

REACH

IDEAS TO CHANGE THE WORLD | 2019

Changing the conversation

Inside CIFAR's new research portfolio



The memory hunters

Beauty in the gut of a fish

Can virtual reality change the way we understand ourselves?

CIFAR

CIFAR

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possession, and our worst enemy.

CIFAR

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About CIFAR

CIFAR is a Canadian-based, global charitable organization that convenes extraordinary minds to address science and humanity's most important questions.

By supporting long-term interdisciplinary collaboration, CIFAR provides researchers with an unparalleled environment of trust, transparency and knowledge sharing. Our time-tested model inspires new directions of inquiry, accelerates discovery and yields breakthroughs across borders and academic disciplines. Through knowledge mobilization, we are catalysts for change in industry, government and society. CIFAR's community of fellows includes 19 Nobel laureates and more than 400 researchers from 22 countries. In 2017, the Government of Canada appointed CIFAR to develop and lead the Pan-Canadian Artificial Intelligence Strategy, the world's first national AI strategy.

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President's Message

A beacon of light for the world

Science has the unique power to help us make sense of the world around us. The process, language and values of science are shared across nations, unifying our shared understanding of our world and its challenges. And science challenges accepted wisdom and ideology. It is these qualities that makes science an ideal voice for open, liberal democratic societies. In these troubled times, science's voice and Canada's voice are needed more than ever.

Canada is a beacon of light, a country known for its compassion, diversity, inclusion, openness to new ideas, and support of science and of evidence-based decision making. As an organization with firmly Canadian roots, CIFAR shares these characteristics. CIFAR was founded on the premise that convening the world's best scientists is essential to address the complex challenges facing science and humanity. Like CIFAR, Canada can be a convener of the world's nations for common cause to address the global challenges of our time.

It is in this context that I am happy to share our cover story in this issue of *Reach*, which introduces our new portfolio of research programs spanning four interdisciplinary theme areas: Life & Health, Individuals & Society, Earth & Space and Information & Matter. This is a significant renewal that will shape our research and impact over the next decade and beyond.

This issue also highlights the impact of our long-term com-

mitment to interdisciplinary, international research teams. You will read about CIFAR's three pioneers of AI — Geoffrey Hinton, Yoshua Bengio and Yann LeCun — who were recipients of the ACM A.M. Turing Award, commonly known as the “Nobel Prize of Computing,” and CIFAR Fellow Paul Romer, who earned the Nobel Prize in Economics. In “The Memory Hunters”, we introduce CIFAR Fellows Paul Frankland, Sheena Josselyn and Blake Richards and examine their search for the physical structure of individual memories in our brains. From the implications of virtual reality on brain science, to what we can learn from the microbes in fish, CIFAR's scope of inquiry highlighted in this issue is broad and deep.

This is an important time for CIFAR and for Canadian science leadership. With the closing of borders and minds happening elsewhere, Canada has been thrust into a new position: more than ever before we are attracting some of the world's brightest young people who are eager to change the world. Our responsibility is to provide young people with the opportunity to do just that.

As a country, we must double down on our investments in fundamental research. Those investments not only advance knowledge: they are the feedstock for innovation. The boom in private sector AI investments in Canada is just one example. We must also provide opportunities for our young people to change the



Dr. Alan Bernstein, O.C.,
President and CEO of CIFAR

world. As a student, my decision to become a scientist was motivated by the desire to use my brain to improve humanity. I think more women and young people from underrepresented groups would choose a career in science if they also saw it as one of the best ways to change the world.

Finally, we must kickstart a global conversation on how best to harness the power and unifying force of science to address the global challenges of our time: renewable energy, antibiotic resistance, urbanization, terrorism, environmental degradation, food, water and energy security, and rising income inequality, to name just a few.

We cannot let today's challenges and opportunities go by without leveraging Canada's growing reputation as a powerhouse of research and innovation to harness science to benefit the world. I hope you join us in this effort.

A handwritten signature in black ink, appearing to read "Alan Bernstein".

Dr. Alan Bernstein, O.C.
President and CEO, CIFAR

Honours

AWARD SPOTLIGHT

CIFAR fellow shares Nobel Prize in Economic Sciences

More than two decades ago, Paul Romer co-founded CIFAR's Economic Policy & Growth program, where he explored his ideas on the importance of technological change to drive economic growth. Those ideas led to the Sveriges Riksbank Prize in Economic Sciences in Memory of Alfred Nobel, which he shared with Yale economist William Nordhaus.

The prize brings the number of Nobel Prize recipients affiliated with CIFAR to 19.

The Economic Policy & Growth program helped establish the important field of endogenous growth theory, which explains why new ideas are so important for economic progress. Together, Romer and Nordhaus explained that new ideas just do not improve our society morally; they are the very engine of a well-functioning economy.



Nobel Prize recipient Paul Romer

ANNOUNCEMENT

Governor General named CIFAR viceregal patron



Her Excellency the Right Honourable Julie Payette, Governor General of Canada, is CIFAR's viceregal patron for the duration of her term in office.

Her Excellency the Right Honourable Julie Payette, Governor General of Canada, is CIFAR's new viceregal patron. By granting her patronage, the Governor General affirmed her support of CIFAR's work: creating transformative knowledge for the benefit of society.

"We are honoured that the Governor General, as The Queen's representative in Canada, has recognized the important work we do," says Dr. Alan Bernstein, president and CEO of CIFAR. Her Excellency has had an extraordinary career both as an astronaut and as a leader at NASA and the Canadian Space Agency.

The Governor General traditionally grants patronage to organizations in recognition of outstanding contributions to Canadian society.

QUANTUM MATERIALS

Taillefer earns Kamerlingh Onnes Prize

Louis Taillefer, the co-director of CIFAR's Quantum Materials program, was awarded the 2018 Kamerlingh Onnes Prize. The prize is awarded every three years for outstanding experiments that illuminate the nature of superconductivity.

Taillefer, a professor at the Université de Sherbrooke, was recognized for "illuminating the nature of superconductivity in unconventional superconductors."

Taillefer is the co-director of the Quantum Materials program, which recently conducted a renewal process with new membership and new scientific objectives.

LEARNING IN MACHINES & BRAINS

Turing Award honours CIFAR's "pioneers of AI"

In March, CIFAR Fellows Yoshua Bengio, Geoffrey Hinton and Yann LeCun were jointly awarded the prestigious ACM A.M. Turing Award for their development of "deep learning."

The award is often referred to as the "Nobel Prize of Computing," and is given by the Association of Computing Machinery for major contributions of lasting importance to the field. It carries a \$1 million prize.

"In 2004, with less than \$400,000 in funding from [CIFAR], Dr. Hinton created a research program dedicated to what he called 'neural computation and adaptive perception.'"

*— The New York Times
March 2019*

Bengio, Hinton and LeCun came together at CIFAR in 2004 when Hinton founded what is now the Learning in Machines & Brains program. The fellows were all interested in asking fundamental questions about how humans learn and how to apply that understanding to machines.

Their work together led to a number of advances, including a breakthrough artificial intelligence (AI) technique called deep learning, which is now integral to computer vision, speech recognition, natural language processing and robotics.

Hinton is a CIFAR Distinguished Fellow and an advisor to the Learning in Machines & Brains program. He is a vice-president and engineering fellow at Google, chief scientific advisor at the Vector Institute and emeritus professor at the University of Toronto.

Bengio is co-director of the Learning in Machines & Brains program, and a professor at the Université de Montréal. He is also a Canada CIFAR AI Chair and the scientific director at Mila.

LeCun is co-director of the Learning in Machines & Brains program, a professor at New York University and vice-president and chief AI scientist at Facebook. He is also a member of the CIFAR AI International Scientific Advisory Committee.



From top to bottom: Yoshua Bengio, Geoffrey Hinton and Yann LeCun

Advances

Highlights from our research programs

BIO-INSPIRED SOLAR ENERGY

Discovery links photosynthesis and solar energy



CIFAR fellows have discovered a mechanism used by photosynthetic plants and algae that makes photosynthesis more efficient. The discovery could result in better materials for solar energy.

In photosynthesis, a pigment energized by a photon passes that excitation energy to another nearby pigment, like passing the baton between runners in a relay. Scientists have long wondered how plants move this energy so quickly and efficiently.

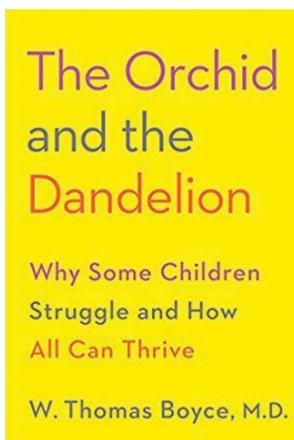
Using computer simulations and experimental data, CIFAR Fellows Alán Aspuru-Guzik of the University of Toronto and Gregory Scholes of Princeton University, found that a protein called PC645 controls where energy goes by tuning the vibrations of pigments to enhance energy transport along specific routes.

“You can imagine these proteins using the vibrations of different pigments like traffic signals that send excitations in one direction or another,” explains Doran Bennett, a post-doctoral fellow who collaborated on the research.

The findings were published in the *Proceedings of the National Academy of Sciences*.

CHILD & BRAIN DEVELOPMENT

Understanding “difficult” children



In his new book *The Orchid and the Dandelion*, W. Thomas Boyce explores the differences between two types of children: hardy “dandelion” children, whose innate resilience helps them to overcome difficult life challenges, and sensitive “orchid” children, whose success in meeting such challenges requires special care, given their emotional and perceptive natures.

“Good parenting matters to all children,” Boyce says. “Even dandelion children, but especially these little sensitive orchid children.”

Boyce is co-director of CIFAR’s Child & Brain Development program and leads the Division of Developmental Medicine at the University of California, San Francisco. The book was published in January 2019 by Penguin Random House.

GRAVITY & THE EXTREME UNIVERSE

Brilliant flashes from beyond the galaxy

McGill astrophysicist Victoria Kaspi, R. Howard Webster Foundation Fellow and director of CIFAR's Gravity & the Extreme Universe program, captivated a Toronto audience at the 2018 CIFAR-Massey Talk with her insights on how the Canadian CHIME telescope is unraveling mysterious "Fast Radio Bursts" from beyond the galaxy.

She explained that the brilliant flashes appear to be the result of cataclysmic events that took place billions of years ago in the universe's farthest reaches.

"The bottom line is, we don't know where they're coming from," says Kaspi.

The CHIME telescope is poised to be the world's top fast radio burst detector. It is located near Penticton, British Columbia and co-funded by several Canadian government partners, with additional support from NSERC and CIFAR.



R. Howard Webster Foundation Fellow and director of CIFAR'S Gravity & the Extreme Universe program, Victoria Kaspi, spoke about Fast Radio Bursts at the 2018 CIFAR-Massey Talk.

AZRIELI BRAIN, MIND & CONSCIOUSNESS

Beyond "levels of consciousness"



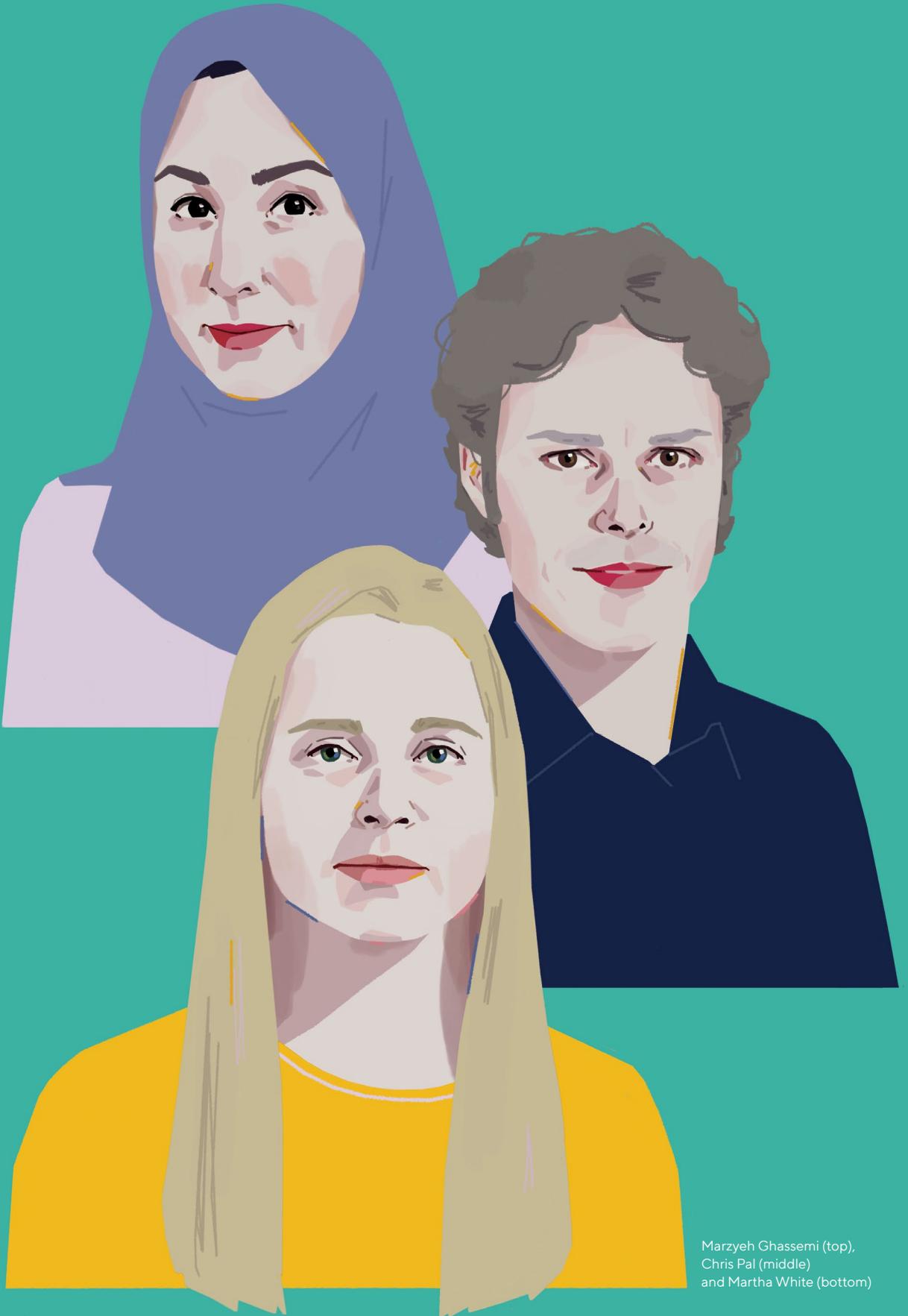
Some people think that drugs like lysergic acid diethylamide (LSD, also known as acid) and psilocybin ("magic mushrooms") elevate you to a higher plane of consciousness. Philosopher Tim Bayne, a fellow in CIFAR's Azrieli Brain, Mind & Consciousness program, argues that this is not a useful way to talk about the phenomenon.

Bayne, a philosopher at Monash University, and co-author Olivia Carter take aim at the notion that consciousness is a phenomenon usefully described by the terminology of "levels."

Although psychedelics might "increase the bandwidth of perceptual experience" (e.g., making colours feel more vibrant), they also impair attention and critical thinking (e.g., causing a reduced ability to understand proverbs).

The authors say that studying psychedelic experiences could help us understand the complex, multivariate phenomenon that is consciousness itself. The paper was published in *Neuroscience of Consciousness*.

Advances continues on page 36



Marzyeh Ghassemi (top),
Chris Pal (middle)
and Martha White (bottom)

In Conversation

Canada's role in the future of artificial intelligence

Illustration: María Hergueta

Reach asked three Canada CIFAR AI Chairs to share their thoughts on the future of AI, Canadian leadership in AI, and the good (and the bad) about the hype.

Marzyeh Ghassemi is a Canada CIFAR AI Chair and a faculty member at the Vector Institute. She was recruited from the U.S. to Canada and the University of Toronto, where she is a professor in the departments of computer science and medicine.

Chris Pal is a Canada CIFAR AI Chair and a faculty member at Mila. He is an associate professor at Polytechnique Montréal, and an adjunct professor with the department of computer science and operations research at Université de Montréal and a principal research scientist at Element AI.

Martha White is a Canada CIFAR AI Chair and a faculty member with Amii. White was recruited from the U.S. to the University of Alberta, where she is an assistant professor in the department of computing science. She is also the director of the University of Alberta Reinforcement Learning and Artificial Intelligence Lab.

“Investing in training is one of the smartest moves that any country can make.”

— *Marzyeh Ghassemi*

Reach: Tell us about your area of research?

Martha White: I work on reinforcement learning, which is a form of machine learning. The idea is that a [software] agent doesn't get to know much information about its world and it attempts to learn how to take action in that world through trial and error interaction. My particular expertise in this area is looking at how the agent can build up a representation or knowledge about its environment so that it can learn how it should take action in a more intelligent way.

Marzyeh Ghassemi: I am focused on identifying what kind of models are healthy in a health care setting. We've seen great advances in application areas like vision, speech and natural language but we're still looking for structures and models that work well based on how health data is generated. I am trying to harness some of the power of the observational data that we have in the Canadian health care system and use machine learning and causal inference methods to create more accurate and scalable recommendations for health.

Chris Pal: I've been doing AI research for over 20 years. I've spent a lot of time on computer vision which has applications for medical imaging. I've

conducted research on segmentation, specifically segmenting brain tumours in medical images. We're looking at deep learning to improve segmentation accuracy of tissue types, which is very useful for clinical decision making.

Reach: What does the future of AI look like?

Marzyeh Ghassemi: Right now we are moving from a space in which everybody is amazed at what AI can do — whether it's speech recognition, predicting mortality or self-driving cars — to a space in which we're starting to care about the nitty-gritty details of how possible technologies might get implemented. That's not something that incentivizes all researchers. AI and machine learning models can work in many settings. We can understand whether machine learning can make predictions about people of all races with equal accuracy, and whether it can be deployed in different countries that have different health care practices without impacting underlying health care.

Martha White: We will start to see that machine learning and reinforcement learning become part of the solution strategies people use to tackle regular problems on a daily basis. Similar to how kids in school today are taking computer

“Today, everyone is interested in talking about what AI might be able to do and it’s encouraging people to think innovatively, and that’s a very positive thing.”

— Chris Pal

programming early on and computer science is seen as a standard skill that many people have, we’ll start thinking of modelling and prediction tools as a standard skill set, and we should absolutely be introducing it earlier at the undergraduate level.

Chris Pal: There’s tremendous potential for AI in health. There are a number of organizational problems that can benefit from AI if we get it right, particularly in medicine. How do we get data out of a clinical setting into the hands of researchers in a way that respects privacy and enables biases to be corrected? The Canada CIFAR AI Chair program helps because researchers can focus on fundamental research and also have access to many resources critical to fully realizing the potential of AI.

Reach: Canada made headlines as the first country to adopt a national AI strategy (the CIFAR Pan-Canadian AI Strategy). What makes Canada suitable to lead in AI?

Marzyeh Ghassemi: When I was at NeurIPS [the Conference on Neural Information Processing Systems], there was a set of playing cards mimicking Cards Against Humanity and one card

asked: “Have you collaborated with the Canadian mafia?” It was a tongue-in-cheek reference, but it pointed out that many of the advances led by researchers in Canada have paid off in terms of neural network architectures and inference methods. This is a result of people being able to work on ideas that were not hot at the time. The payoff that we’re experiencing now is the result of investing early on in allowing people to do the research that really speaks to them.

Chris Pal: It’s a really critical time period where a lot of experienced researchers would have moved on to industrial research activities, resulting in a lot of attrition in academia. Because there is a lot of support in Canada around academic research in AI, more people are working on academic research, and the timing of that is critical. It means that more students will be trained in Canada.

In our case with the creation of the AI Institutes, Amii, Mila and Vector — that’s already starting to have a very positive effect on the environment under which many people with related, complementary interests are co-located. That allows for a lot of the critical mass effects that are not possible in smaller groups. I have collaborations with people outside of

"The focus in Canada is much more on highly qualified personnel, training individuals and funding people rather than projects."

— *Martha White*

Mila's traditional areas because of the critical mass of talent we have in Canada. We're on the radar globally.

Martha White: When AI came on the horizon, fundamental research continued to be funded reasonably well in Canada. And that had a compounding effect because more researchers wanted to come here for research.

Reach: **The CIFAR Pan-Canadian AI Strategy focuses on supporting talent and training for the next generation, whereas other national strategies support commercialization and take a more industrial focus. Is ours a good approach?**

Marzyeh Ghassemi: Investing in training is one of the smartest moves that any country can make. The kinds of people that are going to contribute most to fundamental questions and research want to work on challenging problems and they want to know what other like-minded people have done. It's a huge draw. Bringing in smart people allows them to innovate. That's going to pay off disproportionately more than any other investment you could make.

Martha White: I agree completely. Coming from the U.S. system, where I was for a couple of years, I really feel like the focus in Canada is much more

on highly qualified personnel, training individuals and funding people rather than projects. In other countries, there is a lot less funding for students directly and that calls for more specific research projects that tend to pigeonhole researchers, rather than permitting an open-ended training environment where people can grow and develop in a lot of different ways.

Chris Pal: To fuel startups you need people with a lot of skills, which you almost only get by doing. A lot of times you learn those skills through graduate research or by working in advanced industrial research labs. When students go into a strong graduate program, that's when they start to understand what innovation is. You want to invest in people rather than innovation. That's a powerful component of our funding structure in Canada.

Reach: **What do your next five years as a Canada CIFAR AI Chair look like?**

Marzyeh Ghassemi: In the next five years, I would like to see Toronto, and Canada, really start to lead the charge in machine learning for health. We have some amazing raw resources. We have an inclusive health care system that all people have access to; that's not true of other countries. We also have fantastic hospitals in the Greater Toronto area with access to data from diverse communities and globally ranked medical

schools. One of the things I'm most excited to do is to leverage my AI Chair position towards bridging those communities. Those who train in the medical field generally tend to publish in separate venues and are not always well connected to training and opportunities for publishing research with computer scientists.

I was on the fence when choosing which university to go to, and what really convinced me to come to the University of Toronto and Vector was the opportunity to work with Roger Grosse and Jimmy Ba [also Canada CIFAR AI Chairs]. The fact that I was going to work with colleagues of that calibre and could advise and brainstorm with students created a strong pull. All of the graduate students I'm admitting [into my research projects] have been offered positions at MIT, Stanford University or Carnegie Mellon University. They are choosing us [University of Toronto] over some very competitive schools because of the access to the talent they will have and the ability to work within a larger research mandate.

Chris Pal: The notion of how CIFAR funding can help a professor connect the dots to applications is a concrete impact. As Canada CIFAR AI Chairs, we have funding that is very flexible and stable for five years. It allows us to bring on a PhD student and focus attention on research that will have an impact on the real world. The AI Chairs program allows researchers to maximize impact in whatever way is the most appropriate.

Martha White: Stable funding means that you can work on problems that are important to you. Over the next five years, I'm hoping to make connections that will help put reinforcement learning in practice for more problems. There are a few fundamental challenges but I think we are on the cusp of getting past some of those challenges where we can deploy in more settings. I am investing in this physical system and we'll be trying different algorithms on that system. I'm hoping within the next five years to get some insight out into the real world with some robust algorithms.

Reach: AI is quite the buzzword these days. Should we be excited about AI or is it just hype?

Marzyeh Ghassemi: Yes, we should be excited. As a community we need to make sure we mitigate

some of the damages from that hype. We, as researchers, have to be very realistic about the challenges and the possible negative impact because all new tools have benefits and drawbacks. And we can't account for certain information without bringing humans into the equation. For example, medical doctors with a decade of training need to be involved in assessing the AI tools used in medical settings. We also need to remember that people are biased and therefore models will also be biased.

Martha White: I'm excited that our society is moving to a data-driven one where we actually recognize the utility of gathering data. But it puts the onus on the machine learning community to avoid over-claiming too much because that's never been a good idea.

Chris Pal: I think hype can have a positive impact to the extent that it gets people excited about innovating. It helps people open their mind to doing things in a different ways. One positive aspect of the AI hype is that even a decade ago, if you wanted to get in front of industrial partners, it was almost impossible. Today, everyone is interested in talking about what AI might be able to do. It's encouraging people to think innovatively, and that's a very positive thing.

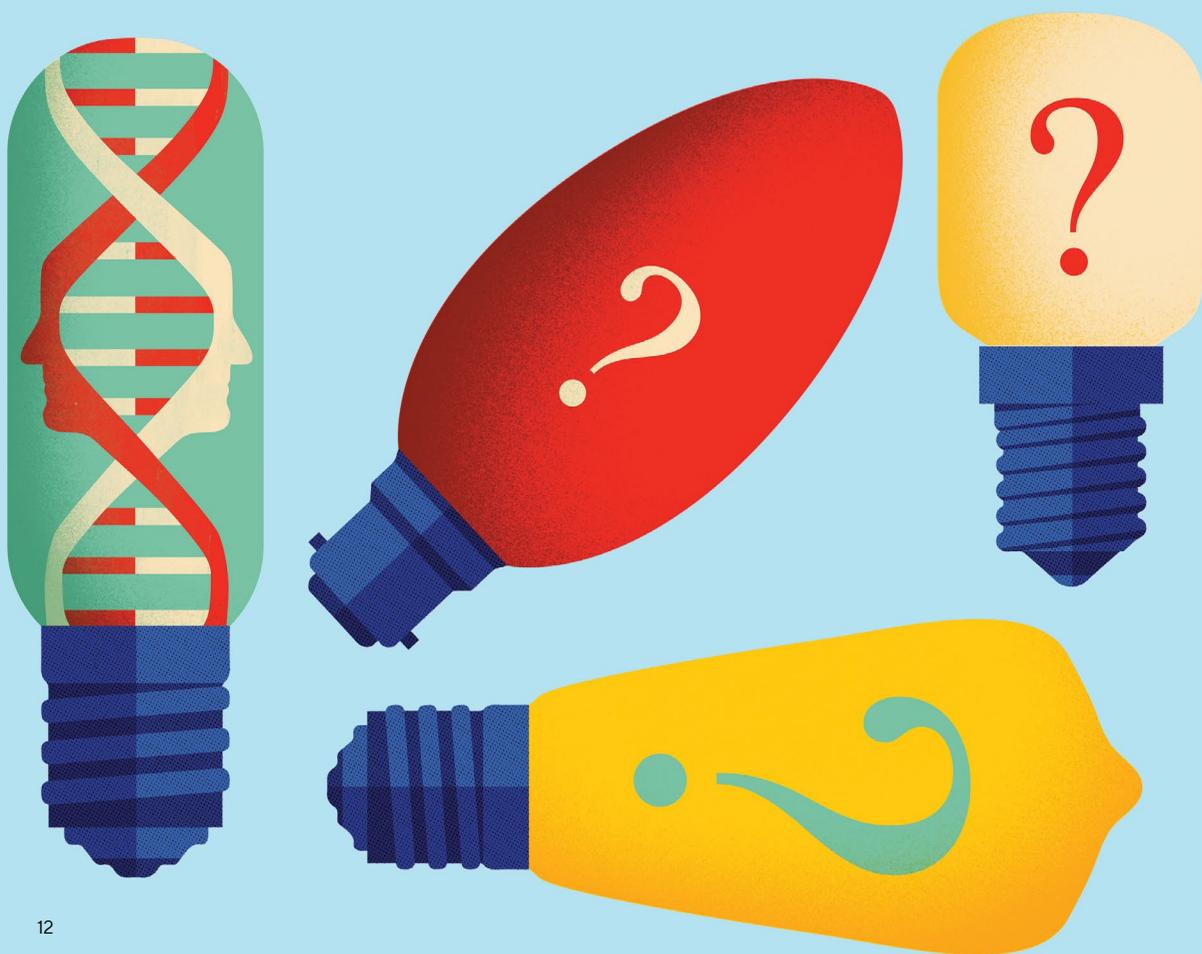
This interview was conducted by Krista Davidson. It has been edited and condensed.

In 2017, the Government of Canada appointed CIFAR to develop and lead the Pan-Canadian Artificial Intelligence Strategy, the world's first national AI strategy.

CIFAR'S new research portfolio tackles science and humanity's most important questions

Changing the conversation

Lead illustration: Mitch Blunt / Program illustrations: Kotryna Zukauskaite





Life & Health

Top scientists and scholars from around the world have new opportunities for collaboration with the announcement of CIFAR's new research portfolio. The 13 CIFAR research programs address critical questions across four interdisciplinary theme areas: Life & Health, Individuals & Society, Information & Matter and Earth & Space.

"For almost 40 years, CIFAR has supported fundamental research and innovation across borders and disciplines," says Dr. Alan Bernstein, president and CEO of CIFAR. "Our new portfolio tackles complex, high risk questions across disciplines and countries. Our goal is to advance knowledge and understanding."

Each program addresses complex questions and engages international and interdisciplinary networks of researchers and scholars. CIFAR provides sustained, long-term commitment by convening meetings and providing catalyst funds for new directions of inquiry. The environment of intellectual freedom fosters deep collaboration and trust between CIFAR fellows. At meetings, they share and critique preliminary findings and data, often prior to publication, and provide insights from peers across disciplines.

"I think CIFAR is going to be particularly catalytic for us," says Barbara Sherwood-Lollar, professor of earth sciences at the University of Toronto and the co-director of the new Earth 4D: Subsurface Science & Exploration program. "The program will enable us to bring together people from extremely different perspectives, and then give them the intellectual freedom to challenge each other, challenge themselves and change thinking."

While CIFAR's impact on the research process is immediate, wider social benefits can take longer to be realized. CIFAR bridges this gap by connecting its research programs to global thought leaders outside of academia through knowledge mobilization. These exchanges enrich research and stimulate new social, economic and technical innovations. For example, CIFAR fellows in the Humans & the Microbiome program are working with public health leaders to create the first educational curriculum on the microbiome and healthy living.

FUNGAL KINGDOM: THREATS & OPPORTUNITIES



What might we uncover in an unknown biosphere?

Co-directors: Leah Cowen (University of Toronto) & Joseph Heitman (Duke University)

Founded: 2019

This program will study the genetic bases of important properties in fungi: their evolution and how they help and hurt plants, wildlife and humans. CIFAR fellows and CIFAR Azrieli Global Scholars will ask fundamental questions, including: Why do some fungi cause disease? How can we predict the next emerging pathogen? What are key features of a vaccine to prevent fungal infections?

Tapping into the biology of fungi is crucial to protecting humans and our environment. It can avert the threat of biological warfare and epidemics. It can help us develop new classes of drugs, vaccines and treatments for antimicrobial resistance. It means we can grow stronger crops and produce better food and biofuels.

Watch interviews with program research directors at youtube.com/c/CIFARVideo

HUMANS & THE MICROBIOME



How do microbes that live in and on us affect our health, development and even behaviour?

Co-directors: B. Brett Finlay (University of British Columbia) & Janet Rossant (University of Toronto)

Founded: 2014

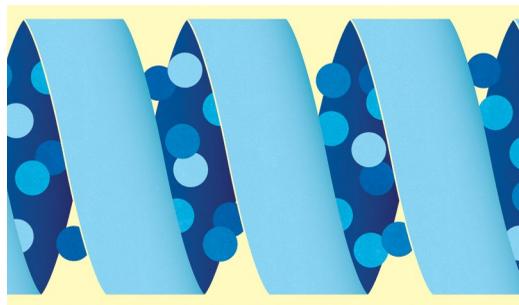
Microorganisms cover our skin and fill our guts. These bacteria, viruses and fungi — collectively called the human microbiome — were, until recently, only considered interesting if they led to disease.

But a growing body of research shows that a properly functioning microbiome has tremendous impact on human health. For instance, the ability to maintain a healthy weight is probably influenced significantly by the microbiota in your gut. A mother's microbiome could affect the healthy development of her fetus's brain. And researchers are learning about the effects of colonization on human groups by examining the microbes in dental tartar of human remains in West Africa.

This program brings anthropologists, biologists and other scholars together to provide biocultural context to host-microbiome interactions. The CIFAR fellows and CIFAR Azrieli Global Scholars are asking new questions about what aspects of individual and societal behaviour are critical to understanding the role of the microbiome in human health and development.

By gaining a complete picture of the relationship between the microbiome and human culture and biology, CIFAR's Humans & the Microbiome program will open up new understanding of the roots of disease, issues of early development, our susceptibility to future pandemics, and even human behaviour.

MOLECULAR ARCHITECTURE OF LIFE



How does life originate and what are the processes that make it possible?

Co-directors: R.J. Dwayne Miller (University of Toronto, Max Planck Institute) & Oliver Ernst (University of Toronto)

Founded: 2014

What is life? How did it originate? What keeps it going? These questions have puzzled humans for thousands of years. With new technology and a unique interdisciplinary approach, the Molecular Architecture of Life program is finding answers.

Until recently, we could only understand the processes of life by looking at static pictures of its building blocks. But life is dynamic, and processes are in constant states of change. Now we have tools such as ultrafast imaging that can record molecules in motion and give scientists the ability to observe living systems at a level that was previously unknown.

Understanding levels of biological function across vastly different lengths and timescales — from the movement of a single atom in a quadrillionth of a second to the much slower processes of cell growth and regulation — is giving CIFAR fellows and CIFAR Azrieli Global Scholars in this program new insights into the processes of life.

Individuals & Society

AZRIELI BRAIN, MIND & CONSCIOUSNESS



What are the origins and mechanisms of consciousness?

Co-directors: Melvyn Goodale (Western University) & Adrian Owen (Western University)

Founded: 2014

The quality of our consciousness is what sets us apart from other species, and seems to be one of the defining traits of being human. Yet the nature of consciousness remains a mystery. The Azrieli Brain, Mind & Consciousness program grapples with the fundamental underpinnings of consciousness, and relates the findings to biology on the one hand and to philosophical questions on the other.

Technological advances in medical imaging make it possible to see the brain in action. The new technology for the first time gives an opportunity to scholars from fields as different as genetics, cognitive neuroscience, artificial intelligence and philosophy of mind to come together and work to understand consciousness. By creating the opportunity for deep collaborations, the CIFAR program will allow fellows to solve one of the most profound questions about human nature.

The Azrieli Brain, Mind & Consciousness program is developing a framework to help fellows from across disciplines understand how our brains give rise to consciousness and our unique perspective on the world around us.

BOUNDARIES, MEMBERSHIP & BELONGING



Is it possible to have a world without “us” and “them”?

Co-directors: Irene Bloemraad (University of California, Berkeley) & Will Kimlycka (Queen’s University)

Founded: 2019

All societies distinguish members from non-members. Indeed, evolutionary biology and psychology suggest that humans are predisposed to distinguish “us” from “them,” and the process can lead to increased trust and cooperation towards members. But it can also lead to prejudice, suspicion and injustice towards non-members.

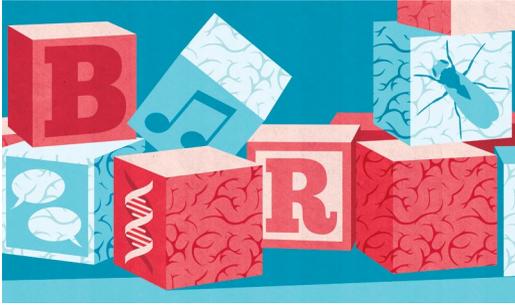
The Boundaries, Membership & Belonging program explores ways to create and empower groups without falling back on ideas that produce pernicious divisions and hierarchies.

As migration and globalization weaken traditional boundaries around the world, many people are searching for a sense of belonging and are staking claims to membership. Recent political events show that if a new, inclusive sense of “we” is not developed, people may turn instead to appeals based on exclusionary boundaries of ethnicity, religion and class.

The program brings together leading social scientists and political and legal theorists who will collaborate to make sense of membership politics. They ask whether we can re-draw boundaries in a way that is inclusive without losing solidarity and the possibility of collective action. In short, why membership matters in a globalizing world.

Individuals & Society

CHILD & BRAIN DEVELOPMENT



How do childhood experiences affect lifelong health?

Co-directors: Candice Odgers (University of California, Irvine) & Takao Hensch (Harvard University)
Founded: 2003

One child is born to a wealthy family. Another is born into a family living in poverty. The child born into wealth will probably live a longer and healthier life — but not always. Some children born into poverty have a resilience that enables them to thrive throughout their lives despite the hardships they experienced when very young.

The Child & Brain Development program examines the effect of the early environment on children, and how adversity can have lifelong effects on health and development. Over the past decade, CIFAR fellows and CIFAR Azrieli Global Scholars in this program have transformed our understanding of the interplay between nature and nurture, and generated important findings related to the biological underpinning of our early experiences as children.

Recent advances in technology, increased access to data, and an interdisciplinary environment are creating new opportunities for the program's fellows and scholars to find the answer to why some children thrive and others do not.

INNOVATION, EQUITY & THE FUTURE OF PROSPERITY



How can innovation be beneficial to all?

Co-directors: Dan Breznitz (University of Toronto) & Susan Helper (Case Western Reserve University)
Founded: 2019

Innovation can promote economic growth and social and cultural well-being. However, innovation is often conceived and implemented in a way that leads to unequal distribution of its benefits. This program takes a multidisciplinary and cross-national look at how, why, and when the benefits of innovation aren't always broadly shared.

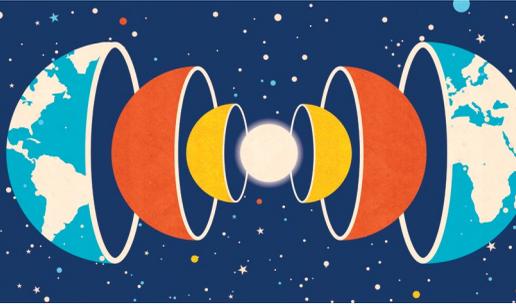
The benefits of innovation tend to be concentrated in a limited number of industries, regions and hands. Innovation that exacerbates — rather than reduces — inequality can undermine public support for science and innovation and contribute to broader political alienation.

CIFAR's Innovation, Equity & the Future of Prosperity program examines how the policies used to generate and diffuse innovation affect the distribution of opportunities and outcomes in society. It also looks at which institutions and other factors facilitate or impede the development and implementation of distribution-sensitive innovation policies, programs and practices.

The program will develop knowledge that can be used to design and implement innovation policies, programs and practices that support equitable economic growth and fair distribution around the globe.

Earth & Space

EARTH 4D: SUBSURFACE SCIENCE & EXPLORATION



How do we understand the life, groundwater and environment lying deep below the surface of a planet?

Co-directors: Barbara Sherwood-Lollar (University of Toronto) & Jack Mustard (Brown University)
Founded: 2019

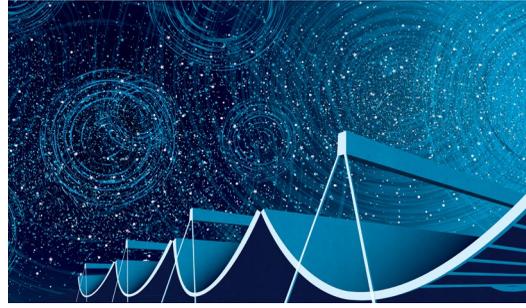
Beneath our feet is a vast, unexplored world consisting of up to tens of kilometres of thick crust containing water, gases, nutrients, resources and various forms of life.

So far we have investigated only a tiny fraction of the Earth's subsurface, although it contains critical information needed to understand the complexities of chemical, physical and biological interactions on the Earth's surface — and our everyday world.

Investigating the interactions between the subsurface and the surface on Earth, the only planet we have ready access to, will inform and expand our understanding of planetary evolution and the possibility of finding life on other planets and moons in our solar system — and beyond.

The Earth 4D program's interdisciplinary team of CIFAR fellows and CIFAR Azrieli Global Scholars focuses on the themes of water, life and space, with time as a fourth theme and overarching lens. No other research group has formalized this broad, disruptive approach and built a diverse intellectual community committed to tackling this challenge.

GRAVITY & THE EXTREME UNIVERSE



What is the nature of extreme gravity, and how can it help us understand the origin and evolution of the universe?

Director: Victoria Kaspi (McGill University)
Founded: 1986

For most of human history, our only information about the universe came from visible light. Later, we learned to detect other forms of electromagnetic radiation, like infrared and radio waves. Today we can finally detect gravitational waves, and that opens the door to fundamentally new ways of observing and understanding the universe.

Gravitational waves are the “ripples” created in spacetime by massive accelerating objects. Combined with other observations, they give researchers brand new tools to understand what's happening in the universe. Questions include the nature of extreme gravity, the origin and evolution of the universe, and the structure of compact objects such as black holes and neutron stars, as well as profound questions about fundamental physics and astrophysics.

CIFAR's Gravity & the Extreme Universe program unites world-leading researchers from a number of relevant fields who are working together and taking advantage of this wealth of new information.

Information & Matter

BIO-INSPIRED SOLAR ENERGY



What can nature teach us about using energy from the sun?

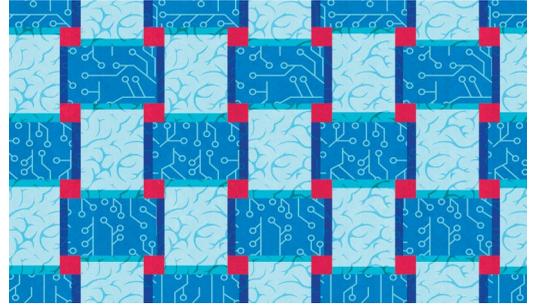
Director: Edward Sargent (University of Toronto)
Founded: 2014

Humans consume one trillion watts of energy annually, and the amount will double by 2050. The fossil fuels that we use to generate most of that energy contribute to global warming, making it vital that we develop renewable energy. This includes finding better ways to generate and store energy from the Sun.

Fortunately, nature has lessons to teach us. The process of photosynthesis, which plants use to turn the Sun's energy into fuel, has been optimized over billions of years of evolution. CIFAR's Bio-inspired Solar Energy program examines the lessons of photosynthetic organisms to create better ways of harvesting, transporting and storing light energy.

The program brings together CIFAR fellows and CIFAR Azrieli Global Scholars from across disciplines to work on questions that could lead to more efficient solar panels, better batteries, new green fuels and other technologies that will feed the world's need for energy without contributing to climate change.

LEARNING IN MACHINES & BRAINS



How do we understand intelligence and build intelligent machines?

Co-directors: Yann LeCun (New York University, Facebook) & Yoshua Bengio (Université de Montréal), Associate Director Hugo Larochelle (Université de Sherbrooke, Google)
Founded: 2004

Artificial intelligence (AI) has created a global industry that touches on every business sector imaginable — from improved banking security to innovation in farming, education, law enforcement, health care, space exploration and customer service.

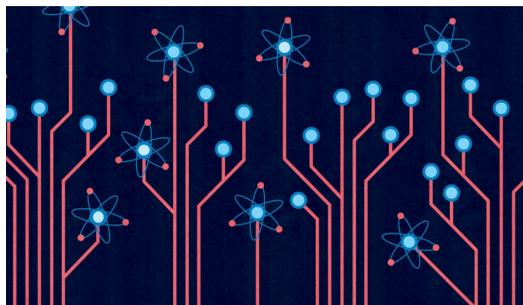
The Learning in Machines & Brains program played a central role in the AI revolution by examining how artificial neural networks could be inspired by the human brain and developing the powerful technique of deep learning.

Now the program is expanding our understanding of the fundamental computational and mathematical principles that enable intelligence through learning, whether in brains or in machines.

Current AI systems are limited in their ability to understand the world around us. This program attacks those limitations by going back to basic questions rather than focusing on short-term technological advances. This fundamental approach has the dual benefit of improving the engineering of intelligent machines and explaining intelligence.

Information & Matter

QUANTUM INFORMATION SCIENCE



How do we harness the power of quantum mechanics to improve information processing?

Co-directors: Aephraim Steinberg (University of Toronto) & David Poulin (Université de Sherbrooke)
Founded: 2002

Computing technology has become so much a part of everyday life that most of us never consider just how amazing the technology is, or the extent of the technological revolution it has created. The next revolution is around the corner: Quantum Information Science.

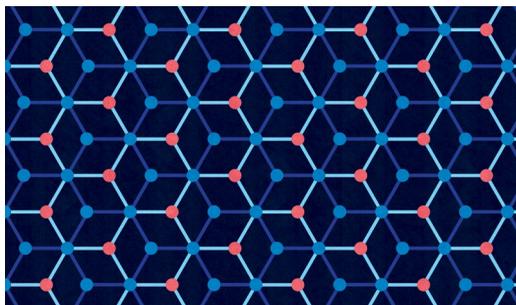
Computer science, aided by quantum mechanical inventions such as the transistor and the laser, has developed further in the past 50 years than we could have imagined. But current computers are binary: a switch is either on or off, one or zero. In this way, they are limited in what they can do.

Quantum Information Science offers the potential to approach quantum mechanics and computer science through a powerful new frame. Potential applications range from cryptography, code-breaking, design and simulation of materials and chemicals, to fast optimization and machine learning techniques.

Many nations are already investing billions of dollars in the field, and spinoff technologies using Quantum Information Science are already being commercialized, including sensors, amplifiers and detectors with applications ranging from medical imaging to oil exploration.

This program connects theorists and experimentalists who address the field's most fundamental questions. This approach will pay dividends by encouraging radically new ideas, at the same time engaging with industry to search for new applications to maximize the positive impact of Quantum Information Science on society.

QUANTUM MATERIALS



How could quantum technologies transform our society?

Co-directors: Leon Balents (University of California, Santa Barbara) & Louis Taillefer (Université de Sherbrooke)
Founded: 1987

The progress of human civilization is intertwined with its ability to make and use materials. We even distinguish the ages of humanity by the material innovations, from the Stone Age to the Bronze Age, the Iron Age and now the Silicon Age.

This program is working towards bringing on the Quantum Age. It explores the fundamental science behind quantum matter — the resource for the quantum technologies that will define the 21st century. These technologies could include room-temperature superconductors that would carry electricity without any energy loss and revolutionize power transmission. Or quantum tech could include the quantum computer that would exploit the entanglement of multiple electrons, resulting in a powerful way to manipulate information. There are also the quantum materials innovations we cannot yet imagine.

This program includes CIFAR fellows & CIFAR Azrieli Global Scholars with three main areas of expertise: materials scientists, who create new materials; experimentalists, who probe materials' properties; and theorists, who invent new concepts and develop our mathematical understanding. Together, they are developing the next big breakthroughs.

“If only there could be an invention that bottled up a memory, like scent. And it never faded, and it never got stale. And then, when one wanted it, the bottle could be uncorked, and it would be like living the moment all over again.” — Daphne Du Maurier, Rebecca

The memory hunters

by Cynthia Macdonald



Memory is at once our most valuable possession and our worst enemy. At any stage in life, it can be fleeting, unreliable, painful or absent. Which is why, like Du Maurier's melancholy narrator, many of us wish our memories lived outside of us: we could then choose their fate, saving the best and consigning others to the trash.

For CIFAR Fellows Sheena Josselyn and Paul Frankland, this kind of control is already happening. In their integrated lab at the Peter Gilgan Centre at Toronto's Hospital for Sick Children (SickKids), the married neuroscientists have been able to implant and enhance memories in their rodent subjects, as well as remove them. New tools allow them to see groups of neurons that represent single memories. They've also been able to eliminate terrifying recollections and contribute significant insights to the fight against Alzheimer's disease.

Memory is mysterious territory indeed, and for all their progress, Josselyn and Frankland admit it remains something of a black box. Although the box is getting more transparent all the time, it will be some years before their research results can be translated from animals to humans. Josselyn says that before we can treat major memory

“We are the sum total of our memories — I mean, that's really who we are. It's the essence of what makes us human.” — Sheena Josselyn

disorders, “we have to be able to understand how the brain works at the most fundamental level. We won't be able to go forward with clinical treatments until that happens.”

The study of memory stretches back thousands of years, but it wasn't until the 20th century that anyone considered looking for a physical trace of it in the brain. Studying psychology as an undergraduate at Queen's University, Josselyn first heard the name of one such person: Karl Lashley. Starting in the 1920s, the American scientist spent many fruitless years searching for

the engram — an elusive neural structure said to house a memory in the brain. Using crude tools that were state-of-the-art at the time (similar to soldering irons), Lashley induced brain lesions in rodents, then watched to see whether they'd forget how to navigate the mazes on which he'd trained them.

In the end, Lashley never found his magic engram, though his research revealed much about the brain (including the fact that memory is stored in various places, not just one). His example stayed with Josselyn, who, after receiving her PhD in psychology, spent time doing clinical work with sex offenders in prison. She says the work was interesting but somewhat rote. Feeling restless, she yearned to make new discoveries. The terrain that most appealed to her was memory.

“It seemed the most fundamental thing,” says Josselyn, who is a fellow in CIFAR's Azrieli Brain, Mind & Consciousness program. Still enchanted by her chosen field over 20 years later, she says, “We are the sum total of our memories — I mean, that's really who we are. It's the essence of what makes us human.”

In the modern era, Josselyn felt she might be able to succeed where Lashley had not. “He's kind of overlooked now, because he didn't find what he was looking for and his tools were very blunt,” she says. “But he really had some important ideas. So what I've tried to do in my career is apply new techniques to answer questions that couldn't be answered in the old days.”

Today, in the midst of what Josselyn calls a “renaissance period” for neuroscientists, one of these tools is the viral vector. Using this approach, scientists can re-engineer viruses to express genes of interest (rather than viral genes). In this way, neurons deep in the brain can be made to overexpress a transcription factor called CREB, which has been linked to memory.

During her post-doctoral work with Mike Davis at Yale and Alcino Silva at UCLA, Josselyn showed that increasing CREB levels in a small portion of neurons deep within the brains of mice enhanced fear memory — an easy form of memory to study, because it's so strong. Evolution has wired us to avoid danger; children may need repeated practice to remember multiplication

tables, but easily recall the experience of touching a hot stove. Emotional memories of this type are stored in the amygdala, an almond-shaped structure located deep within the temporal lobe.

In these experiments, mice were given a small foot shock, paired with a sound tone. “The foot shock isn’t enough to hurt them, just enough to scare them,” Josselyn says. The shock caused them to exhibit a characteristic freezing response. CREB handily intensified the mice’s memory: when the sound tone was played on its own, they instantly froze in fear of the remembered shock.

Another significant find? These improved memories could now be seen by directly examining groups of neurons.

“For the first time, we could really look at what those cells were doing,” Josselyn says. “Certain cells seemed to be recruited over others: into this memory engram, and not for those things the mice learned before or after the manipulation that increased CREB.” Lashley’s engram had been found. Confirmation of this came later at SickKids, where Josselyn was able to remove a selected fear memory by eliminating the neurons that represented it.

Adding memories. Taking them away. If this type of cerebral modification were made available to humans, would it be a bane or a blessing? The answer is complicated. On the one hand, if certain memories are awful enough to interfere with our quality of life, the case for their excision is clear. On the other, there’s a healthy reason why we remember terrible events more clearly than pleasant ones: to stop us from making the bad choices that may have sparked their creation.

As for the enhancement of memory — well, there can’t be anything wrong with that. Or can there? A 2017 paper co-authored by Paul Frankland suggests that the answer isn’t so easy.

Frankland’s office is right next door to Josselyn’s. Like his wife, he holds a PhD in psychology. The pair met while completing their doctorates and seem perfect complements to each other. The Cleveland-born Josselyn is talkative and funny, while Frankland, a native of England, speaks with

Adding memories. Taking them away. If this type of cerebral modification were made available to humans, would it be a bane or a blessing?

polite reserve and care. Both have great memories, of course. She knows every Madonna lyric; he’s a walking encyclopedia of soccer statistics.

Frankland, a fellow in CIFAR’s Child & Brain Development program, has long been absorbed by the question of neurogenesis, the term for new nerve cell formation in the brain’s hippocampus (it also takes place in the olfactory bulb). Less than 100 years ago, adult neurogenesis was deemed impossible. Even today, some neuroscientists are skeptical about whether it occurs naturally in adult humans.

Frankland is not among them. Two years ago, he and CIFAR Fellow and Canada CIFAR AI Chair Blake Richards published a literature review in *Neuron*, with the Daliesque title “The Persistence and Transience of Memory.” It was widely picked up by the popular press, with most articles headlined by some variation on the idea that “forgetting makes you smarter.”

The review referenced work from Frankland’s own lab, showing that as new neurons are formed in the hippocampus, existing circuits are remodelled. This process overwrites old memories, making them harder to access. But that, says Frankland, isn’t necessarily a bad thing.

“Certain kinds of forgetting are beneficial,” affirms Frankland. “The world’s changing all the time, so you don’t need outdated information from a week, a month or two years ago. It’s no longer useful to you.” Frankland adds that you wouldn’t want to remember events perfectly anyway, because then you’d expect subsequent events to be identical. That would just be confusing.

His co-author Blake Richards offers an example. “Imagine that you work somewhere where you’ve got an intern named Matt, who then leaves. The next year, an intern named Mike starts. But if your brain stores the name ‘Matt’ permanently, every

time you want to speak to Mike you're going to call him Matt. An easier solution is just to forget Matt's name — why bother storing it, if you're no longer working with him? Then you'll have a higher chance of getting Mike's name right."

In other words: a good memory is not necessarily one that's packed with information, but one that selects for the most useful information. And it can only do that by erasing data that isn't relevant anymore.

If adults do this regularly, it turns out that children do it even better. A key focus in Frankland's lab is the question of infantile amnesia, a term coined by Freud. Most of us can't remember anything from before the age of three, and very little from before the age of seven. Yet small children have much better memories than adults for the details of their experiences. Frankland wanted to explore this, and the couple's daughter Charlotte, now 10, provided part of the inspiration.

"... when you try to design an AI agent and get it to interact with the world, you rapidly discover the need for memory." — Blake Richards

One day about seven years ago, the family was at the Bowmanville Zoo in Ontario, Canada. After being frightened by a loud duck near the pond, Charlotte was relieved when Frankland scooped her up and headed for a more benevolent animal.

"For months she would tell people this story about the zoo," he says. "Then one day it was completely gone. She didn't remember it at all."

Frankland led a team investigating why this might be. They found that young mice experience neurogenesis in the hippocampal region at a much higher rate than adults do, making them superior at encoding the details of their experiences — but also inclined to forget them faster.

Still, the question remains: are those vanished memories truly erased, or just hard to retrieve? Frankland's most recent experiment supports

the latter theory. He tagged clusters of neurons representing memories of locations that mice appeared to have forgotten. Then, weeks later, he stimulated the clusters. As if by magic, the mice once again recognized the forgotten places. Their recovery was incomplete, though, suggesting that the experience wasn't perfectly preserved.

"We know this from our own experience," Frankland says. "Even really important memories are not as detailed and precise as we imagine. When Sheena and I got married, or when our daughter was born — I have a sense of how those days unfolded, and what my feelings were. But I don't remember those events with the kind of precision I have when remembering my flu shot this morning."

Still, when memories are called up repeatedly, the synaptic connections supporting them are strengthened. This may explain people like Jill Price, the much-written-about hyperthymestic who intentionally remembers most days of her life in perfect detail. A person with hyperthymesia spends large amounts of time thinking about their own past, and has an extraordinary ability to remember events from it. Most people, though, are too busy living in the present, creating new memories and sacrificing old ones.

Much of what we know about memory comes from research on model animal species, such as snails, zebrafish and mice. Can the extraordinary discoveries neuroscientists have made with animals be translated to humans? There is very good reason to think so. The era of genomic sequencing has revealed greater similarities between mice and humans, for example, than had been previously thought. It has also allowed for gene editing, another potential avenue of discovery and cure. Humans share key biological pathways with a wide variety of other living beings.

At the same time, there are key structural differences between animal and human brains. "How things differ is in the way the brain seems to be wired up," says Josselyn. "We've solved Alzheimer's disease in mice," she says, but not in people.

In 2017, she and Frankland stimulated neurogenesis in the hippocampi of mice, both young and old, who had genetic mutations associated with Alzheimer's — with very promising results. Initially, the mice exhibited the brain plaques typical of the disease, as well as obvious memory difficulties. After the stimulation, their memories were improved, regardless of age, and plaque was reduced. Can this be done in humans? Not yet.

“There's something that we're missing,” Josselyn says, “and it's still kind of tricky to figure out exactly what that is.”

Blake Richards, a fellow in CIFAR's Learning in Machines & Brains program and Canada CIFAR AI Chair, says even the study of a brain that isn't alive can give valuable insights into how memory works.

Richards comes to neuroscience not from psychology but from artificial intelligence. As a student in the lab of CIFAR Distinguished Fellow Geoffrey Hinton, he became fascinated with the idea of neural nets: machine learning agents that mimic human brain processes.

“The reason I got into memory specifically,” he says, “is that when you try to design an AI agent and get it to interact with the world, you rapidly discover the need for memory. Because without learning and memory there is simply no way to get a computer to do the sort of stuff that you want it to do.”

One hundred billion neurons fill the human brain, connected by 100 trillion synapses. The brain is also powered by a chemical elixir of neurotransmitters, peptides and lipids. Naturally, a robot brain lacks all of this, and is much simpler. But it's faced with similar functional challenges.

“If you come up with an AI solution to driving a car or managing someone's personal accounts, it won't relate to the human in terms of chemistry at all. But in terms of certain mathematical details, it might,” Richards says. Like humans, neural nets can experience memory problems if their store of irrelevant memories isn't cleared — a phenomenon known as overfitting.

Neural nets currently lack many of the human brain's chemical and cellular details, because the presence of such complicating elements could interfere with scientists' ability to train them using mathematical analysis. Now, however, Richards is conducting research into designing computa-

tional models of artificial brains that are more brain-like than ever before. He says this may lead to better drug design for Alzheimer's and other diseases and a greater general understanding of brain functioning.

“We could perturb components in the model to make predictions about how doing so impacts the system's memory capabilities,” he says. “You can think of this as being almost akin to what we do with climate models, since climate is another incredibly complex interconnected system.”

Richards, Frankland and Josselyn have worked together investigating memory — Richards completed a post-doctoral fellowship in Frankland's lab. Their separate interests dovetail and diverge, but all three agree that studying memory from different angles provides a richer view of the problems it presents. Their membership in different CIFAR programs has been helpful.

“Coming to Paul and Sheena's lab was really good for me, because it was a different perspective on memory than I'd ever encountered,” says Richards. “Our ability to get out of a certain pattern of thinking and refocus on something else is aided significantly by exposure to people with different aspects of expertise. That's what makes the CIFAR programs such a febrile ground for new ideas.”

Together, the three neuroscientists are helping to redefine what we mean by a “good memory.” Instead of one packed with readily retrievable information, it's one that is imperfect and constantly changing, free of unnecessary flotsam, enriched only by the content that serves it best. And if the sunny day you remember is rainy in someone else's recollection, that's all right too.

“Not to get too philosophical, but this just comes back to the point that we are living in the present,” says Richards. “All we can say for sure is what's happening to us right now. If you can get comfortable with the idea that your past is something that informs the present but may disappear over time, that's probably best. Because that's your reality.”

To see interviews with Sheena Josselyn, Paul Frankland and Blake Richards, visit: cifar.ca/memory-hunters

Art of Science

Beauty in the gut of a fish

When a zebrafish is mature, its horizontal bands of dark and light scales bring to mind its namesake on the savannah. Not an ugly fish, but not remarkable either.

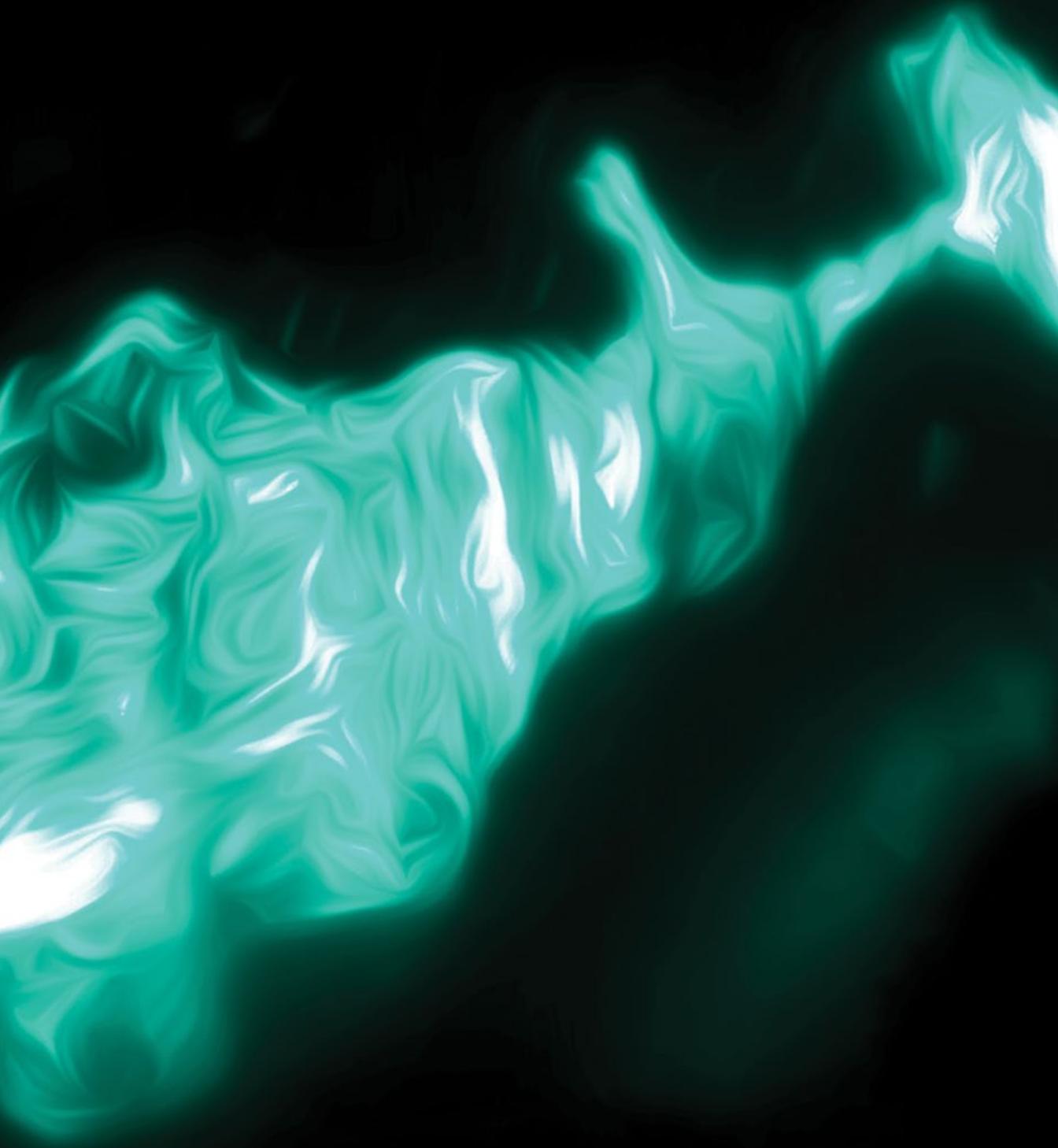
In its larval stage, however, it's another story. For about three days after they emerge from their eggs, zebrafish are completely transparent. This makes them beautiful to biologists such as Karen Guillemin, a fellow in CIFAR's Humans & the Microbiome program, and her post-doctoral fellow Travis Wiles, because the inner processes of the fish can be captured with a microscope.

The bright, swirling patterns shown here might bring to mind deep water caves, the aurora borealis or mysterious astrophysical phenomena. But the truth is much smaller: this is a long-exposure photograph, taken over a few seconds, of fluorescent *Vibrio* bacteria moving in the intestine of a larval zebrafish. At actual size, the pictured area would fit on the head of a pin.

The bacteria swim and bustle at quite a clip, some reaching speeds of a tenth of a millimetre per second. "If you scale that up based on body length to human scale, that would be like the average-sized person running 600 kilometres an hour," Wiles says.

Understanding the dynamics of how bacteria live and move inside another creature can have big implications for health and well-being. CIFAR's Humans & the Microbiome program is exploring just that. Their work seeks to explain how microbes that live in and on us affect our health, development and even behaviour.

— Jon Farrow





Hannah Carter

Towards personalized cancer diagnosis and treatment

by Cynthia Macdonald

By understanding the details of how genetic mutations turn into tumours, CIFAR Azrieli Global Scholar Hannah Carter is paving the way for better, more personalized diagnosis and treatment.

A single faulty copy of a gene inherited from our parents can predispose us to cancer. But the precise way in which genetic mutations lead to cancer's actual onset and development remains a mystery — particularly the interplay between inherited “germline” mutations and acquired “somatic” mutations.

2017 CIFAR Azrieli Global Scholar Hannah Carter is a computational biologist and assistant professor of medicine at the University of California, San Diego, who studies this very question. Working with giant data sets, she uses algorithms and cutting-edge software tools to discover how tumours develop at the molecular level.

“By understanding more about genetic background and the potential for a tumour to evolve,” says Carter, “we can project not just the likelihood of someone getting cancer in their lifetime, but perhaps where cancer will occur in their body, or whether the cancer will be more or less aggressive. And that will help inform screening.”

In an important 2017 paper published in *Cancer Discovery*, Carter and her team analyzed more than two million inherited cancer variants from 10,000 patient genomes in The Cancer Genome Atlas (TCGA), a landmark cancer genomics program started in 2006. They were able to locate more than 400 such variants that suggested where and how a malignant tumour might evolve.

Data gleaned from TCGA has ushered in a new era of cancer research. “We have all these different data layers that we can look at and study together. Which has given us an incredibly rich resource — there really isn't another one like it,” says Carter.

For too long, cancer treatment has suffered from a one-size-fits-all approach. Relatively few patients are enrolled in any given clinical trial; and of those, only a small minority stand to benefit, since the effect of their particular genetic background isn't considered.

The advent of molecular oncology has changed this. Targeted therapies such as monoclonal antibodies and immunotherapy are now able to

alter cell function in very particular ways. In some cases, results have been dramatic: even people with advanced metastatic disease have seen their tumours regress rapidly.

But there is still progress to be made. According to Carter, “tumours are challenging to deal with because they will eventually resist whatever therapies you throw at them. So we have to get smarter, and continue our efforts to understand them.”

The past two years have been eventful for Carter’s lab. In addition to providing clues as to how our germline and somatic genomes interact in the cancer process, she and her colleagues have also answered significant questions about how the immune system might be boosted more effectively to fight the spread of tumour cells.

Though an expert in both machine learning and genetics, the Kentucky native actually began her professional career as an electrical engineer. (“There was a sharp left turn in there somewhere,” she says wryly.) Initially thinking she’d like to develop neuroprostheses, she enrolled in a program at Johns Hopkins University that allowed her to attend first-year medical school classes.

“I just became absolutely fascinated with the genetic and molecular basis of diseases — and so I switched at that point and joined a lab that was doing computational molecular biology,” she says. Her engineering background proved tremendously helpful as she built critical skills in machine learning and computational modelling.

Right now, Carter says, the biggest challenge in her field is amassing the data needed to make truly big cancer discoveries. Though much has been collected, much more is still needed. With the right tools, she and her colleagues are poised to make extraordinary advances in the years to come.

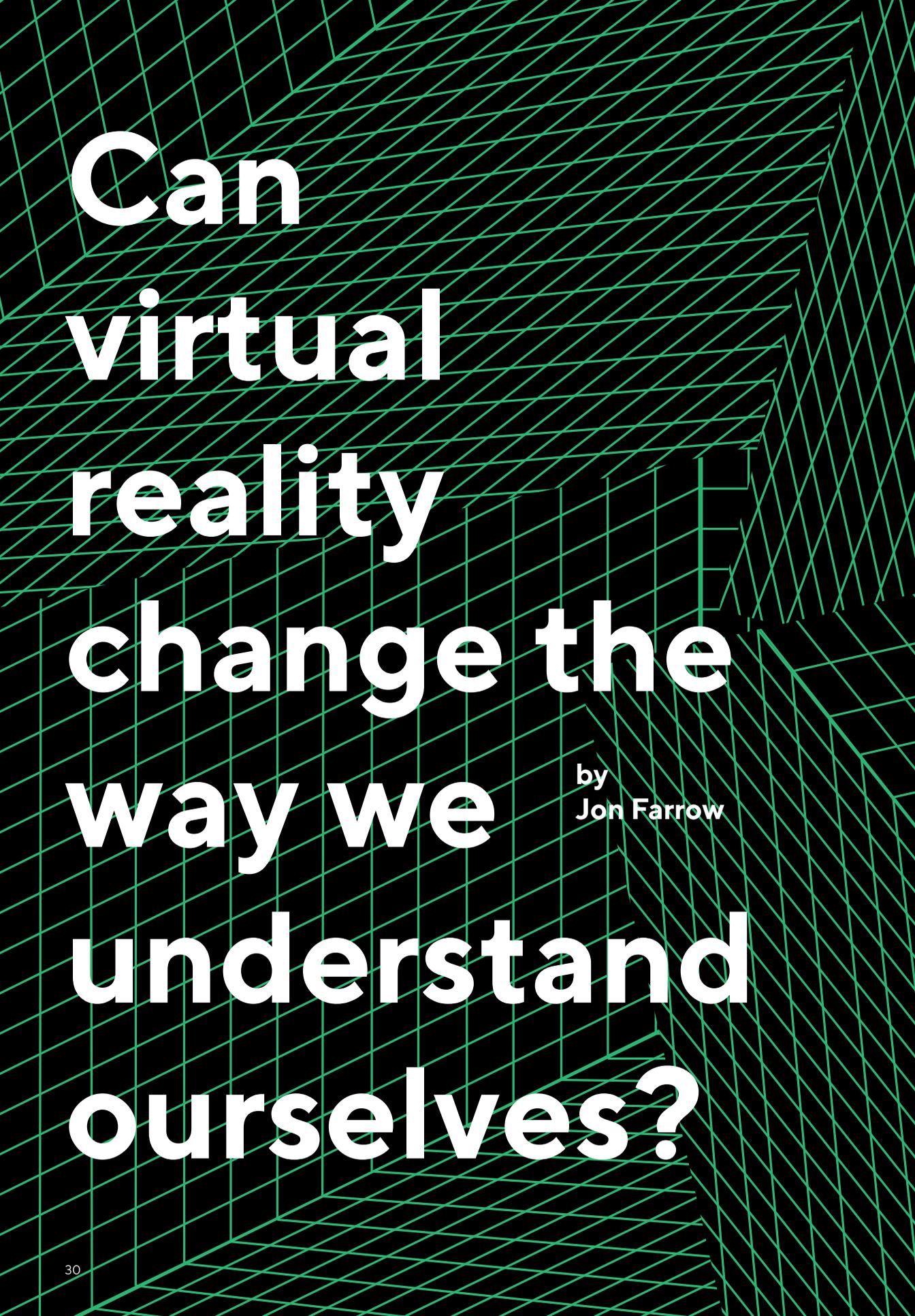
“Definitely this is an exciting time for cancer research,” she says. “The sheer number of studies and publications is daunting — it’s almost impossible to keep on top of the literature. But we’ve really made good inroads on understanding mechanistically how tumours are developing. We’re starting to come up with strategies to try to directly intervene in that development, and to further personalize cancer therapy.”

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**Can
virtual
reality
change the
way we
understand
ourselves?**

by
Jon Farrow

Virtual reality (VR) technologies could open a window on the nature of consciousness, while advances in neuroscience are expected to lead to better VR experiences. CIFAR is bringing researchers and industry together to make this “virtuous circle” a reality.

Virtual reality lets you immerse yourself in another reality within seconds of slipping on a headset. The applications for entertainment are obvious, but virtual reality has the potential to be much more than a new entertainment medium.

“VR represents a revolutionary paradigm shift that is not only going to change every domain of human experience, but also has some deeper philosophical shifts,” says Kent Bye, a journalist who has been preoccupied with the potential of virtual reality for the last half decade.

Bye embarked on a quest to create what he calls a “real-time oral history” of VR shortly after slipping on the first commercially available headset in early 2014. He has been interviewing neuroscientists, tech CEOs, artists and programmers about VR ever since.

And Bye isn’t the only one with high hopes for what VR can do. Ryan Chapman is CEO of Motive, a Vancouver-based company that develops immersive VR training experiences. He too has a vivid memory of his first time entering a VR world: “I was floored by how real everything felt.”

Chapman wants to use the technology to train people for expensive or dangerous scenarios without ever leaving the office. Already, companies such as Walmart are rolling out VR training programs for once-a-year events like Black Friday, and U.S.-based Verizon has started using VR training for employees who need to learn to work at heights. Chapman also sees applications for doctors, pilots and the military.

There is research that shows VR training can be more effective than other methods. Chapman and other

industry players have a question: how close is VR to the real thing?

This is where researchers like Anil Seth come in. A fellow in CIFAR’s Azrieli Brain, Mind & Consciousness program, Seth is interested in how the brain constructs reality. He uses VR in his lab to study embodiment — the experience of being a self and having a body. In a virtual environment like the one presented inside a VR headset, the limits of physics don’t apply.

“With VR, I can give you a virtual hand and then mess around with it in some way — delay it, change its colour or change its size, and see how that affects your experience of what is your body,” says Seth.

Neuroscience labs are often far removed from the game developers and programmers who will be able to implement research findings to build more immersive VR experiences. So, as part of the knowledge mobilization (KM) strategy for the Azrieli Brain, Mind & Consciousness program, CIFAR’s KM team has been working on ways to bring these communities together.

At last year’s Game Developers Conference (GDC) in San Francisco, CIFAR sponsored a panel on neuroscience and VR, which included two neuroscientists from the program — Alona Fyshe and Craig Chapman (both of the University of Alberta) — as well as Kent Bye and Jake Staunch, a tech CEO who has developed a lightweight EEG headset that integrates with gameplay. With nearly 200 people crowding into the small room, it was clear that game developers are keen to learn more about neuroscience.

“We had never been to GDC before, so we weren’t sure if people would be interested in a panel about VR and neuroscience. But seeing the packed room and the discussions afterwards, we knew there was something in this,” says Rebecca Finlay, vice-president of engagement & public policy at CIFAR.

To build on this interest, the KM team is convening a workshop for consciousness researchers like Anil Seth, industry leaders like Ryan Chapman and connectors like Kent Bye in New York this May. The idea is to explore common challenges and foster new collaborations.

INSPIRED GIFTS TO SCIENCE

“Every field of human endeavour—from the environment, to medicine, to social well-being and more—benefits from a world-class research system.”

— Naomi Azrieli

The philanthropists behind the great discoveries

Researchers are celebrated for the advances they make in science, technology, innovation and scholarship. Behind the great discoveries are often visionary philanthropists who understand the importance of risk-taking.

The discovery of DNA, the structure of the atom and the moons of Jupiter, the invention of the thermometer and the polio vaccine: these great scientific advances changed the course of history. None might have been possible without support from individuals who were both generous and visionary.

The idea that scientific research is wholly funded by government and industry only became entrenched around the mid-20th century. Before that, scientists often relied on private patronage to fund their projects — when they didn't pay for them on their own.

The silent partners behind our greatest inventions sometimes do not get the credit they deserve. These include the Duke of Devonshire, who founded the famed Cavendish laboratory where Watson and Crick conducted their Nobel Prize-winning research into DNA. And shipping magnate Daniel Ludwig, whose \$2.5 billion fortune has funded decades of cancer research.

To this list we can add a growing body of committed donors who are shaping the future of science — many of them by giving to CIFAR. Science philanthropists are both idealistic and adventurous, realizing that the eventual rewards of basic research can far outweigh the risks.

“CIFAR's donor community gives us the means and the relationships we need to be bold and to address the most important questions of our time,” says Dr. Alan Bernstein, CIFAR president and CEO. “Their support and personal interest in our work is both essential and inspirational.”

Some donors fund entire research programs that span a period of years. Others support aspects of our research programs or other organizational priorities. “We have loyal supporters who have been contributing over a long period of time and we couldn't operate without their sustained generosity,” says Dr. Bernstein.

Whatever their level of support, donors to fundamental research understand that research is the driver of real impact in the world.

CIFAR donors are no exception. They are knowledgeable and forward-thinking, and many advocate for and invest in science. In the May 7, 2017 issue of *Maclean's*, a group of science philanthropists — including long-time CIFAR supporters Naomi Azrieli and Lorne Trottier — wrote an op-ed urging governments to join them in backing the cause of fundamental research.

“Every field of human endeavour — from the environment, to medicine, to social well-being and more — benefits from a world-class research system,” says Azrieli, Chair and CEO of the Azrieli Foundation. “I believe that each and every Canadian has the potential to help create that kind of system for our country.”

Like others who give to science, Azrieli cares deeply about the state of the world she will eventually leave behind. Science philanthropists often cite climate change and the fate of the oceans as two areas of obvious and critical concern. Disease research is another.

In this new climate of science philanthropy, CIFAR's donors and partners are not just a critical source of support for the research efforts of our fellows. In their willingness to support long term, high risk fundamental research, they are very much discoverers themselves.

— Cynthia Macdonald

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Pan-Canadian Artificial Intelligence Strategy: Canada CIFAR AI Chairs named

CIFAR announced 29 researchers to the Canada CIFAR AI Chairs program at the AICan conference in Montreal in December 2018. The event brought together researchers, academic leaders, members of government and industry representatives to inspire discussion and collaboration around AI research in Canada. An additional 17 chairs were announced in April 2019.

Parliamentary Secretary David Lametti of the Ministry of Innovation, Science & Economic Development joined Dr. Alan Bernstein, CIFAR president and CEO, and Dr. Elissa Strome, Executive Director, CIFAR Pan-Canadian Artificial Intelligence Strategy, to kick off AICan with the announcement of the Canada CIFAR Artificial Intelligence Chairs program.

The Canada CIFAR AI Chairs were named as part of the CIFAR Pan-Canadian Artificial Intelligence Strategy, which aims to maintain Canada's leadership in AI research and attract and retain academic talent. Nearly half of the chairs were attracted from the U.S. and elsewhere to their new faculty positions in Canada. The Canada CIFAR AI Chairs were nominated by three national AI institutes: Amii (Edmonton), Mila (Montréal) and the Vector Institute (Toronto).

In 2017, the Government of Canada appointed CIFAR to develop and lead the Pan-Canadian Artificial Intelligence Strategy, the world's first national AI strategy. For more information on the Pan-Canadian Artificial Intelligence Strategy, visit cifar.ca/ai.

Knowledge Mobilization: CIFAR partners on international AI & Society workshops

CIFAR, in partnership with the French National Centre for Scientific Research (CNRS) and UK Research and Innovation (UKRI), has launched a series of international AI & Society research workshops to examine the economic, ethical, policy and legal implications of artificial intelligence (AI) on society.

Administered and managed by CIFAR with support from CNRS and UKRI, the workshops explore the global implications of AI on a range of topics — from future conflicts in the Arctic and societal trust in AI systems to how AI may impact the practice of medicine. Each workshop will receive up to \$50,000 for a total combined commitment of \$400,000 from all three organizations for this joint call. This is the second call for workshop proposals issued by CIFAR's AI & Society program.

Child & Brain Development: Building a fly brain on a computer

Despite having simple visual system, fruit flies can tell each other apart using sight alone. Researchers have now built a neural network that mimics the

fruit fly's visual system and can distinguish and re-identify flies.

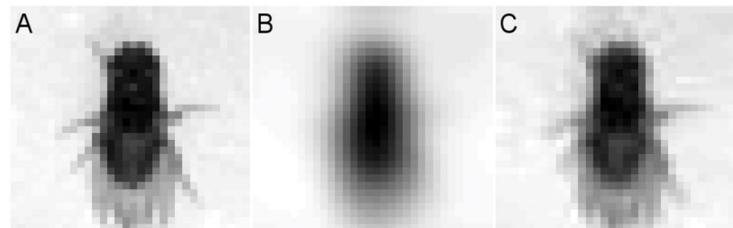
The technology could be helpful for lab workers who study fruit flies. Because it is designed to operate within the same constraints as an actual fly brain, it also provides clues to biologists about how their brains function.

The project, funded by a CIFAR Catalyst grant, brought together Joel Levine, a fellow in the Child & Brain Development program and a biologist at the University of Toronto Mississauga, and Graham Taylor, a CIFAR Azrieli Global Scholar in the Learning in Machines & Brains program.

Genetic Networks: "Genome Jenga" reveals cell health clues

By removing genes from cells in combination, fellows in CIFAR's Genetic Networks program uncovered how different genes work together to keep cells alive. The research will help scientists understand how faults in multiple genes combine to drive common conditions such as cancer or heart disease.

The study, led by program co-director Charles Boone (of the University of Toronto) and Fellows Brenda Andrews (also of the University of Toronto) and Chad Myers (of the University of



Building a fly brain on a computer: A) Illustrates the resolution that a fly's eye is capable of seeing. B) Illustrates what researchers thought the fly actually perceived. C) is the more detailed image that researchers now believe is what the fly actually perceives.

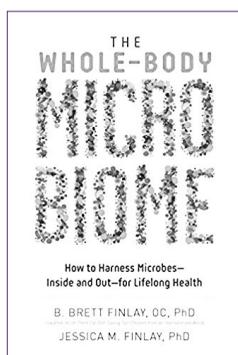


CIFAR Fellows Brenda Andrews (University of Toronto), Charles Boone (University of Toronto) and Chad Myers (University of Minnesota) examined the importance of gene combinations to health.

Minnesota, examined how various combinations of three genes help maintain normal cell physiology.

They compared their findings to a giant game of Jenga, with genes standing in for wooden blocks. While most single blocks can be taken out without compromising the structure, when critical combinations of blocks are removed, the system collapses. The research was published in *Science*.

Humans & the Microbiome: Better living through germs



B. Brett Finlay, co-director of CIFAR's Humans & the Microbiome program and a professor at the University of British Columbia, published *The Whole-Body Microbiome* with his daughter Jessica Finlay in January 2019. The book examines the ways

that a healthy microbiome contributes to human health and longevity.

"You should be petting your dog and playing on the rug with your grandkids, because a lot of studies show you need this healthy microbial exposure," Finlay says.

Finlay's previous book, *Let Them Eat Dirt*, is the basis for a new documentary with the same name, produced and directed by Rivkah Beth Medow and written and produced by Brad Marshland.

Molecular Architecture of Life: Mapping the cell for new drug creation

CIFAR's Molecular Architecture of Life program is working with global pharmaceutical and advanced scientific manufacturing equipment companies to explore how better mapping the functions of the cell could catalyze drug discovery. Program co-directors Oliver Ernst and R.J. Dwayne Miller have hosted two knowledge mobilization engagements on their topic with more planned for 2019. To learn more visit cifar.ca/exchange.

Quantum Information Science: Quantum crypto to protect the blockchain

Blockchain technologies like Bitcoin depend on digital "fin-

gerprints," cryptography that guarantees a shared file cannot be altered without detection. The cryptography that guarantees the integrity of the blockchain is so mathematically complex that it is considered unbreakable.

Advances in quantum computing could soon make that cryptography easy to break, says Alexander Lvovsky, a fellow in CIFAR's Quantum Information Science program and a physicist at Oxford University.

Using a technique called quantum key distribution, he and a team from Moscow's Russian Quantum Centre have created a solution. With the system, two people can generate a secret key over a secure quantum channel, and then use that key to keep their information encrypted while communicating on a public channel.

"A lot of quantum research is just interesting for physics and has intellectual merit, but the quantum threat to the security of cryptocurrencies is something that will affect all of us, and quite soon," says Lvovsky. The work was published in the online journal *arXiv*.

The Early Years Report



Twenty years ago, a landmark CIFAR report showed that the first six years of life are the most important of all.

The Early Years Report: Reversing the Real Brain Drain was issued in April 1999. Co-chaired by CIFAR founder Dr. Fraser Mustard (1927–2011) and CIFAR Advisory Committee Member Margaret Norrie McCain, it revealed early childhood as a critical period for brain development — a “make or break” time that sets the stage for an individual’s future mental and physical well-being.

Marshalling evidence from genetics, neuroscience, education, social work and other fields, the report offered a unique scientific rationale for public investment in children. Several important government initiatives, such as the implementation of full-day kindergarten and the establishment of parenting centres, can be traced to this groundbreaking research.

Some of Dr. Mustard’s enduring legacies resulted from his advocacy for children. His relentless passion for the cause inspired others across the globe — including billionaire George Soros, who committed to investing millions toward early childhood education in Eastern Europe.

In concert with Stuart Shanker and Kerry McCuaig, Mustard and McCain would go on to author two further Early Years reports. These efforts live on today in CIFAR’s Child & Brain Development program, an interdisciplinary group of CIFAR fellows & CIFAR Azrieli Global Scholars dedicated to the generation of important scientific findings by analyzing the psycho-social effects of our earliest experiences.

— Cynthia Macdonald

In a changing world, knowledge is power.

CIFAR will launch an exciting new series of public events in 2019.

To be the first to learn more, join our mailing list at cifar.ca/public





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