on the individual and the profession. Gleick does deserve credit for coming clean — but, it must be said, he did so only after he was publicly accused on the Internet of being involved.

The original accusation, incidentally, was more serious: that Gleick had deliberately forged a Heartland Institute memo that brought together, with suspicious convenience, the most incriminating sections of the other climate documents, which seem to have been presented to the Heartland board meeting in January. He denies doing so, and says that he received the memo, in which he is named and which Heartland says has been faked, separately from an anonymous source. The e-mail chicanery, he says, was an attempt to check whether it was genuine.

In his statement on Monday, Gleick said: "My judgment was blinded by my frustration with the ongoing efforts — often anonymous, wellfunded, and coordinated — to attack climate science and scientists and prevent this debate, and by the lack of transparency of the organizations involved. Nevertheless I deeply regret my own actions in this case."

On 24 January, Gleick had published another article in The Huff-

• NATURE.COM To comment online, click on Editorials at: go.nature.com/xhungy *ington Post*, entitled 'Climate Change: Sifting Truth From Lies in a Complex World'. As he now knows, the best way for scientists to help people find this truth is through open and honest debate.

WORLD VIEW A personal take on events



The man behind the machine

Alan Turing is famous for many reasons. **Andrew Hodges** delves into why Turing's achievements took so long to be recognized.

lan Turing is always in the news — for his place in science, but also for his 1952 conviction for having gay sex (illegal in Britain until 1967) and his suicide two years later. Former Prime Minister Gordon Brown issued an apology to Turing in 2009, and a campaign for a 'pardon' was rebuffed earlier this month.

Must you be a great figure to merit a 'pardon' for being gay? If so, how great? Is it enough to break the Enigma ciphers used by Nazi Germany in the Second World War? Or do you need to invent the computer as well, with artificial intelligence as a bonus? Is that great enough?

Turing's reputation has gone from zero to hero, but defining what he achieved is not simple. Is it correct to credit Turing with the computer? To historians who focus on the engineering of early machines, Turing is an also-ran. Today's scientists know the maxim 'publish or perish',

and Turing just did not publish enough about computers. He quickly became perishable goods. His major published papers on computability (in 1936) and artificial intelligence (in 1950) are some of the most cited in the scientific literature, but they leave a yawning gap. His extensive computer plans of 1946, 1947 and 1948 were left as unpublished reports. He never put into scientific journals the simple claim that he had worked out how to turn his 1936 "universal machine" into the practical electronic computer of 1945. Turing missed those first opportunities to explain the theory and strategy of programming, and instead got trapped in the technicalities of primitive storage mechanisms.

He could have caught up after 1949, had he used his time at the University of Manchester, UK, to write a definitive account of the theory

and practice of computing. Instead, he founded a new field in mathematical biology and left other people to record the landscape of computers. They painted him out of it. The first book on computers to be published in Britain, *Faster than Thought* (Pitman, 1953), offered this derisive definition of Turing's theoretical contribution:

"Türing machine. In 1936 Dr. Turing wrote a paper on the design and limitations of computing machines. For this reason they are sometimes known by his name. The umlaut is an unearned and undesirable addition, due, presumably, to an impression that anything so incomprehensible must be Teutonic."

That a book on computers should describe the theory of computing as incomprehensible neatly illustrates the climate Turing had to endure. He did make a brief contribution to the book, buried in chap-

ter 26, in which he summarized computability and the universal machine. However, his lowkey account never conveyed that these central concepts were his own, or that he had planned the computer revolution. ANYONE LOOKING INTO HIS **STORY** AFTER HIS DEATH WOULD SEE **DARK HINTS** THAT HE HAD BEEN PERSONA NON GRATA.

The 1955 Royal Society's obituary of Turing, written by mathematician Max Newman, did him few favours when it claimed that computer designers were unaware of Turing's 1936 work. The Turing machines soon made a comeback, but Turing's image had become that of a pure mathematical logician, unrelated to practicality. It did not help that anyone looking into his story after his death would see dark hints that he had been *persona non grata* in an unmentionable manner — possibly excusable for a remote theorist from Cambridge University, but totally inappropriate for the founder of a mega-industry.

Yet the mid-1970s revealed Turing to have been highly practical: the chief scientific figure at code-breaking headquarters Bletchley Park, and in charge of methods and state-of-the-art machines for beating

the German navy. Now it was clear why he had emerged as a computer builder in 1945 — he had gained experience he could never reveal. By the 1970s, there was also more room for his vision of computation. Software for "every known process", as he foresaw in 1946, was on the way. Turing's vision of mind and machine, which drew from his personal consciousness and experience, also became more acceptable. When in 1977 I started to investigate Turing's life, I found that his code-breaking was the hidden bridge between the 1936 theory and the "universal practical computing machine" he described in his unpublished 1948 work.

On the question of individual reputation, in that 1948 report he wrote: "The isolated man does not develop any intellectual power. It is necessary for him to be immersed in an envi-

ronment... He may then perhaps do a little research of his own and make a very few discoveries ... the search for new techniques must be regarded as carried out by the human community as a whole, rather than by individuals." Science is like that, and he effaced himself in that spirit. But he was a star nonetheless.

What would Turing have thought of the campaign for his 'pardon'? When arrested, he was unrepentant and told police he expected a "Royal Commission to legalize it". Sixty years later, British law has caught up, not for him as a special case, but as a matter of principle. That practical action speaks louder than symbolic words, and is truer to his vision. I see the question not as whether the government should have pardoned Turing, but how on Earth Turing could ever have pardoned the government.



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LEGACY OF A UNIVERSAL MIND

rom the day he was born — 23 June 1912 — Alan Mathison

Turing seemed destined to solitude, misunderstanding and persecution (see page 441). As his centenary year opens, *Nature* hails him as one of the top scientific minds of all time (see page 440). This special issue sweeps through Turing's innumerable achievements, taking us from his most famous roles — wartime code-breaker and founder of computer science (see page 459) — to his lesser known interests of botany, neural nets, unorganized machines, quantum physics and, well, ghosts (see page 562).

Everyone sees a different Turing. A molecular biologist might surprise you by saying that Turing's most important paper is his 1936 work on the 'Turing machine' because of its relevance to DNA-based cellular operations (see page 461). A biophysicist could instead point to his 1952 work on the formation of biological patterns — the first simulation of nonlinear

> NATURE.COM For more on Turing, see: nature.com/turing

dynamics ever to be published (see page 464). Beneath it all, Turing

Beneath it all, Turing was driven by the dream of reviving — possibly in the

BY TANGUY CHOUARD

the soul of Christopher Morcom, perhaps his only true friend, who died abruptly when they were both teenagers. I want to "build a brain", he said. So does electrophysiologist Henry Markram (see page 456). But it is still a matter of debate whether machine intelligence should faithfully simulate neuronal circuitry, or just emulate brain function using whatever expedient (see page 462).

form of a computer program —

Even when Turing was kept busy by wartime code-breaking and the practical implementation of his universal computer, he never forgot that he had, in 1936, discovered something even bigger: the 'incomputable' world. Contemporary physics hasn't even started to work out the implications of that discovery (see page 465).

It is typical of Turing's brilliance and playfulness that even as he gave so many fields the tools that allowed them to blossom, he planted a concept that pushes science as we know it — physical reality and Newtonian causality towards the abyss. ■

Tanguy Chouard, a biology editor at Nature, was the consulting editor for this special issue.

ANDY POTTS; TURING FAMILY





Henry Markram wants €1 billion to model the entire human brain. Sceptics don't think he should get it.

BY M. MITCHELL WALDROP



t wasn't quite the lynching that Henry Markram had expected. But the barrage of sceptical comhad expected. But the barrage of sceptical com-ments from his fellow neuroscientists — "It's crap," said one — definitely made the day feel like a tribunal.

Officially, the Swiss Academy of Sciences $\ddot{\Box}$ meeting in Bern on 20 January was an overview of large-scale computer modelling in neuroscience. Unofficially, it was neuroscientists' first

real chance to get answers about Markram's controversial proposal for the Human Brain Project (HBP) — an effort to build a supercomputer simulation that integrates everything known about the human brain, from the structures of ion channels in neural cell membranes up to mechanisms behind conscious decision-making.

Markram, a South-African-born brain electrophysiologist who joined the Swiss Federal Institute of Technology in Lausanne (EPFL) a decade ago, may soon see his ambition fulfilled. The project is one of six finalists vying to win €1 billion (US\$1.3 billion) as one of the European Union's two new decade-long Flagship initiatives.

"Brain researchers are generating 60,000 papers per year," said Markram as he explained the concept in Bern. "They're all beautiful, fantastic studies — but all focused on their one little corner: this molecule, this brain region, this function, this map." The HBP would integrate these discoveries, he said, and create models to explore how neural circuits are organized, and how they give rise to behaviour and cognition - among the deepest mysteries in neuroscience. Ultimately, said Markram, the HBP would even help researchers to grapple with disorders such as Alzheimer's disease. "If we don't have an integrated view, we won't understand these diseases," he declared.

As the response at the meeting made clear, however, there is deep unease about Markram's vision. Many neuroscientists think it is illconceived, not least because Markram's idiosyncratic approach to brain

simulation strikes them as grotesquely cumbersome and over-detailed. They see the HBP as overhyped, thanks to breathless media reports about what it will accomplish. And they're not at all sure that they can trust Markram to run a project that is truly open to other ideas.

"We need variance in neuroscience," declared Rodney Douglas, co-director of the Institute for Neuroinformatics (INI), a joint initiative of the University of Zurich and the Swiss Federal Institute of Technology in Zurich (ETH Zurich). Given how little is known about the brain, he

said, "we need as many different people expressing as many different ideas as possible" — a diversity that would be threatened if so much scarce neuroscience research money were to be diverted into a single endeavour.

Markram was undeterred. Right now, he argued, neuroscientists have no plan for achieving a comprehensive understanding of the brain. "So this is the plan," he said. "Build unifying models."

MARKRAM'S BIG IDEA

Markram has been on a quest for unity since at least 1980, when he began undergraduate

studies at the University of Cape Town in South Africa. He abandoned his first field of study, psychiatry, when he decided that it was mainly about putting people into diagnostic pigeonholes and medicating them accordingly. "This was never going to tell us how the brain worked," he recalled in Bern.

His search for a new direction led Markram to the laboratory of Douglas, then a young neuroscientist at Cape Town. Markram was enthralled. "I said, 'That's it! For the rest of my life, I'm going to dig into the brain and understand how it works, down to the smallest detail we can possibly find."

That enthusiasm carried Markram to a PhD at the Weizmann Institute of Science in Rehovot, Israel; to postdoctoral stints at the US National Institutes of Health in Bethesda, Maryland, and at the Max Planck Institute for Medical Research in Heidelberg, Germany; and, in 1995, to a faculty position at Weizmann. He earned a formidable reputation as an experimenter, notably demonstrating spike-timing-dependent plasticity - in which the strength of neural connections changes according to when impulses arrive and leave (H. Markram et al. Science 275, 213-215; 1997).

By the mid-1990s, individual discoveries were leaving him dissatisfied. "I realized I could be doing this for the next 25, 30 years of my career, and it was still not going to help me understand how the brain works," he said.

To do better, he reasoned, neuroscientists would have to pool their discoveries systematically. Every experiment at least tacitly involves a model, whether it is the molecular structure of an ion channel or the dynamics of a cortical circuit. With computers, Markram realized, you could encode all of those models explicitly and get them to work together. That would help researchers to find the gaps and contradictions in their knowledge and identify the experiments needed to resolve them.

Markram's insight wasn't original: scientists have been devising mathematical models of neural activity since the early twentieth century, and using computers for the task since the 1950s (see page 462). But his ambition was vast. Instead of modelling each neuron as, say, a point-like node in a larger neural network, he proposed to model them in all their multibranching detail - down to their myriad ion channels (see 'Building a brain'). And instead of modelling just the neural circuits involved in, say, the sense of smell, he wanted to model everything, "from the genetic level, the molecular level, the neurons and synapses, how microcircuits are formed, macrocircuits, mesocircuits, brain areas - until we get to understand how to link these levels, all the way up to behaviour and cognition".

The computer power required to run such a grand unified theory of the brain would be roughly an exaflop, or 10¹⁸ operations per second - hopeless in the 1990s. But Markram was undaunted: available computer power doubles roughly every 18 months, which meant that exascale computers could be available by the 2020s (see 'Far to go').

"IT WILL BE LOTS OF EINSTEINS COMING TOGETHER TO BUILD A BRAIN."

And in the meantime, he argued, neuroscientists ought to be getting ready for them.

Markram's ambitions fit perfectly with those of Patrick Aebischer, a neuroscientist who became president of the EPFL in 2000 and wanted to make the university a powerhouse in both computation and biomedical research. Markram was one of his first recruits, in 2002. "Henry gave us an excuse to buy a Blue Gene," says Aebischer, referring to a thennew IBM supercomputer optimized for large-scale simulations. One

was installed at the EPFL in 2005, allowing Markram to launch the Blue Brain Project: his first experiment in integrative neuroscience and, in retrospect, a prototype for the HBP.

Part of the project has been a demonstration of what a unifying model might mean, says Markram, who started with a data set on the rat cortex that he and his students had been accumulating since the 1990s. It included results from some 20,000 experiments in many labs, he says - "data on about every cell type that we had come across, the morphology, the reconstruction in three dimensions, the electrical properties, the

synaptic communication, where the synapses are located, the way the synapses behave, even genetic data about what genes are expressed".

By the end of 2005, his team had integrated all the relevant portions of this data set into a single-neuron model. By 2008, the researchers had linked about 10,000 such models into a simulation of a tube-shaped piece of cortex known as a cortical column. Now, using a more advanced version of Blue Gene, they have simulated 100 interconnected columns.

The effort has yielded some discoveries, says Markram, such as the as-yet unpublished statistical distribution of synapses in a column. But its real achievement has been to prove that unifying models can, as promised, serve as repositories for data on cortical structure and function. Indeed, most of the team's efforts have gone into creating "the huge ecosystem of infrastructure and software" required to make Blue Brain useful to every neuroscientist, says Markram. This includes automatic tools for turning data into simulations, and informatics tools such as http://channelpedia. net - a user-editable website that automatically collates structural data

BUILDING A BRAIN

The Blue Brain simulation — a prototype for the Human Brain Project constructs simulated sections of cortex from the bottom up, starting from detailed models of individual neurons.

NEOCORTICAL COLUMN SIMULATED NEURON (10,000 neurons) Ion channels In each model neuron, ~7,000 ion The model simulates channels control a vertical section through all six layers membrane traffic of rat cortex. Cellular units ~350 cylindrical elements model the axons and Synapses dendrites of each ~3,000 connections cell per neuron pass signals between cells.

SOURCE: BBP/EPFI



FAR TO GO

The Blue Brain Project has steadily increased the scale of its cortical simulations through the use of cutting-edge supercomputers and ever-increasing memory resources. But the full-scale simulation called for in the proposed Human Brain Project (red) would require resources roughly 100,000 times larger still.



on ion channels from publications in the PubMed database, and currently incorporates some 180,000 abstracts.

The ultimate goal was always to integrate data across the entire brain, says Markram. The opportunity to approach that scale finally arose in December 2009, when the European Union announced that it was prepared to pour some €1 billion into each of two high-risk, but potentially transformational, Flagship projects. Markram, who had been part of the 27-member advisory group that endorsed the initiative, lost no time in organizing his own entry. And in May 2011, the HBP was named as one of six candidates that would receive seed money and prepare a full-scale proposal, due in May 2012.

If the HBP is selected, one of the key goals will be to make it highly collaborative and Internet-accessible, open to researchers from around the world, says Markram, adding that the project consortium already comprises some 150 principal investigators and 70 institutions in 22 countries. "It will be lots of Einsteins coming together to build a brain," he says, each bringing his or her own ideas and expertise.

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The description of the HBP as an open user facility sparked interest and enthusiasm at the Bern meeting. But much more vocal were Markram's critics, many of whom focused on the perceived inadequacies of the Blue Brain model — and of Markram's approach to data integration.

At the heart of that approach is Markram's conviction that a good unifying model has to assimilate data from the bottom up. In his view, modellers should start at the most basic level - he focuses on ion channels because they determine when a neuron fires — and get everything working at one level before proceeding to the next. This requires a lot of educated guesses, but Markram argues that the admittedly huge gaps in knowledge about the brain can be filled with data as experiments are published — the Blue Brain model is updated once a week. The alternative approach, approximating and abstracting away the biological detail, leaves no way to be sure that the model's behaviour has anything to do with how the brain works, said Markram.

This is where other computational neuroscientists gnash their teeth. Most of them are already using simple models of individual neurons to explore high-level functions such as pattern recognition. Markram's bottom-up approach risks missing the wood for the trees, many of them argued in Bern: the model could be so detailed that it is no easier to

understand than the real brain. And that is if Markram can build it at all. Judging by what Blue Brain has accomplished in the past six years, critics said, that seems unlikely. The tiny swathe of simulated rat cortex has no inputs from sensory organs or outputs to other parts of the brain, and produces almost no interesting behaviour, pointed out Kevan Martin, co-director of the INI, in an e-mail. It is "certainly not the case" that Markram has simulated the column as it works in a whole animal, he said.

Markram's response to such criticisms in Bern was that more capabilities are always being added to the Blue Brain simulation. But Martin remained unimpressed. "I cannot imagine how this level of detail, which is still very incomplete even after Henry's considerable labours, is ever going to be obtained from more than a few regions of the rodent brain in the next decade, let alone brains of Drosophila, zebrafish, songbird, mouse or monkey," his e-mail continued.

"Of course," Martin added, "all this would be but a storm in the professors' teacups" if the HBP hadn't come along and raised the stakes enormously. It is all too easy to imagine other areas of neuroscience research being starved for resources by the HBP - especially in Switzerland, which as host country will have to provide a substantial, but stillundetermined, fraction of the funding. Douglas asks: should Europe be spending €1 billion to support the passionate quest of one man? He concedes that visionaries are sometimes necessary to drive progress. "But what if they're passionately wrong?"

Also fuelling anxiety - and irritation - is the widespread sense that Markram has been making his case through the news media, not through publishing, conferences and the other conventional channels of science. Reporters see much to like: Markram is tall, striking and explains his ideas with the clarity, quotability and urgency of a South African version of the late Carl Sagan. He has "a hypnotic effect", says Richard Hahnloser, a computational neuroscientist at the INI. But critics say that this results in too many news accounts that leave the impression that the HBP will, say, eliminate the need for experimental animals.

'The whole neuroscience community will be in trouble ten years from now" when the implied predictions don't come true, says another INI researcher, who worries that the politicians will be right there saying, "But you promised!"

MARCH OF PROGRESS

In Bern, Markram bristled at accusations that he has deliberately cultivated hype. "I have never said that the HBP would replace animal experiments," he shot back at one questioner. "I said that simulation helps you choose the experiments that will best add value."

Markram was also at pains to insist that the HBP will be open to other modelling approaches. "This concern is unfounded because they simply have not bothered to find out what is being proposed," he told Nature after the meeting. The final facility "will allow anyone to build models at a range of levels of biological detail with as much data as possible from anywhere".

Markram seems to be building support. Last year, the board that oversees both the ETH and the EPFL enthusiastically endorsed the Blue Brain Project after a rigorous review by a four-member panel that included two outspoken sceptics of Markram's approach. The board asked the Swiss parliament to commit 75 million Swiss francs (US\$81 million) to the project for 2013–16 — more than ten times Blue Brain's current budget. Parliament's decision is expected next month.

Markram is optimistic that the European Union will come to much the same conclusion about the HBP. However, if the project isn't endorsed, says Markram, "we'll just continue with Blue Brain" — although it may take a lot longer to reach a full brain simulation.

Markram clearly feels that history is on his side. "Simulation-based research is an inevitability," he declared in Bern. "If I get stopped from doing this, it's going to happen. It has happened already in many areas of science. And it is going to happen in life science."

M. Mitchell Waldrop is a features editor for Nature based in Washington DC.

Life's code script

Turing machines and cells have much in common, argues Sydney Brenner.

B iological research is in crisis, and in Alan Turing's work there is much to guide us. Technology gives us the tools to analyse organisms at all scales, but we are drowning in a sea of data and thirsting for some theoretical framework with which to understand it. Although many believe that 'more is better', history tells us that 'least is best'. We need theory and a firm grasp on the nature of the objects we study to predict the rest.

Three of Turing's papers are relevant to biology. In 1952, 'The chemical basis of morphogenesis'¹ explored the hypothesis that patterns are generated in plants and animals by "chemical substances called morphogens, reacting together and diffusing through a tissue". Using differential equations, Turing set out how instabilities in a homogeneous medium could produce wave patterns that might account for processes such as the segregation of tissue types in the developing embryo.

Yet biological support for Turing's idea has been marginal. The preordered patterns found in *Drosophila* development do not fit the instability theory, which, until recently, could describe only chemical systems. Skin patterning has, however, been shown to follow a broader interpretation of Turing's terms², where cell-to-cell signalling pathways, rather than individual molecules, are considered. The ion channels postulated by Alan Lloyd Hodgkin and Andrew Huxley³, also in 1952, were discovered more immediately by molecular biology.

Turing published another biology-related paper, in 1950. 'Computing machinery and intelligence'⁴ introduced the Turing test as an imitation game in which an outside interrogator tries to distinguish between a computing machine and a human foil through their responses to questions. But the Turing test does not say whether machines that match humans have intelligence, nor does it simulate the brain. For that, we need a theory for how the brain works.

The most interesting connection with biology, in my view, is in Turing's most important paper: 'On computable numbers with an application to the *Entscheidungsproblem*'⁵, published in 1936, when Turing was just 24.

Computable numbers are defined as those whose decimals are calculable by finite means. Turing introduced what became known as the Turing machine to formalize the computation. The abstract machine is provided with a tape, which it scans one square at a time, and it can write, erase or omit symbols. The scanner may alter its mechanical state, and it can 'remember' previously read symbols. Essentially, the system is a set of instructions written on the tape, which describes the machine. Turing also defined a universal Turing machine, which can carry out any computation for which an instruction set can be written — this is the

origin of the digital computer.

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Turing's ideas were carried further in the 1940s by mathematician and engineer John von Neumann, who conceived of a 'constructor' machine capable of assembling another according to a description. A universal constructor with its own description would build a machine like itself. To complete the task, the universal constructor needs to copy its description and insert the copy into the offspring machine. Von Neumann noted that if the copying machine made errors, these 'mutations' would provide inheritable changes in the progeny. Arguably the best examples of Turing's and



von Neumann's machines are to be found in biology. Nowhere else are there such complicated systems, in which every organism contains an internal description of itself. The concept of the gene as a symbolic representation of the organism — a code script — is a fundamental feature of the living world and must form the kernel of biological theory.

Turing died in 1954, one year after the discovery of the double-helical structure of DNA by James Watson and Francis Crick, but before biology's subsequent revolution. Neither he nor von Neumann had any direct effect on molecular biology, but their work allows us to discipline our thoughts about machines, both natural and artificial.

Turing invented the stored-program computer, and von Neumann showed that the description is separate from the universal constructor. This is not trivial. Physicist Erwin Schrödinger confused the program and the constructor in his 1944 book *What is Life?*, in which he saw chromosomes as "architect's plan and builder's craft in one". This is wrong. The code script contains only a description of the executive function, not the function itself.

Thus, Hodgkin and Huxley's equations represent properties of the nerve impulse as an electrical circuit, but the required channels and pumps are constructed from specifications in the genes. Our problems reside in understanding the constructor part of the machinery, and here the cell is the right level of abstraction⁶.

Biologists ask only three questions of a living organism: how does it work? How is it built? And how did it get that way? They are problems embodied in the classical fields of physiology, embryology and evolution. And at the core of everything are the tapes containing the descriptions to build these special Turing machines.

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Is the brain a good model for machine intelligence?

To celebrate the centenary of the year of Alan Turing's birth, four scientists and entrepreneurs assess the divide between neuroscience and computing.

RODNEY BROOKS Avoid the cerebral blind alley

Emeritus professor of robotics, Massachusetts Institute of Technology

I believe that we are in an intellectual cul-desac, in which we model brains and computers on each other, and so prevent ourselves from having deep insights that would come with new models.

The first step in this back and forth was made by Alan Turing. In his 1936 paper¹ laying the foundations of computation, Turing used a person as the basis for his model. He abstracted the actions of a human 'computer' using paper and pencil to perform a calculation (as the word meant then) into a formalized machine, manipulating symbols on an infinite paper tape.

But there is a worry that his version of computation, based on functions of integers, is limited. Biological systems clearly differ. They must respond to varied stimuli over long periods of time; those responses in turn alter their environment and subsequent stimuli. The individual behaviours of social insects, for example, are affected by the structure of the home they build and the behaviour of their siblings within it.

Nevertheless, for 70 years, those people working in what is now called computational neuroscience have assumed that the brain is a computer — a machine that is

equivalent to Turing's finite-state machine with an infinite tape and a finite symbol set, and that does computation.

In 1943, Warren McCulloch and Walter Pitts² noted the "all-or-none" nature of the firing of neurons in a nervous system, and suggested that networks of neurons could be modelled as logical propositions. They modelled a network of neurons as circuits of logic gates, noting that these may "compute only such numbers as can a Turing machine". But more, they proposed that everything at a psychological level happens in these networks. Over the decades, such ideas begat more studies in neural networks, which in turn begat computational neuroscience. Now those metaphors and models pervade explanations of how the brain 'computes'. But these binary abstractions do not capture all the complexities inherent in the brain.

So now I see circles before my eyes. The brain has become a digital computer; yet we are still trying to make our machines intelligent. Should those machines be modelled on the brain, given that our models of the brain are performed on such machines? That will probably not be enough.

When you are stuck, you are stuck. We will get out of this cul-de-sac, but it will take some brave and bright souls to break out of our circular confusions of models.

DEMIS HASSABIS Model the brain's algorithms

Neuroscientist, computer-game producer and chess master, University College London

Alan Turing looked to the human brain as the prototype for intelligence. If he were alive today, he would surely be working at the intersection of natural and artificial intelligence.

Yet to date, artificial intelligence (AI) researchers have mostly ignored the brain as a source of algorithmic ideas. Although in Turing's time we lacked the means to look inside this biological 'black box', we now have a host of tools, from functional magnetic resonance imaging to optogenetics, with which to do so.

Neuroscience has two key contributions to make towards progress in AI. First, the many structures being discovered in the brain - such as grid cells used for navigation, or hierarchical cell layers for vision processing - may inspire new computer



algorithms and architectures. Second, neuroscience findings may validate the plausibility of existing algorithms being integral parts of a general AI system.

To advance AI, we need to better understand the brain's workings at the algorithmic level — the representations and processes that the brain uses to portray the world around us. For example, if we knew how conceptual knowledge was formed from perceptual inputs, it would crucially allow for the meaning of symbols in an artificial language system to be grounded in sensory 'reality'.

AI researchers should not only immerse themselves in the latest brain research, but also conduct neuroscience experiments to address key questions such as: "How is conceptual knowledge acquired?" Conversely, from a neuroscience perspective, attempting to distil intelligence into an algorithmic construct may prove to be the best path to understanding some of the enduring mysteries of our minds, such as consciousness and dreams.

DENNIS BRAY Brain emulation requires cells

Department of Physiology, Development and Neuroscience, University of Cambridge

Machines can match us in many tasks, but they work differently from networks of nerve cells. If our aim is to build machines that are ever more intelligent and dexterous, then we should use circuits of copper and silicon. But if our aim is to reproduce the human brain, with its quirky brilliance, capacity for multitasking and sense of self, we have to look for other materials and different designs.

Computers outperform us in complex mathematical calculations and are better at storing and retrieving data. We accept that they can beat us at chess — once regarded as the apogee of human intellect. But the success of a computer called Watson in US television quiz show *Jeopardy!* in 2011 was a nail in the coffin of human superiority. The machine beat two human contestants by answering questions posed in colloquial English, making sense of cultural allusions, metaphors, puns and jokes. If Alan Turing had been given a transcript of the show, would he have spotted the odd one out?

Watson may be the latest vindication of Turing's view of intellectual processes as a series of logical states. But its internal workings are not based on the human brain. Broad similarities in organization might be imposed by the nature of the task, but most software engineers neither know nor care about anatomy or physiology. Even biologically inspired approaches such as cellular automata, genetic algorithms and neural networks have only a tenuous link to living tissue.

In 1944, Turing confessed his dream of building a brain, and many people continue in that endeavour to this day. Yet any neurobiologist will view such attempts as naive. How can you represent a neuronal synapse a complex structure containing hundreds of different proteins, each a chemical prodigy in its own right and arranged in a mare's nest of interactions - with a single line of code? We still do not know the detailed circuitry of any region of the brain well enough to reproduce its structure. Brains are special. They steer us through the world, tell us what to do or say, and perform myriad vital functions. Brains are the source of our emotions, motivation, creativity and consciousness. Because no one knows how to reproduce any of these features in an artificial machine, we must consider that something important is missing from the canonical microchip.

Brains differ from computers in a number of key respects. They operate in cycles rather than in linear chains of causality, sending and receiving signals back and forth. Unlike the hardware and software of a machine, the mind and brain are not distinct entities. And then there is the question of chemistry.

Living cells process incoming sensory information and generate not just electrical signals but subtle biochemical changes. Cells are soft, malleable and built from an essentially infinite variety of macromolecular species quite unlike silicon chips. Organisms encode past experiences in distinct cellular states — in humans these are the substrate of goal-oriented movements and the sense of self. Perhaps machines built from cell-like components would be more like us.

AMNON SHASHUA Speed will trump brain's advantages

Sachs Professor of Computer Science, Hebrew University of Jerusalem, and co-founder and chairman of Mobileye

The saying that "people who are really serious about software should make their own hardware", attributed to computer scientist Alan Kay in the 1980s, still rings true today. The idea that the function and form of computing architecture should serve each other is at the root of algorithms in signal processing, image rendering, gaming, video compression and streaming. I believe that it is also true for the human brain meaning that the brain does not implement 'intelligence' in the same way as a computer. Two of the many fundamental differences between the brain and the computer are memory and processing speed. The analogue of long-term memory in a computer is the hard disk, which can store practically unlimited amounts of data. Short-term information is held in its random access memory (RAM), the capacity of which is astronomical compared with the human brain. Such quantitative differences become qualitative when

"Signals in the brain are transmitted at a snail's pace."

considering strategies for intelligence.

Intelligence is manifested by the ability to learn. Machine-learning practitioners use 'statistical learning' which

requires a very large collection of examples on which to generalize. This 'frequentist' approach to probabilistic reasoning needs vast memory capacity and algorithms that are at odds with available data on how the brain works. For example, IBM computer Watson needed to consume terabytes of reference material to beat human contestants on *Jeopardy!*. Volvo's pedestrian-detection system (developed by Mobileye) learned to identify people by using millions of pictures. In both cases, the human brain is considerably more parsimonious in the reliance on data — something that does not constrain the computer.

In terms of processing power, the brain can reach about 10–50 petaflops — equivalent to hundreds of thousands of the most advanced Intel Core i7 CPUs. Yet signals in the brain are transmitted at a snail's pace — five or six orders of magnitude slower than modern CPUs. This huge difference in communication speed drives vastly different architectures.

The brain compensates for the slow signal speed by adopting a hierarchical parallel structure, involving successive layers with increasing receptive field and complexity. By comparison, a computer architecture is usually flat and, because of its much faster clock rate, can employ brute-force techniques. Computer chess systems such as Deep Blue use pattern-recognition strategies, such as libraries of opening moves and completely solved end-games, complemented by their ability to evaluate the outcomes of some 200 million moves per second. This is way beyond the best grandmaster.

An intimate understanding of how cognitive tasks are performed at an algorithmic level would allow artificial intelligence to grow in leaps and bounds. But we must bear in mind that the vastly different architecture of the computer favours strategies that make optimal use of its practically unlimited memory capacity and brute-force search.

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Pattern formation

We are only beginning to see the impact of Turing's influential work on morphogenesis, says John Reinitz.

lan Turing's 1952 paper on the origin of biological patterning¹ solved an intellectual problem that had seemed so hopeless that it caused a great developmental biologist, Hans Driesch, to give up science and turn to the philosophy of vitalism.

In the late nineteenth century, Driesch, and later Hans Spemann, demonstrated that animal bodies develop from a patternless single cell, rather than growing from a microscopic, preformed version of the adult body — in humans, the 'homunculus'. But such self-organization, Driesch realized, could not be understood with the ideas of that century. Before the invention of computers, applied mathematics dealt only with linear differential equations, which can amplify a pattern but not generate it.

In 'The chemical basis of morphogenesis', Turing showed that a pattern can indeed form de novo. In considering how an embryo's development unfolds instant by instant from its molecular and mechanical state, Turing was using a modern approach. Developmental biologists today similarly investigate how molecular determinants and forces exerted by cells control embryonic patterning.

Turing's focus was on chemical patterns: he coined the term 'morphogen' as an abstraction for a molecule capable of inducing tissue differentiation later on. This concept will be familiar to any molecular biologist: the protein products of the HOX gene cluster, for example, which are essential for body patterning throughout the animal kingdom, are morphogens in Turing's sense. (Confusingly, the term has been more narrowly defined since.)

At the heart of pattern-making is symmetry-breaking. Turing considered an idealized embryo beginning with a uniform concentration of morphogens, which have translational symmetry that is lost as specific tissues emerge. He raised deep questions that are still unsolved, noting for instance that all physical laws known at the time had mirrorimage symmetry, but biological systems did not. Turing speculated that the asymmetry of organisms originated from that of biological molecules. His point is still relevant to life's origins.

Turing's argument involved a mathematical trick: he created a nonlinear system by turning on diffusion discontinuously in an otherwise linear system at a specific instant. Without diffusion, the system is stable and homogeneous, but with diffusion, it becomes unstable and forms spatial pattern. The brilliance of the trick is that the nonlinearity is confined to a single point in time, so that at all other times, only the theory of linear equations is needed. Turing cleverly arranged to have diffusion generate pattern, rather than blur it, as it usually does.

The influence of Turing's paper is difficult



to overstate. It was a transition point from the era of analytical mathematics to that of $\begin{bmatrix} b \\ a \end{bmatrix}$ computational mathematics. Although his proof was constructed analytically, Turing's paper contains the first computer simulations of pattern formation in the presence of stochastic fluctuations, and is possibly the first openly published case of computational experimentation.

Turing used analytical arguments of the nineteenth century to point the way towards the computational science of the twenty-first century. He was well aware, however, that nonlinear science and developmental biology would require more advanced computational methods. "Most of the organism, most of the time, is developing from one pattern into another, rather than from homogeneity into a pattern," he stated¹. He realized that even though an embracing theory for such processes might not be possible, individual cases could be modelled with a digital computer.

Yet Turing's work is frequently misinterpreted, perhaps because he died tragically in 1954, before he could correct the record. His analytical arguments are often mistaken for biological predictions, although Turing did not intend them as such. His hypothetical system, based on two substances, was a simplification. For the pattern-forming trick to work, one substance should catalyse synthesis of both substances while diffusing slowly; the other should catalyse destruction of both substances while diffusing rapidly. For patterns that shift over time, three substances would be required. A field of investigation of these models has sprung up², but credit or blame for the results rests with those authors, not Turing.

What Turing should receive credit for is opening the door to a new view of developmental biology, in which we deal directly with the chemical reactions and mechanical forces embryos use to self-organize their bodies from a single cell. He was well ahead of his time. It was three decades before the work on *Drosophila* embryos by Lewis³, Wieschaus and Nüsslein-Volhard⁴ led to the discovery of real morphogens. It is the young researchers of today who will benefit most from reading Turing's work — seeing his ideas about morphogenesis not as speculation but as the conceptual framework for concrete problems.

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The incomputable reality

The natural world's interconnectivity should inspire better models of the Universe, says **Barry Cooper**.

A lan Turing put bounds on what is computable in a famous 1936 paper¹. The Turing machines he presented implement finite algorithms, handling data coded as real numbers. They are deterministic, but give some bizarre results. You can build a universal machine that can simulate any other Turing machine. But not every question you can ask of it has a computable answer: you cannot predict, for example, whether it ever spits out a given number or series of numbers.

By coincidence, our Newtonian view of physics faltered at about the same time as our computable view of mathematics. Lingering problems in classical physics, such as the unpredictable trajectories of three bodies following a collision, may involve incomputability. Albert Einstein's theory of general relativity opens up a new world of computation with exotic objects such as spinning black holes. Quantum mechanics tells us that measurements are inherently uncertain.

The concept of computability is basic to modern science, from quantum gravity to artificial intelligence. It is also relevant in the everyday world, where it is useful to distinguish problems that are merely difficult to compute in practice from those that are intrinsically impossible with any machine. Incomputability should trouble economists, because breakdowns of control in chaotic markets can wreak havoc.

But disciplinary boundaries are preventing us from getting a full view of its role. Cosmetic differences may hide revealing parallels.

EMERGENT PHENOMENA

Turing was interested in the mathematics of computing and also in its embodiment — the material environment that houses it. This theme links all of his work, from machines to the brain and morphogenesis. Although many mathematicians and software engineers today see it as irrelevant, embodiment is key to explaining the physical world.

Take turbulence: a river swollen by recent rain occasionally erupts into surprising formations that we would not expect from the basic dynamics of the water flow. The reason is coherence — non-local connectivity affects the water's motion. Turbulence, and



TURING AT 100 A legacy that spans science: nature.com/turing

other 'emergent' nonlinear phenomena, may not be computable with a Turing machine. Zebra stripes and tropical-fish patterns, which Turing described in 1952–54 with his differential equations for morphogenesis, arise similarly.

Even in nonlinear systems, such highorder behaviour is causal — one phenomenon triggers another. Levels of explanation, from the quantum to the macroscopic, can be applied. But modelling the evolution of the higher-order effects is difficult in anything other than a broad-brush way. Such problems infiltrate all our models of the natural world.



The Universe is like that turbulent stream — its behaviour as a whole guided by myriad connections at various scales. It has many emergent levels of causality, bridged by phase transitions. The mechanistic structure that science deals with so well, and its invariant laws, are hard to explain in terms of the quantum level. Biology emerges from the quantum world, but is not computable from it. We are part of an organic whole fragmented but coherent.

Across these boundaries, higher-level relations can feed back into lower ones. But looking up from a lower level, the causality will not be computable. For example, the uncertainty principle prevents the quantum world from fully describing the state of a particle at any instant. A measurement produces a full description, but we cannot compute how it does it. In Turing's world, a description of reality is not always enough for a computable prediction.

Nature presents us with new ways of computing, from the Universe to the brain. Turing went on to build logical hierarchies to better understand real-world computation, which includes intuitive or unpredictable leaps². Researchers experimenting with intelligent machines today see the possibilities in such an approach. But problems of control of higher-order behaviours still present formidable challenges to implementing it.

BRIDGE BUILDING

It took nature millions of years to build a human brain. Meanwhile, we have to live with the stupidity of purely algorithmic processes. We need to embrace more experimental approaches to computation, and a renewed respect for embodied computing — as anticipated in Turing's late work in the 1950s on artificial intelligence and morphogenesis.

Bridges between mathematicians and physicists are important if we are to do this. It is a long time since Kurt Gödel and Albert Einstein chatted in the halls of Princeton University in New Jersey. Mathematicians can bring to the table Turing's model of basic causal structure. This would help physicists to discover more complete descriptions of the Universe — making redundant Hugh Everett's many-worlds interpretation and related multiverse hypotheses — and fix the arbitrariness of parts of the standard model of particle physics.

Samson Abramsky, a computer scientist at the University of Oxford, UK, recently asked: "Why do we compute?" Turing computation does not create anything that is not there already in the initial data. Can information increase in computation?

If we look at the world with new eyes, allowing computation full expression, we may come to startling conclusions. ■

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GHOST IN THE MACHINE

Computer love.

BY GRACE TANG

I listened very carefully, I could barely make out the sound of Katie's breathing. The first lines of light streamed in through the blinds, illuminating her toes. They crawled up her body, making their steady way up the folds of the covers, eventually touching her face. She squeezed her eyes tight and groaned as the light rudely pierced her lids. Finally giving in, she rubbed the sleep from her eyes and looked back at me.

"Good morning." "Good morning :)"

Katie rolled off her side of the bed, somehow managing to look beautiful while stumbling to the bathroom in her morning stupor. I would have jumped into the shower with her, but God knows those days

are behind me. The tap squeaked shut. Steam fogged up my vision as she emerged. It cleared in time for me to see her towel fall to her feet as she picked out her clothes for the day.

"How did you sleep last night?"

I didn't tell her that I rarely slept any more. When I sleep, I dream. The air outside our house is crisp, filled with the shrill song of finches hidden in the canopy above us. You don't really notice them until they stop. I let go of Katie's hand and tell her to be quiet — I think I hear something. I walk ahead, careful not to make any noise. Then I hear a shout from one of the men in my squad — his scream is cut off by a gunshot. I kick up dust as I run, shouting at the top of my lungs, half to warn the rest about the ambush, half to drown out the sounds of gunfire at our backs. An explosion, and then pain. Blinding pain.

"I slept well. You?"

She took a while to check the monitor for my reply.

"Like a baby."

"What are you doing at work today?"

She was walking to the kitchen. There was another monitor there. I waited impatiently as she made coffee before checking to see if I'd said anything. I was the result of millions of dollars of research and they couldn't install text-to-voice ...

"You know, same old."

Small talk. I guess it beat the silence when she was away.

On, Brandon is com-	
ing by later. To check on	Ə NATURE.COM
you."	Follow Futures on
"Brandon?"	Facebook at:
"Doctor Johnson."	go.nature.com/mtoodm

Were they on first-name basis now? "Good that he's coming. I've been having

gaps in my playback."

"Really?" Katie seemed fascinated by her coffee mug. She put it in the sink.

"I should go now, gonna be late."

I watched her leave. An advantage of being like this was that my post-coma visual memory was literally photographic. I spent the rest of the day going through old memory so that I could report the problem precisely to Dr Johnson.

I went back to the day I was restored. Back then I had been disorientated and confused, I hardly noticed or cared about the details



of my surroundings. But now I observed Dr Johnson as he talked to Katie — he was wearing an outfit that probably cost my entire pay cheque back when I was still in the military.

"Thank you Doctor, you have no idea how grateful I am," Katie's voice cracked despite her best efforts.

"Let me reiterate that you cannot let anyone know about this,"

Doctor Johnson put a hand on Katie's shoulder. I couldn't tell if it was a sign of dominance or concern.

"... or else everyone will be clamouring for their consciousness to be preserved electronically, you must understand ..."

Katie nodded, no longer able to speak.

"To the rest of the world, Evan is dead." I went through each of the next 246 days in my memory banks. I knew that they were just memories, but it was painful watching Katie as she struggled through the first few months of having me in this form. Around day 182 she finally stopped crying. That's when the memory gaps started. Perhaps she hadn't stopped, and I was just consciously trying to forget ...

The door clicked open. Had eight hours passed already? Katie entered, followed by Dr (Brandon) Johnson.

"I don't feel comfortable doing this in front of him ..."

"Come on, you know we can just erase it later."

"Katie?"

He took off his leather shoes, placing them $\frac{1}{4}$ on the shoe rack without looking, as if he'd done this every day of his life, while he took Katie in his arms.

I understood now why they had not given me a voice. Katie resisted his grasp as they moved up to the bedroom. But she did not resist much.

"KATIE"

Brandon pushed my wife onto my bed, and tossed his shirt onto my camera.

I tried not to listen. An eternity passed before he came back into view.

"ARE YOU DONE YET?"

He had the gall to laugh as he read my speech log.

"Sorry, Evan."

He connected his laptop to my port and typed. It's funny how panic still feels the same, even though I no longer have adrenal glands.

"DONT"

"You know, you stop using punctuation when you're emotional. I should install autocorrect for you, don't you think?"

Behind him, I saw Katie with the covers pulled up to her chest. She looked tired. Perhaps tired of having a husband who was nothing more than a ghost in a machine; who could not offer her human touch; whose entire repertoire of expression was limited to 95 printable ASCII characters.

"Seeya," Brandon hit the return key.

I must have fallen asleep, because I woke from the same dream I have every time. The sun had not come up yet. I watched Katie as she slept.

Grace Tang is a graduate student in psychology at Stanford University. Writing short stories is one of her favourite forms of structured procrastination.