# REACH

IDEAS TO CHANGE THE WORLD | SPRING 2018

## Seeing Life

CIFAR fellows ask the biggest question

CIFAR

**Connecting the best minds for a better world.**

CIFAR

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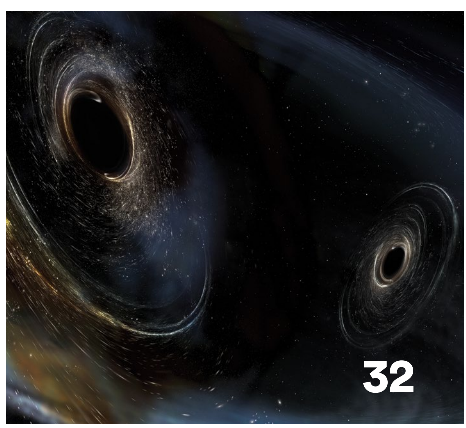

# CIFAR
# REACH Magazine
## Spring 2018
## Volume 17, Issue 1

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**About CIFAR**
CIFAR brings together outstanding researchers from across disciplines and borders to identify and address important global challenges. CIFAR is supported by the governments of Canada, Alberta, British Columbia, Ontario and Quebec, as well as individuals, foundations and corporations across Canada and the world.

# President's Message

**Alan Bernstein**
President & CEO

I'm excited to share with you this issue of Reach magazine. As always, it is full of interesting stories highlighting some of the fascinating and important research happening at CIFAR, and the people who make it possible.

This has been a landmark year for CIFAR, one that saw the development of our new five-year Strategic Plan, Advancing Excellence, Increasing Impact, the launching of our next Global Call for Ideas and the Pan-Canadian AI Strategy, and our next cohort of CIFAR Azrieli Global Scholars. Since our earliest days, CIFAR has brought together outstanding researchers from across disciplines and countries to work on problems of global importance. We have had many successes in that time, from contributing novel insights into population health, to the life-long effects of the early years, to the groundbreaking work that led to the first detection of gravitational waves.

One important advance that is in the news is artificial intelligence (AI), which promises to change everything from transportation to financial services to science itself. Much of the credit for modern AI goes to Distinguished Fellow Geoff Hinton and other members of our Learning in Machines & Brains program, co-directed by Yoshua Bengio (Université de Montréal) and Yann LeCun (New York University, Facebook). Inside, you can read about CIFAR's expanded work in AI, including the launch of the $125 million Pan-Canadian AI Strategy, which is building Canada's AI research strength, including our AI & Society program, which will examine the effects of AI on how we live, work and think about ourselves.

Our cover story looks at our Program in Molecular Architecture of Life, which plans to create a Human Genome Project for the cell — an attempt to understand life at its most fundamantal level. This program could set the stage for a new understanding of disease and the basis of life itself.

Also in this issue you can read about Charles Nelson, a senior fellow in CIFAR's Child & Brain Development program, and his efforts to understand the effects of neglect and abuse on children from Romania to Bangladesh to Canada. His work is leading to a new understanding of how profoundly abuse and neglect affect children.

This issue also includes a conversation between CIFAR Fellows Tobias Rees and Thomas Bosch in our Humans & the Microbiome program. As anthropologists and evolutionary developmental biologists they discuss how CIFAR brought them together and led to an influential paper that questions the very idea of an individual human self, seeing the human instead as a collective being made up of billions of co-existing organisms.

# Advances
# New highlights from our research network

Scientists must discover new materials to fully harness wind power. Artificial Intelligence can accelerate this search.

## Using AI to develop clean energy

Artificial intelligence (AI) and machine learning may be the key to speeding up the development of clean energy — from better batteries to more efficient solar cells.

That's the argument recently advanced in *Nature* by a team of prominent researchers, including CIFAR's Bio-inspired Solar Energy Program Heffernan Director **Ted Sargent** (University of Toronto, Engineering), Senior Fellow **Alán Aspuru-Guzik** (Harvard University), and Learning in Machines & Brains Program Co-Director **Yoshua Bengio** (Université de Montréal).

Solar and wind power have seen dramatic reductions in cost in recent years; however, in order to displace significant amounts of fossil fuels, they urgently require further improvements in conversion efficiency and energy storage.

Sorting through all possible materials to determine the very best ones to use for this purpose is a task for which humans are ill-equipped. The integration of AI, robotics and materials science could speed up the discovery of materials at least by a factor of ten — from 20 years to one to two years.

"What we'd like to see is more collaboration between the artificial intelligence community and the clean energy community," says Phil De Luna (MSE PhD candidate), an author on the paper.

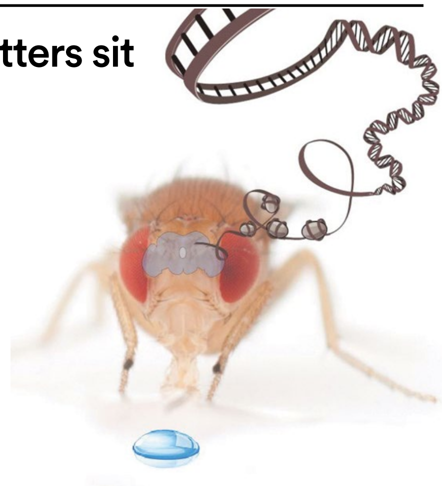
## Facebook invests in CIFAR, AI research

Facebook announced a major investment with CIFAR, a result of the Institute's leadership in the field of artificial intelligence (AI). The US$2.625 million investment over five years will continue Facebook's support of CIFAR's Learning in Machines & Brains program, and will also fund a Facebook-CIFAR Chair in Artificial Intelligence at the Montreal Institute for Learning Algorithms (MILA).

Facebook made the announcement at a ceremony at McGill University in Montreal, attended by Prime Minister Justin Trudeau and CIFAR President & CEO **Alan Bernstein**. Facebook also announced funding for a Facebook AI Research (FAIR) Lab to be headed by McGill's **Joëlle Pineau**, a CIFAR senior fellow in the Learning in Machines & Brains program.

"Facebook's investment in CIFAR and in the Canadian AI community recognizes the strength of Canadian research in artificial intelligence. I'm proud of the major part that CIFAR played in helping to spark today's AI boom, and the part we continue to play in the AI sphere," said Dr. Bernstein.

## Why roving fruit flies rove, and sitters sit



There is an epigenetic key to foraging.

When it comes to behaviour, researchers have moved beyond the "nature versus nurture" debate. It's understood that genes and environment both play a role. However, how they interact at a molecular level to shape behaviour is still unclear.

A paper published in PNAS reveals how epigenetics — changes in gene expression that do not change DNA — interact with genes to shape different feeding behaviours in fruit flies. This research unlocks the molecular mechanism that leads "rover" flies to forage for food more than "sitter" flies. It is the first study of its kind to show a causal link between epigenetics, genetics and behaviour.

"We have an empirical example of how this interaction is important for differences in many sorts of behaviour," says lead author Ina Anreiter. She adds that these findings could help researchers understand how individuals' behaviours differ, whether fruit flies, mice or even humans.

Anreiter is a PhD student in CIFAR Weston Fellow **Marla Sokolowski**'s lab at the University of Toronto. Sokolowski is the co-director of CIFAR's Child & Brain Development program and has been studying the "foraging gene" in fruit flies since she first discovered it in the 1980s. The research was funded partly by CIFAR and conducted in collaboration with Jamie Kramer at Western University.

The researchers began by isolating gene products and identifying which ones were key to shaping the different feeding behaviours of rovers and sitters. Findings showed that the different genetics of rovers and sitters interact with epigenetic mechanisms to regulate behavioural differences.

The research was inspired by discussions in the Child & Brain Development program with experts ranging from fruit fly geneticists to clinicians.

## How to create a conscious car

Imagine driving, and your fuel light goes on. Your car has a GPS that can tell it where the nearest gas station is. But the fuel light and the GPS are unaware of each other. If your car had access to information from all its parts and was self-aware — in other words, it knew what it knew — if it could direct itself to the gas station. It would be functionally conscious.

So argue CIFAR Fellows **Stanislas Dehaene** and **Sid Kouider**, members of CIFAR's Azrieli Program in Brain, Mind & Consciousness, in a review paper published in *Science*.

The review looks at existing knowledge about the neuroscience of consciousness and proposes that consciousness results from specific types of information processing carried out by the brain. Today's artificial intelligence does not have these abilities, the researchers say.

In order to achieve a functional consciousness similar to that of humans, Kouider, Dehaene and their colleague Hakwan Lau say that machines need to adopt two types of information processing already present in the brain.

The first is "global availability," the act of selecting and making a piece of information accessible for processing and decision-making by the whole system. Global availability highlights or draws attention to a piece of information that was, up until that moment, unconscious.

Though the brain possesses a deep hierarchy of specialized modules that operate non-consciously and are dedicated to specific tasks, it also possesses a "global neuronal workspace" where information is selected and shared across all modules. Information present in this global area at any given time is what we call "conscious."

But for a machine to act as though it was conscious it is not enough for information to be globally accessible. The researchers point to a second computational process that they believe is key — self-awareness.

"Humans do not just know things about the world, they actually know that they know or that they do not know," the authors state in the paper.

Photo credits: Wind Turbines, Master Wen via Unsplash; Fly, Ina Anreiter, University of Toronto

CHIME captures radio frequencies that tell the history of the universe.

## Novel Canadian telescope unveiled

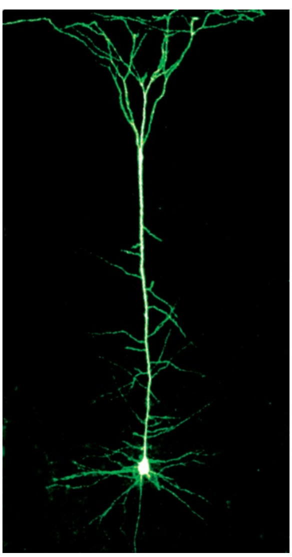
A Canadian telescope with unprecedented abilities to image the sky and capture signals from space was recently unveiled in Kaleden, B.C. The newly completed radio telescope will open the universe to a new dimension of scientific study thanks to key contributions from CIFAR researchers.

The Canadian Hydrogen Intensity Mapping Experiment (CHIME) is a radio telescope made up of "half-pipe" reflectors with an array of radio receivers along the focus. Unlike other radio telescopes, it has no round dish and no moving parts. CHIME will survey more than half the sky each day as the Earth turns.

In addition to mapping the universe, CHIME captures a frequency range that is ideal for studying fast radio bursts and radio pulsars.

"CHIME's unique design will enable us to tackle one of the most puzzling new areas of astrophysics today — fast radio bursts. The origin of these bizarre extragalactic events is presently a mystery," said R. Howard Webster Foundation Fellow **Victoria Kaspi** (McGill).

## Deep learning in the human brain?



Tree-like neurons have the right shape for deep learning.

Deep learning has brought about machines that can "see" the world more like humans can, and recognize language. And while deep learning was inspired by the human brain, the question remains: does the brain learn this way?

In a study published in *eLife*, CIFAR Fellow **Blake Richards** and his colleagues unveiled an algorithm that simulates how deep learning might work in our brains. The network shows that certain mammalian neurons have the shape and electrical properties that are well-suited for deep learning. Furthermore, it represents a more biologically realistic way of how brains could do deep learning.

Their algorithm employed neurons in the neocortex, which is responsible for higher-order thought.

"Most of these neurons are shaped like trees, with 'roots' deep in the brain and 'branches' close to the surface," says Richards. "These roots receive a different set of inputs than the branches that are way up at the top of the tree."

Knowing the neurons' structure, Richards built a model that similarly received signals in segregated compartments. These sections allowed simulated neurons in different layers to collaborate, achieving deep learning.

## 'American dream' moving out of reach

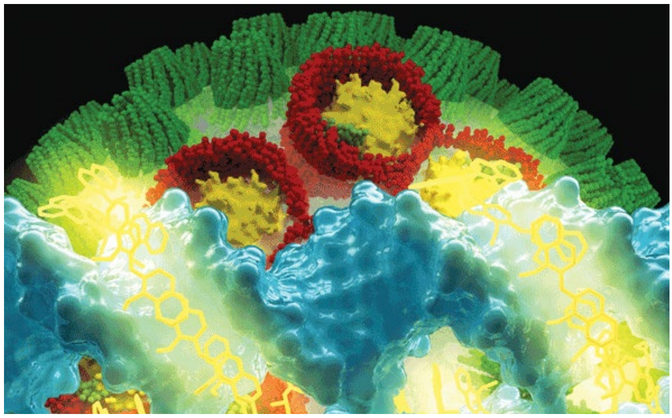
A key component of the "American dream" is that children will earn more than their parents. This was a near guarantee during the post-World War II boom, but has recently been moving out of reach.

A *Science* paper co-authored by Senior Fellow **David Grusky** (Stanford University) chronicles the striking decline of upward-income mobility in the United States over a half-century. It shows that from 1940 to 1984, the percentage of children earning more than their parents fell from 92 per cent to 50 per cent. The paper concluded that restoring former levels of upward mobility would require GDP growth to be shared much more broadly.

The sharpness of this decline surprised Grusky, who has studied inequality for more than 30 years.

Although maintaining high rates of upward mobility is an important commitment in the United States, it has gone unmeasured largely because doing so requires panel data. This study became possible by analyzing de-identified tax records pertaining to more than 10 million child-parent pairs and then combining those data with census and survey data.

The Equality Opportunity Project, led by co-author Raj Chetty, will use "big data to identify new pathways to upward mobility." Grusky is one of his collaborators on a team examining ways to improve the country's capacity to measure the health of the American dream over time.



Researchers organized pigments on a DNA "origami" scaffold.

## Photosynthesis informs efficient synthetic circuit

CIFAR fellows and colleagues designed a new synthetic structure that can harvest light energy in a way similar to naturally occurring photosynthetic bacteria.

"The idea was to develop an excitonic circuit to direct absorbed energy," said **Gabriela Schlau-Cohen** (MIT), a co-author on the paper and CIFAR Azrieli Global Scholar. "The goal of these types of systems is to get energy as far as possible as efficiently as possible."

The paper, published in *Nature Materials*, aligns closely with the work being carried out in CIFAR's Bio-inspired Solar Energy program, which seeks to uncover the nanoscale mechanisms photosynthetic organisms employ to harvest energy from the sun, and create artificial devices that can do the same.

"This is a keystone paper related to our CIFAR BSE program," said Senior Fellow **Alán Aspuru-Guzik** (Harvard University).

The synthetic circuit built by Aspuru-Guzik, Schlau-Cohen and their fellow authors organizes molecules to form a supramolecular structure where energy gets shared across the entire structure.

"In natural systems, you see energy moving through two different types of mechanisms, a more incoherent or hopping-type transport and a more coherent or wave-like motion," said Schlau-Cohen. "We were able to develop a system that can control the balance of these."

In nature, photosynthetic organisms use light-harvesting pigments and reaction centres to convert light energy from photons into chemical energy. In this process, photons are captured by pigments, turning them into energized versions of themselves called "excitons." Excitons pass energy from one molecule to another until they reach a reaction centre where light energy is converted into chemical energy.

Controlling the direction and flow of excitons in synthetic systems is something that scientists have struggled with. Senior author Mark Bathe (MIT) designed a synthetic DNA "origami" scaffold that allows researchers to control the absorption of photons and the transportation of excitons.

Photo credits: CHIME, Andre Renard, Dunlap Institute of Astronomy & Astrophysics, U of Toronto; Deep Learning, Black Richards; DNA scaffold courtesy of Gabriela Schlau-Cohen


CIFAR Senior Fellow Daron Acemoglu spoke about robotics, AI and the future of work at the 2017 David Dodge CIFAR Lecture in Ottawa.

## Lessons from the past for an AI future

As society looks to the future and the potential of artificial intelligence (AI) and robotics, CIFAR Senior Fellow and MIT economist **Daron Acemoglu** reminds us that we must first look to the past.

"We have been here before," Acemoglu told the crowd at the sold-out David Dodge CIFAR Lecture in Ottawa last spring, citing a 1930 essay by British economist John Maynard Keynes.

"We are being afflicted with a new disease of which some readers may not have heard the name, but of which they will hear a great deal in the years to come … namely, technological unemployment," Keynes wrote.

Although Acemoglu said AI will never replace the human mind, it will continuously take over tasks that humans have previously performed. Some soon-to-be-obsolete jobs he listed include telemarketers, radio operators, drivers, assembly-line workers and construction workers.

So where will new jobs come from? Acemoglu's hope is that new technologies will create new tasks resulting in higher-skill jobs. However, his fear is that in the short term, job growth will be focused on low-paying service jobs. Over the last 35 years, he says, there has been an "alarming" decline in employment rates and wages.

Lessons on how to adapt may be found by looking at society's response to the Industrial Revolution. There was essentially no wage growth from around 1760 to about 1850, despite very rapid technological change in Britain.

Growth came in the second half of the 19th century when Britain enacted institutional changes. These included labour unions, female suffrage, moving toward a democratic system of government and introducing universal education. Acemoglu said similar changes may be necessary today.

"I think we are really very much in the middle of some very transformative changes. The way to deal with these changes is to understand them better; to make knowledge-based, quantitatively sound assessments about what they are doing and what they are likely to do; and change our own investments, our own policy positions and our own institutions in a way that is coherent with this picture," he said.

# How the nervous system regulates the microbiome

An ancient animal has revealed one way nerves shape the microbiome, and has opened up a whole new area of research on gut–brain interaction.

Hydras are miniscule freshwater creatures with a tubular body and tentacles. They don't exactly have a gut or brain, but they do contain a community of microbes and are among the earliest organisms to evolve a nervous system.

Using hydras, researchers have observed the first proof of the nervous system cooperating with the microbial community. These findings, published in *Nature Communications*, show how neurons regulate the composition and distribution of microbes.

"Microbes are everywhere. They're on the body, on the skin, in the gut and the oral cavity, but they follow very strict spatial rules. Yet nobody really knows who controls that spatial organization," says **Thomas Bosch**, a senior fellow in CIFAR's Humans & the Microbiome program who led the research team at Kiel University.

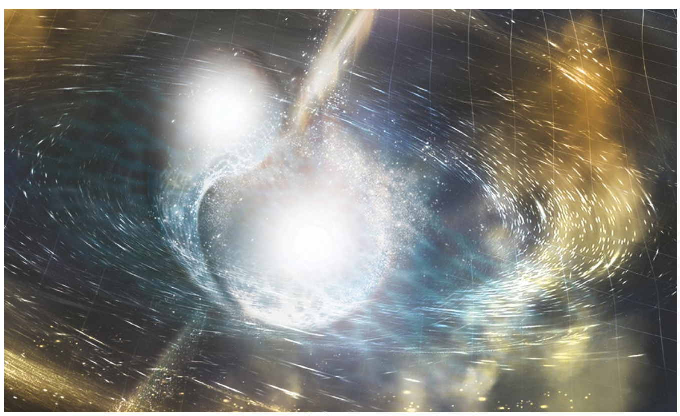
Bosch's team found an answer by eavesdropping on the conversations between the "brain" and "gut" in hydras. Their nervous system communicates with the microbiome through neuropeptides, molecules secreted by nerve cells. These neuropeptides keep away unwanted microbes and maintain a balance of desired microbes. They also organize bacteria along specific areas of the Hydra's body.

The research shows that this communication goes both ways. "It's not only that the microbiome communicates with the microbes on this one side of communication, but on the other side the neurons also actively communicate with the microbiome," Bosch says.

A freshwater polyp Hydra.

Bosch has been studying hydras for 40 years because they offer a unique view into how organisms have evolved. His current research was inspired in part by conversations in the Humans & the Microbiome program, which includes biologists, bacteriologists, immunologists, historians and anthropologists.

# Neutron stars collide



GW170817 sent out gamma rays and gravitational waves.

For the first time, scientists directly detected gravitational waves from the spectacular collision of two neutron stars, and at the same time detected visible light from the merger. The discovery, reported by a collaboration of scientists from around the world, marks the first time that a cosmic event has been detected through both light and gravitational waves — the ripples in spacetime predicted a century ago by Albert Einstein's general theory of relativity.

The result heralds a new era of multi-messenger astronomy, in which different kinds of electromagnetic radiation and gravitational waves combine to teach us more about the universe than either could by itself. Five CIFAR researchers in the Gravity & the Extreme Universe program are involved in the discovery: **Harald Pfeiffer**, **Gabriela Gonzalez**, **Vicky Kalogera**, **Daryl Haggard** and **Parameswaran Ajith**.

Photo credits: Daron Acemoglu, byfieldpitman photography; Hydra, Dr. Alexander Klimovich; Colliding Neutron Stars, LIGO-Virgo/Aaron Geller/Northwestern University

In Conversation

# THE MICROBIOME AND THE SENSE OF SELF

New understanding of the human microbiome — the billions of microbes that live in and around us — have given unexpected insights into human health, development, and evolution. But CIFAR Fellows Tobias Rees (University of California, Berkeley) and Thomas Bosch (Kiel University) think the implications go further than that, to the fundamental question of what it means to be a human being. Rees, an anthropologist, and Bosch, an evolutionary developmental biologist, met through the CIFAR Humans & the Microbiome program. With colleague Angela E. Douglas, they published a paper in *PLOS Biology* called "How the Microbiome Challenges the Concept of Self." Reach talked with the two about their work. The interview is edited for length and clarity.

Top: Tobias Rees
Bottom: Thomas Bosch

Photo credits: CIFAR Archives

## Reach: What got you thinking about these ideas in the first place?

**Tobias Rees:** Thomas and I met in 2015, at the first meeting of the Humans & the Microbiome program. The first talk was by Thomas. He asked whether the immune system really is, as had classically been assumed, a self/not-self recognition system. You know, the idea that the immune system is basically a defence system that can tell self apart from not-self or microbe, killing the latter.

His suggestion was to drop the self/not-self idea and to instead rethink the immune system in terms of a meta-organism — that is, from the perspective of a fully integrated system between the human body and our microbial cells. If looked at from the perspective of a meta-organism, Thomas suggested, not-self or bacteria are part of self and hence the idea of the immune system as a self/not-self recognition system whose main job is defence falls apart. Could it perhaps be that the major job of the immune system is less defence than a selection of the microbes the meta-organism needs to flourish?

His talk triggered a wild discussion amongst all the members, and Thomas and I were both vigorously defending the idea that we are multi-organismal, and in the heat of this discussion a beautiful friendship was born.

**Thomas Bosch:** We immediately realized that we're a perfect complement of each other because I was in a natural sciences community, but realized that we need advice and explanations from outside the natural sciences, and particularly anthropology, and Tobias provided this.

## Reach: What was the new science that led to these new ideas?

**Bosch:** The paradigm shift was with this new insight that both the innate immune system and the adaptive immune system are based in part on microbial input. That means microbes are an essential part of our immune system, meaning that non-self is part of what was previously believed to be self.

The immune system has been considered one of the three pillars of the definition of self.

**"... microbes are an essential part of our immune system, meaning that non-self is part of what was previously believed to be self."**

The others are the brain and the genome. We know that the brain certainly is heavily affected by the microbial community, and the same is of course true of the genome. We can trace about 37 per cent of the human genome to a bacterial origin.

So facts that were believed 20 or 30 years ago to be the definition of an individual self — the immune system, your brain and also your genome — are is getting very blurry and have to be rethought. That's the point of this paper.

**Rees:** Let me follow up on this and use you as a guinea pig, if you don't mind: imagine that we actually don't know where you end and your microbiome begins, as if there were an overlap.

**Reach: Mm-hmm.**

**Rees:** If this is true then that means that there is an indistinguishability in the middle, where you are literally microbial. Can one rethink the body from the perspective of this indistinguishability? This is the challenge. The microbes that live in and on you produce waste products that we call metabolites, and these metabolites are actively involved in gene regulation. They were actively involved in the growth of your organism when you were a baby and they're actively involved in many organic functions in your body right now, as we talk.

If one thinks about our organisms in evolutionary terms then this overlap in the middle, this indistinguishability where you are literally microbial, this is actually where you're coming from.

About three billion years ago there were only bacteria. Every living organism we now know evolved out of this microbial scene. That is, they evolved out of but also in a microbial world, a world rich in metabolites. As multi-cellular organism and later plants and animals evolved, there were bacteria and they shielded themselves from some but made use of others.

It is this recognition that we are animals with microbial origins and are living in a microbial world that led to a rethinking of the immune system, the brain and the genome.

From the1930s onward, the idea that the immune system is purely a system that defends our boundaries against non-self was very firmly established. And then in a series of papers, mostly by Sarkis Mazmanian, Margaret McFall-Ngai and Thomas, a different conceptualization of the immune system emerged. The recognition that microbes are part of the immune system led them to suggest that we better understand the immune system as an evolutionarily preserved joint ecological management system between microbes and human cells.

You can see a similar process of rethinking with respect to the brain. Until recently, neurobiology tended to think about the brain as an enclosed system, set apart from the rest of the body by the blood–brain barrier. And then, only a few years ago, researchers discovered that, a) there is a direct path of communication between the bacteria in our gut and the brain and, b) that a good number of the neurotransmitters in our brain seem to be produced by gut bacteria.

It's a little more complicated because it's not the actual neurotransmitters but precursors, but if you just take that story then you cannot say that the brain is, as had been assumed, a self-enclosed system. On the contrary. In fact, if microbes are part of the nervous system, then it is a bit as if discoveries of microbiome researchers extended the brain beyond itself, as if the brain — traditionally another locus of self — were inseparably interwoven with microbes in our gut — that is, not-self.

And the third example is the genome. And as Thomas said, about 37 per cent of the genes we find in our genome have homologues in bacteria, i.e., they already existed in bacteria and are of bacterial origin. And that while we have about 23,000 genes in our nuclear genome, we have up to 20 million genes in our microbiome, many of which seem to be part, in one way or another, of our normal physiology: as especially Thomas has shown with his work on hydra, many of the pathways of interaction between genome and microbiome are evolutionarily preserved.

How wild is this?

The challenge here, again, is to understand that what we traditionally called self, the genome, is inseparably integrated with not-self — that is, the microbiome.

**"...nothing in cell and evolution history makes sense except in the light of the microbiome because they were there before we were there."**

**Reach: You see this as a profound difference in how we see ourselves. We haven't just extended the boundaries out a little more than we used to — this is a major change in our self-conception; is that right?**

**Rees:** It has the potential to be one. People can choose to ignore it, or people can begin learning about it. It redefines our place on the planet, our understanding of ourselves.

**Bosch:** Darwin's hypothesis put humans in the context of other living organisms, and human life is nothing else but another organism, another animal. And the microbiome research now makes more or less this same point. We get people saying, "Wow, we are just — our cells are the minority in our body and microbial cells are the majority." So our functioning is actually the sum of these parts, that's what we really are.

**Rees:** And I can push that further because, as Thomas said, for Darwin we were biological organisms among biological organisms, but we still could exist separate unto ourselves. But with the microbiome that's an impossible claim; you're completely and inseparably interwoven with the microbial world in which we live.

The oxygen we breathe is produced by microbes, the biogeochemistry on which we rely when we eat plants or animals that eat plants is done by microbes. How can one rethink what it means to be human, to live on the planet, how can one rethink politics in terms of giving microbes, so to speak, their fair share? It doesn't mean that microbes should vote, but it does mean that the stakes of politics extend far beyond the human, and when it comes to society we also might actually rethink what living together means. Who lives with whom?

If I'm at my most provocative I say that this figure of the human as set apart from the rest of the world as defined by our mind — by the meaning that we produce — this figure of the human doesn't actually exist in the wild. It's an artificial abstraction.

**Bosch:** If I can extend on that, this is exactly what one can say now about any fundamental processes of life. Multicellular life originated on a biofilm of 3.5 billion years of microbes that have invented everything in terms of communication, in terms of competition, in terms of synergy and cooperation.

All these features were there at a highly sophisticated level and then at some point it became multicellular. So today I think nothing in cell and evolution history makes sense except in the light of the microbiome because they were there before we were there, and "we" includes the most simple animal forms we have on this earth.

**Rees:** Thomas here de-centred the human, so to speak, from the centre of the world and put us a little on the side. And then when we have to rethink the human from the perspective of a microbial world, that's exactly what I'm intrigued by. For the humanities, for philosophy and anthropology, this a huge challenge.

**Reach: Do you think that this fits into a larger philosophical conversation about human identity and our place in the universe? For instance, I understand that Buddhism has always seen the self as an illusion.**

**Rees:** I would say that's actually a way more complicated question than one thinks. On the surface of things the answer is simply yes. As a matter of fact I'm organizing right now, with another member of CIFAR, Liping Zhao, a workshop in China where traditional Chinese philosophers, microbiome researchers from the east and the west and a couple of philosophers from the west meet to discuss the figure of the human that emerges from microbiome research and that very clearly corresponds with concepts from classical Chinese medicine.

Now, that being said, I think it is important to note and understand that classical Chinese philosophy and microbiome research are different fields that revolve around different goals. One is about science, the other is concerned with wisdom. Chinese philosophy doesn't need to be verified by microbiome research — and microbiome research doesn't need to be dignified by Chinese philosophy. But, I repeat, there are certainly corresponding ideas. This is also true, for example, for microbiome research and the history of landscape painting in Europe — think of a painter like Cezanne and the naked bodies that he painted where humans are basically fading into the environment and are dissolved in it without actually losing their contours. There are multiple traditions for rethinking the human and the natural worlds. Rather than blurring them all, I am interested in their differences and the correspondences that become visible through these differences.

**Reach: Going out as far as you can with this idea, does this create a sense of self that is completely interconnected with the rest of nature so that a separate sense of identity is a misunderstanding of who we are?**

**Rees:** I think we are a piece of nature and nothing but that. In fact we are a complicated piece of microbial matter with some more. This is one thing that is maybe controversial in the humanities and the human sciences. In the 17th century, the concept of the human as more than mere animal and as qualitatively different from a mere machine emerges. And in fact authors like Descartes and many who came after him thought that all animals and all plants are kind of machines. It also means that nature — and this includes the human body — can be described in terms of math and mechanics. But the human mind, because we have reason, cannot be described in terms of math and mechanics.

And so when you now say that humans are just a piece of nature, then you seem to suggest that the human sciences are illegitimate or that they're wrong or that they're building on an illusion or that the knowledge or the wisdom they have collected is not relevant, and I think that that's not at all the case.

I think on the contrary that the challenge is to rethink the human in terms of the knowledge produced by the microbiome, and thereby make the microbiome a kind of philosophical field. Or, differently put, if what's at stake in the study of microbes is the human, then that means that microbiome researchers must learn to talk to people in the humanities and human sciences, and people in the humanities and human sciences must learn to talk to microbiome researchers and explore that field in a shared way. •

> **"The challenge is to rethink the human in terms of the knowledge produced by the microbiome, and thereby make the microbiome a kind of philosophical field."**

# SEEING

# LIFE

# TO ANSWER THE BIGGEST QUESTION, WE HAVE TO UNDERSTAND THE WORLD AT THE SMALLEST SCALE

**BY JUANITA BAWAGAN**

**ILLUSTRATIONS BY KOTRYNA ZUKAUSKAITE**

When light hits your eye, hundreds of things happen before you see it. The process starts with a single group of atoms whose presence is responsible for the colour of the retina. They are part of a larger protein that absorbs the light, and as it does, this protein changes shape, bending and binding partners before it sets off a cascade of events that spark an electrical signal transmitted by rod cells to the optical nerve and, finally, to your brain. This all takes place nearly instantaneously, across different scales of space and time.

As colleagues working together at the University of Toronto, Dwayne Miller and Oliver Ernst were interested in the role played in this reaction by a light-sensitive receptor protein called rhodopsin. It triggers nerve stimulation with a 65 per cent quantum yield for every photon of light absorbed. This is one of the most evolutionarily optimized chemical reactions of its kind. And, as Miller and Ernst would later show, this reaction is also one of the fastest chemical reactions known, working at the quantum speed limit, happening in mere quadrillionths of a second.

The two researchers thought that if they could understand the mechanics of rhodopsin, and learn about the design principles in optimization of the protein structure, it would provide clues to unlock countless other biological processes. When they heard about CIFAR's 2013 Global Call for Ideas, they thought they had the beginnings of a proposal. But they also knew they had to think bigger.

"And so, what's the biggest idea? Well, we were sort of talking about, 'What is life?, That's the biggest single question you could imagine in the field of biology," recalled Miller. "It was pretty gutsy. I thought we might get shot down, that it was maybe too big."

Instead, they were chosen to create and co-direct CIFAR's Molecular Architecture of Life program. Although the questions around the meaning of life are broad and long-standing, Miller and Ernst thought that for the first time science had the tools to address the question directly. Advances in theory and in experimental approaches and especially recent advances in technology meant that science could bring a whole new set of techniques to understanding the very basics of life, right down to an atomic level. Four years into the program, the two researchers think they've made a start at answering the biggest question.

## MOLECULAR MOVIES

Over the course of a few years, Miller and Ernst had watched decades of research converge to answer the basic questions required to understand living systems. The way scientists observed the world had shifted. Before, they could only see life in static states, but now, science was making a jump from molecular photography to molecular movies.

These advances were in no small part due to technological advances. Ultrabright electron sources, a table-top particle accelerator, developed by Miller, and billion-dollar X-ray facilities could light up molecules in motion. Major advances in imaging hold promise to be able to map the chemistry behind such key life-giving processes as molecular self-replication. The challenge to connect all this information is daunting. But with machine learning and increased computing power, the researchers have pointed the way to make the connections between fundamental biochemistry and physics of nonlinear systems to the emergence of life.

Ernst points to the example of cryo-electron microscopy (cryo-EM), whose innovators were recognized with the 2017 Nobel Prize in Chemistry. Cryo-EM freezes molecules to capture three-dimensional snapshots of them in motion. The approach had been in development for more than 30 years, but detector technology and improved computational programs only caught up five years ago, Ernst said.

"I still think the best is yet to come," said Ernst. For him, atomic resolution of how biological systems work within the living cell is the gold standard.

"If you can look at something that is in motion, you understand how things are related to each other, and this is of course much more complicated. I only hope it will not take another 30 years to get there."

When they proposed the Molecular Architecture of Life program, Miller and Ernst hoped to create a program that could grow to the scope of the Human Genome Project. To achieve something on that scale, they had to build a team that would drive both technological development and understanding of the fundamental biology, chemistry and physics that underlie living systems. The Molecular Architecture of Life program includes fellows with backgrounds ranging from physics, chemistry, biochemistry and genetics to basic medicine; they come from Canada, the United States, England, Germany, Switzerland, China and Korea.

> "And so, what's the biggest idea? Well, we were sort of talking about, 'What is life?, That's the biggest single question you could imagine in the field of biology."

“We're at a new time in science where we can actually get at this great question everybody asks.”

# A WINDOW INTO THE BRAIN

“I really look at this as a collection of people with different backgrounds, expertise and knowledge. This heterogeneity makes the system much more powerful because it looks at every problem from a different angle,” said Krzysztof Palczewski, a professor at Case Western Reserve University’s Department of Pharmacology. He is a senior fellow in the Molecular Architecture of Life program and one of its first recruits.

For Palczewski, who is best known for solving the structure of rhodopsin, the answer to life’s greatest questions can be found in the eye.

“The eye is like a window into your brain,” he said.

The eye evolved before the brain and the information it processes is interconnected with the entire nervous system, he explained. The eye is also accessible for existing methodologies and techniques in biochemistry, pharmacology and imaging.

Palczewski has spent his career studying the chemistry and biology of vision, but CIFAR’s program allowed him to examine them in a new way. In a recent paper, Palczewski and Senior Fellow Daniel Figeys at the University of Ottawa revealed multiple signaling pathways involved in phagocytosis, the renewal of photoreceptor cells.

Every day, photoreceptor cells in the retina get replaced as new membranes and proteins are synthesized. We would go blind over time without this process. Scientists have long known that phagocytosis takes place, but there has been little progress in understanding exactly how. Figeys is a specialist in proteomics, a field of biotechnology that looks at the complex connections and data involved with protein networks. By looking at these connections, he and Palczewski are working toward unraveling the molecular basis of this process and others.

Exploring the pathways within the eye extends to a greater understanding of our bodies as a whole. The eye is home to light-sensitive receptors, which are part of the G protein-coupled receptor (GPCR) family. These receptors act as a “gateway to the cell” and help it to sense its environment. They are also crucial to drug design; approximately half of all medications today target this kind of receptor.

In textbook illustrations, GPCRs look like pool noodles threaded together, or curly ribbons along the membrane of a cell. These ribbons wiggle and bend to send messages and shape when and where hormones bind to specific receptors. But up until the last few decades, scientists had no idea what they looked like or if they existed as a molecule.

CIFAR Advisor Brian Kobilka was jointly awarded the Nobel Prize in Chemistry for his studies in the 1980s that led to the discovery of the GPCR family. In 2011, he would go on to capture the first image of a receptor just as it was activated by a hormone. The Nobel committee described it as “a molecular masterpiece.”

## BETTER DRUGS

Another paradigm shift in GPCR research came from Senior Fellow Michel Bouvier at the Université de Montréal. Bouvier discovered that many mutations led to disease because of misfolding proteins. Furthermore, he uncovered a way to restore the folding of disease-causing genetically mutated receptors using "pharmacological chaperones."

"It changed our hope to build new treatment for these diseases, to bring these 'chaperones' into the clinic," Bouvier said. One of the diseases targeted by Bouvier's group for the development of therapeutic pharmacological chaperone is familial early onset severe obesity.

Bouvier's studies also led to the concept of GPCR functional selectivity, whereby compounds can selectively regulate subsets of the activities controlled by a given GPCR. This opens the avenue to develop more effective drugs with fewer side effects in many clinical indications.

In the quest to understand life and how it arose, CIFAR fellows are helping to design better drugs, revolutionize technologies and change the way we see ourselves and our world. This hits at the crux of the Molecular Architecture of Life program. Miller and Ernst agree that "seeing is believing" and, most importantly, understanding.

This idea comes across through their research as well as their outreach. Miller is the founder of Science Rendezvous, Canada's nation-wide science festival. He launched the festival in 2008 to bring science out of the lab and into the streets. Since then, more than 200,000 Canadians, including over 6,000 volunteers, have had hands-on experiences that change how they see science in their everyday lives. To help better explain science using the principle "seeing is believing," Ernst recently developed the first interactive virtual reality biochemistry lecture with his graduate student. Using special molecule viewers from Autodesk, audience members were able to watch a protein in motion and imagine what life might be like within a cell.

"It is very important for us to reach out of from the science we are doing and make it accessible," said Ernst. "Then we can illustrate what, for example, is going on in the world at the molecular level … and they can explore it themselves."

## THE GREAT QUESTIONS

The Molecular Architecture of Life program is already examining the three characteristics that determine whether something is alive — whether it can reproduce, whether it can mutate and whether it is catalytic, or self-balancing. They can be hard questions to answer. They also blend together and the result is more likely a better way to test a question than to provide an answer.

When they do answer "the great question," it will bring forward many ethical issues. Some are already playing out with artificial intelligence, but a whole new debate would emerge about organisms that could potentially be created independent of another living system.

"We're at a new time in science where we can actually get at this great question everybody asks and we think, given the fullness of time, we'll be able to answer what makes a living system," said Miller.

When asked whether it will be possible to see this within his lifetime, Miller offers a confident "yes."

"You will get very old," said Ernst with a smile.

As their laughter settled, they quickly launched into an itemized list of things that need to happen from new technologies and detectors to better physics. It would be enormous to accomplish that in a lifetime, but as Miller and Ernst agree, they don't even have that kind of time.

"You'll see in 10, 20 years, somewhere in there," said Miller. "I think I'll make it." •

# HEROISM AND HOPE

BY CYNTHIA MACDONALD

**Charles Nelson studies what happens to children under the worst of conditions, from refugees in Dhaka to orphans in Romania. And while the results of abuse and neglect on the developing brain are grim, the lessons Nelson is learning provide hope that these children can be helped.**

**DHAKA DOESN'T JUST HAVE ONE SLUM AREA — IT HAS THOUSANDS OF THEM.** With 500,000 people moving from rural Bangladesh to its capital each year, the city is said to be growing faster than any other on Earth. Services and infrastructure have been stretched well beyond the breaking point. Before they are even born, the children of Dhaka must contend with the brute reality of its poverty.

"This is a place where there are dirt roads, a very high density of people, tremendous pollution, open sewers," says developmental neuroscientist Charles Nelson. "Because of unclean water and poor sanitation, the kids have chronic diarrhea. And on the psychosocial side, they live with high levels of domestic violence and maltreatment."

Nelson is a senior fellow in CIFAR's Child & Brain Development program, professor of pediatrics at Harvard, and head of the Laboratories of Cognitive Neuroscience at Boston Children's Hospital. Using sophisticated imaging techniques, he has spent much of his career studying the ways in which severe adversity affects the developing brains of young children. And in Dhaka, the forms of adversity are apparently endless. "A goal of our project is to understand how they work individually and in aggregate, to impact the course of it all," he says from his office in Boston.

On a dusty Dhaka street, Nelson's research team has managed to install a neuroimaging lab in a small apartment building that also houses a medical clinic. This is no small feat, considering that four months before the lab opened, the building had no grounded electricity and a gaping construction hole in front of it. But with strong local partnerships and funds from the Bill & Melinda Gates Foundation, it's been up and running for over three years.

During that time, Nelson has been following a double cohort of children who were first screened at the ages of six months and three years, respectively. Initial test results — using MRI, EEG and a newer technique known as functional near-infrared spectroscopy (fNIRS) — have shown the three-year-olds to be "way behind" on cognitive development, with reduced metabolic activity (inferred from fNIRS) and altered connectivity (inferred from EEG). The study is intended to be longitudinal; it will follow the same children over several years, so it will be some time before Nelson can say definitively which insults, among the many faced by his Dhaka cohort, are worse than others.

He has some ideas, however. "We think that psychosocial features, such as violence in the house, may exert bigger effects than growth stunting. Growth stunting usually results from malnutrition; everybody assumes it's bad for the brain, and it certainly is. But we may be showing that psychosocial adversity is even worse."

## THE GRIM LESSONS OF ROMANIAN ORPHANAGES

Dhaka is not the only place that Nelson has studied children living in the worst of conditions. Since 1999, a landmark study he has coled in Romania, known as the Bucharest Early Intervention Project (BEIP), has revealed much about how a child's brain responds — in some cases, permanently — to his or her environment during the first years of life.

The tragic story of Romania's orphanage system is now well-known. In the misguided belief that population growth would lead to economic riches, former leader Nicolae Ceauşescu effectively banned both abortion and contraception. The consequence of this thinking was that, from the 1960s until the repressive dictator was executed in 1989, hundreds of thousands of unwanted children were placed in a series of grim, poorly run orphanages.

One survivor referred to the orphanages as "slaughterhouses of souls"; when Nelson and his team first started working in them, they made a pact with each other not to cry in front of the children. Babies lay in unchanged diapers, staring at white ceilings all day and developing permanently crossed eyes in the process; small children were often totally withdrawn, or clung wildly to strangers.

Romania was a far different environment from Dhaka — with modern plumbing and sanitation, the European children were far less afflicted by enteric disease. But without the benefit of the kind of familial attention seen in Dhaka, they've suffered profoundly from the trauma of extreme neglect.

Brain imaging has shown the tragic results of neglect in Romanian orphanages.

"The kids in Dhaka are being clobbered with experiences that are not healthy for brain development," Nelson says. "Whereas the kids in Romania were just not getting experiences. And it juxtaposes the differences. How does the brain wire itself if it doesn't get a set of instructions? And how does it wire itself if the instructions it gets are less than optimal?"

The MRIs administered to children in Romania clearly showed that eight-year-olds had marked deficits in both grey matter (governing, among many other things, intelligence and emotional regulation) and white matter (the brain's information highway, responsible for transmitting its thoughts and impulses). "In the Romanian orphanages, we found that the entire brain was affected," Nelson says. "We believe these children may have fewer brain cells, or fewer connections."

## CRITICAL TIMING

Children thrive on loving attention, good nutrition and a safe environment, and the absence of any one of these is likely to be dangerous in some way. But Nelson's work has revealed that early deprivation does not simply make children unhappy: because it interrupts their brain development, it may damage them beyond repair. The harsh truth is that without proper intervention, such damage can make leaving the grinding cycle of poverty all the more difficult.

To prevent this, timing is critical. Nelson has been able to show that when intervention occurs early enough, some pernicious effects can be reversed. Half of the 136 children in the Romanian study were placed in foster care, while the rest stayed in institutions. But when children were placed in a foster care environment before age two, their IQ and social functioning improved to a degree Nelson calls "overwhelming." Children placed later improved, too, though not nearly as much.

In Dhaka however, "we can't really examine critical periods very well, because we're not manipulating anything," Nelson says. "We just see delays and deficits. But the fact that we're not seeing too much at six months — and a lot at 36 months — makes me wonder if kids need to be in these bad environments for a while before the brain goes off track."

He has also noticed that functions such as cognition appear more amenable to recovery than other abilities, such as the goal-setting and self-control mechanisms known as executive functions.

"How does the brain wire itself if it doesn't get a set of instructions?" Nelson asks.

Mike Carroll

Megan Gunnar is a psychologist and associate fellow in CIFAR's Child & Brain Development (CBD) program whose research has also centred on early adversity in children, with an emphasis on those adopted from orphanages. She's seen similar results in North America. While many of the children she has studied do succeed in life, especially those with resourceful parents, "they often struggle with attention problems," says Gunnar. "The prefrontal cortex is very sensitive to early experiences, and we see disturbances in the development of the circuitry that supports executive function. We see this in imaging, and in the kind of tasks they're able to do."

Essential brain functions don't come on all at once. Though the stage for poor outcomes may be set early in life, the results of adversity are only revealed in the fullness of time. This argues for the necessity of studying children, as Nelson does, in a longitudinal fashion.

In infancy, researchers can tell whether vision, hearing and motor skills are developing properly. But it's only when children enter school that the abilities to read, write and get along with peers become measurable. In adolescence, other deficits may emerge, such as those related to executive functioning and intimate partner relationships. Among the Romanian orphans, psychosis and paranoia have just started to appear in teens who've been institutionalized their whole lives.

"One concern we've already had is that of those 136 kids who started life in an institution, 68 are girls. And of those, nine of them had had babies by the time they were 15," says Nelson. "So we'd like to follow that up."

## ETHICAL CONSIDERATIONS

Naturally, many ethical questions surround the study of children living in squalor. The BEIP was a randomized control trial; as with others of this type, half the subjects received treatment and half didn't. Unlike other such trials, though, it was likely from the outset that children removed from orphanage care would fare better than those left in it. Wouldn't it have been preferable to just close the orphanages, and place every single child with a caring foster family?

Unfortunately, that option wasn't available in Romania in the early 2000s. The country did not have a foster care system, and most of the parentless children were not, in fact, literal orphans: without proper resources to raise them,

Photo credit: Mike Carroll

“WE CAN INTERVENE IN DOMESTIC VIOLENCE, AND IN CHILD MALTREATMENT. WE CAN CLEAN UP THE WATER, WE CAN IMPROVE THE VACCINATION RATE, WE CAN CURE THEIR ENTERIC DISEASE.”

their parents had simply abandoned them in orphanages.

Still, after a lengthy interview process and the cooperation of local NGOs, Nelson’s team managed to find, train and fund enough competent adults to foster about half of his cohort. When the initial research period was over, they staged a press conference in Bucharest to draw attention to the radical differences between orphanage and home care. They then called on the government to pay for foster parenting.

That system is now in place. While institutional care hasn’t been fully eradicated in Romania, it is forbidden for children under the age of two (except in cases of severe disability).

Nelson admits that fixing the situation in Dhaka will be far more difficult. With a current population of 18 million, its numbers swell every day with the presence of “climate refugees” driven toward the city from a receding coastline. Many of these live in the slums.

“But there are concrete steps we can take,” Nelson insists. “We can intervene in domestic violence, and in child maltreatment. We can clean up the water, we can improve the vaccination rate, we can cure their enteric disease.”

## NO SIMPLE ANSWER

Any one of these problems could prove harmful to the developing brain. The widespread presence of potentially harmful gut pathogens in Dhaka is a relatively recent concern for neuroscientists, given new research on the relationship between microbiota and the brain. But Nelson wants to use a combination of therapy and imaging technology to identify the most pressing needs first, so that interventions can be precision-targeted.

“I don’t think we ever expected a simple answer,” says behavioural geneticist Marla Sokolowski, co-director of CIFAR’s CBD program. “Now, at least, scientists know what many of the problems are. Physical abuse used to be the only thing that was thought to affect children in a very negative way. But now we know that the slow drip of neglect, even without physical abuse, can be just as bad. Because adversity is so multidimensional, we need to bring together people from all kinds of disciplines. Chuck brings expertise in psychology, as well as in neuroscience.”

On occasion, those brain images are surprising. Even with everything against them, a minority of children are able to survive, thrive and lead relatively normal lives. “Some kids are exposed to horrible experiences, but don’t show any developmental sequelae because of them,” Nelson says. “In Romania we tried to identify key protective factors, but there’s still this issue of individual differences — a combination of genetics and other things that we don’t yet fully understand. So we expect there will be some kids in Dhaka who look unfazed by these experiences. And others who will be profoundly impacted. And the big question for us is, which is which, and why is that?”

He’s also availed himself of new techniques. Scanning babies in an MRI machine might once have seemed impossible, given the punishing din of this particular test on adults, but the team has developed a technique to test infants who are fully asleep, clad in special “swaddle sacks.”

But while MRI reveals a lot about the brain’s structure, other technology is needed to mea-

The children of Dhaka deal with a multitude of threats, including pollution, malnutrition and microbial illness.

Photo Credit: Courtesy of Charles Nelson

sure how it's actually functioning. For this, scientists have traditionally relied on functional MRI scanning (fMRI). But fMRI tests aren't easy on children, in that they require them to sit still for long periods of time. Instead, Nelson uses fNIRS, which is shorter and more readily accommodates a fidgety patient. He also uses EEG, which measures electrical activity in the brain.

And the people of Dhaka are involved not only as test subjects, but as data collectors, too. "We have a staff of about maybe 15 local people," Nelson says. "They operate the lab there. Some of them are the physicians who see these kids, and have gotten to know them really well. The other thing is that we've brought them here to Harvard a couple of times for training. So even long after our study is over, they'll have the intellectual capital there to continue this work on their own."

Nelson's studies are well-known to psychologists working with children in impoverished societies around the world, in places far removed from the relative comfort of North America. Are these issues relevant to our own society?

"I think they are," says Sokolowski. "I mean, if you look at the Indigenous population on reserves — I don't have to say any more. This is happening in Canada. And even in wealthy populations there's abuse and neglect that isn't spoken about. This is not, about 'them and us.' It's about all of us."

Nelson's career is unique in that it has involved three distinct domains: developmental psychology, neuroscience and humanitarianism. Emotionally, it has been extremely draining. But it's also had a directly positive effect on the lives of many, and promises to do so for years to come. Thanks to Nelson's work, we can be sure that while nature is a powerful determinant in brain development, nurture plays a large part, too. He has ensured that children's brains can be studied both ethically and effectively. He is ferreting out the greatest dangers to a vulnerable cerebrum. And, perhaps above all, he is making direct interventions that save lives.

"Chuck is a fantastic researcher and he'll go anywhere in the world to find the answers to questions that he's asking," says Sokolowski. "Everyone wants the best for their children, no matter what their circumstances. They're happy that someone is thinking and caring about them, so that they can have better lives. Heroic — that's the word for what he does." •

# THE LEADING EDGE

## CIFAR is keeping Canada at the forefront of AI

BY EVA VOINIGESCU

The 19th-century facade of the Power Corporation of Canada headquarters in Montreal belied the cutting-edge technology being discussed inside on a Tuesday evening this past April. Some of Canada's most prominent business leaders were hearing from a selection of the world's foremost experts on artificial intelligence (AI), including CIFAR Senior Fellows Yoshua Bengio and Joëlle Pineau, and celebrating the tremendous success of the Québec AI ecosystem.

The success in Montreal is a microcosm of what's going on nationally, thanks in part to the Pan-Canadian Artificial Intelligence Strategy and CIFAR's leadership in AI. It's an example of how a strong partnership among research, government and industry can retain and attract the world's top talent and keep Canada at the leading edge in a field that will significantly shape the way we live for years to come.

Canadians and Canadian-funded research have long been at the forefront of developments in AI. CIFAR recruited Geoffrey Hinton, now a CIFAR Distinguished Fellow and chief scientific advisor at the Vector Institute in Toronto, to Canada in the 1980s. At the time, most AI researchers saw neural networks as a dead end. But Hinton started what is now CIFAR's Learning in Machines & Brains program, and the foundational work he and others did within the program helped spark the deep learning technology we know today. Now, deep learning fuels everything from smart cars, to personalized medicine and diagnostics, to science itself.

So when the federal government announced its $125 million investment in the Pan-Canadian AI Strategy in March 2017, it looked to CIFAR for help.

"CIFAR's long track record of supporting pioneering AI research and success in bringing together research leaders from across disciplines and around the world to tackle tough problems made us the obvious choice for delivering on the goals of our national AI research strategy," says Elissa Strome, executive director, Pan-Canadian AI Strategy at CIFAR.

The strategy aims to cement Canada's international leadership in AI research and training through four primary areas. The first is to establish three centres of excellence in AI research across the country: Vector Institute

CIFAR Senior Fellows Yoshua Bengio and Joelle Pineau are leaders in AI research. They helped celebrate Montreal's AI leadership at a CIFAR event in April.

Photo credits: Pat Pinotti, Les Productions Studio 55 Inc. (photos); Kotryna Zukauskaite (background illustration)

in Toronto, MILA in Montreal and the Alberta Machine Intelligence Institute (Amii) in Edmonton. The institutes' leadership includes current and past members of CIFAR's Learning in Machines & Brains program, from Rich Zemel in Toronto, to Bengio in Montreal, to CIFAR Associate Fellow Rich Sutton in Edmonton.

The second, and hallmark activity, the Canada CIFAR Chairs in AI program, is dedicated to recruiting and retaining leading AI researchers to Canada as well as fostering the next generation of talented AI scientists. The program will see 50 Canada CIFAR Chairs in AI appointed across the three institutes. CIFAR is working closely with the AI institutes as they identify possible candidates, and in February appointed seven members to the Pan-Canadian AI Strategy's International Scientific Advisory Committee. This committee, comprised of internationally distinguished individuals from leading universities and companies from the US, the UK, France and the Netherlands, will review nominations for the CCAI Chairs program and provide strategic advice and guidance on the overall strategy.

Already, support from federal funding, and the significant provincial contribution ($50 million in Ontario and $100 million in Québec) and private sector investment is drawing AI leaders to Canada. Carnegie Mellon professor Garth Gibson has been appointed CEO of Vector. The newly established Microsoft Research Montreal recruited Geoff Gordon, also from Carnegie Mellon, and CIFAR Senior Fellow Alán Aspuru-Guzik left Harvard to join Vector and the University of Toronto as a Canada 150 Research Chair.

Further investments have focused on expanding the pool of talented individuals in Canada who have skills and expertise in AI. Last October, the Ontario government increased its commitment to AI training, investing an additional $30 million in Vector over five years to work with universities to build a strong cohort of AI master's students.

"The Province of Ontario saw an important opportunity to respond to demand from students and employers alike for expanded training opportunities in AI. The goal is that by the end of five years, Ontario will be graduating 1,000 master's students per year in AI-related fields. That kind of density of tal-

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**The AI & Society Program lets us tackle the questions that are important, but may not necessarily be getting attention right now...**

ent can lead to significant positive economic impact," says Strome.

The third component of the strategy is the creation of a national AI program of activities to encourage greater coast-to-coast collaboration in research. These activities include workshops, a December meeting of the CIFAR Chairs in AI in Montreal and a series of hands-on summer schools dedicated to helping young people, from high school to graduate school and beyond, develop skills and expertise in AI that will be beneficial to their careers.

Two summer schools worth highlighting are the upcoming annual CIFAR Deep Learning/Reinforcement Learning Summer School, hosted by the Vector Institute and University of Toronto this July for 250 graduate and post-graduate trainees; and McGill University, MILA and the OSMO Foundation's AI for Social Good Summer Lab, which provides women with machine learning skills and practical experience to increase their career opportunities.

The national AI program's workshops, Aix (or AI to the power of X), will also provide opportunities for researchers to get together with machine learning and AI experts to think about how to apply AI approaches to their particular domain. One workshop this January with the CIHR's Institute of Population and Public Health brought together public health researchers and AI researchers. A second workshop, AI for Neuroscience, is coming this fall.

"The Tri-Council Agencies just launched a call for proposals for AI, Health and Society projects so we're already seeing outcomes as a result of the workshops that CIFAR helped to organize and facilitate," says Strome.

The fourth and final component of the strategy is perhaps the one of most interest to a media-consuming general public already intrigued by how AI will impact our daily lives. CIFAR's AI & Society Program will support research and policy outreach on the ethical, legal, economic and policy opportunities and issues AI presents for society by convening working groups and publishing the results in non-specialist publications that are accessible to a broad audience.

"The AI & Society program lets us tackle the questions that are important, but may not necessarily be getting attention right now. It also gives us the chance to engage internationally and across perspectives," says CIFAR Director of Public Policy Brent Barron.

"If we look at what's going to help the world respond in a way that best takes advantage of this technology, it's research capacity, but also policy innovation and business leadership. We need to be able to bring all of those sectors together," he says. Two lines of activities will serve this goal.

A call for workshops seeks proposals from around the world in three areas: policy implications; global dynamics; and creativity and discovery. These themes were selected to open the door to greater involvement from researchers in the social sciences and humanities.

"The vast majority of the people I've talked to are really interested in engaging across disciplines and across borders. We aren't seeing many other mechanisms that are focused on supporting that kind of engagement."

The workshops will build connections, and will also provide a pipeline for knowledge mobilization. Conclusions will be published as white papers, briefing documents and reports, for example, aimed at the government community, professional associations, NGOs and beyond.

The second part of the AI & Society program is a national series of policy foresight labs that will bring early career professionals in government, together with people from think tanks, advocacy groups and the broader public sector, to explore policy issues posed by AI. The aim is to spark discussions about the potential of technology, across policy domains.

As Barron sees it, Canada has all the pieces in place to contribute to the world's moral compass on AI.

"If you look at everything that's happening in Montreal, for example, on ethics and social responsibility, together with the Government of Canada's investment in CIFAR on AI & Society, it seems as if Canada will be able to fulfil its traditional middle power influence in the world. As a global convenor and peacekeeper that exemplifies the values of diversity and inclusivity, this could be Canada's time to shine."

The scope of CIFAR's AI efforts is necessarily ambitious. The overwhelming appetite for leadership and engagement on this issue, and the sheer number of players rushing into the field, makes the task of connecting everyone a challenge. Fortunately, CIFAR's model of convening diverse groups of actors to address broad questions of global importance has been refined and implemented successfully over 35 years.

"Because we're very much in the early start-up phase of the strategy, outreach is really a critical component. One of the things that we are tracking very closely is all of the events and workshops and conferences and panels that we're participating in, and our public visibility as the leaders of implementing the strategy," says Strome.

So what is the vision for one year out from now?

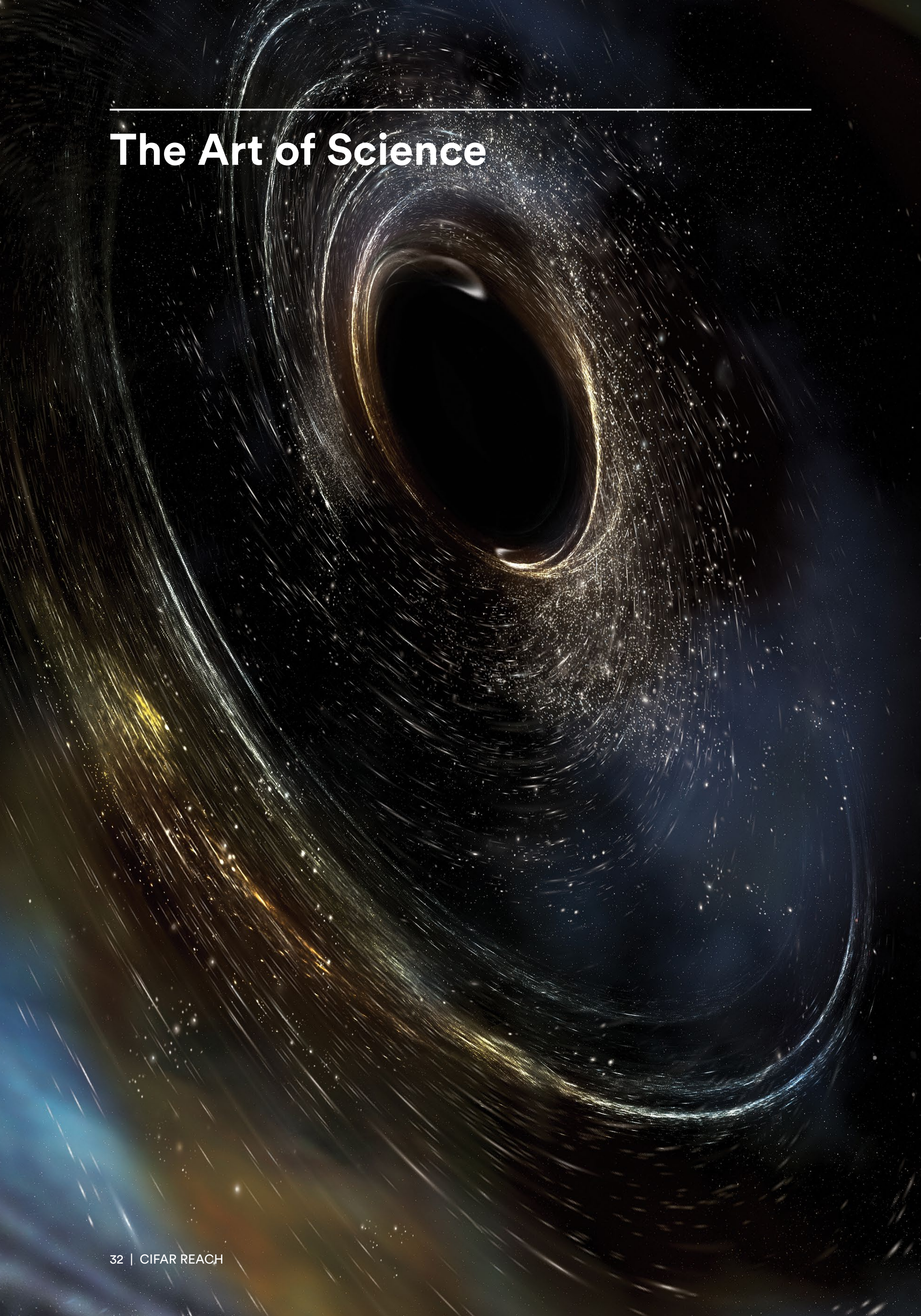
"The AI Institutes will be buzzing with activity and undertaking leading-edge research to continue to advance AI technology," says Strome. "We will have named a cohort of incredibly strong, diverse and internationally leading researchers who have come to Canada, or remained in Canada, and taken up roles as Canada CIFAR Chairs in AI. Our national program of activities will have reached a wider audience and brought experts from across disciplines and across the country together And, finally, our AI & Society program activities will have seeded new areas of research that help inform decision-making across a variety of sectors.

"It is ambitious," acknowledges Strome, "but we have great partners on the ground and a shared vision across the country. The Pan-Canadian AI Strategy is off to an amazing start." •

**"**

**...we have great partners on the ground and a shared vision across the country. The Pan-Canadian AI Strategy is off to an amazing start**

# The Art of Science



# Spacetime rippling

**ON SEPTEMBER 14, 2015,** a postdoctoral student in Germany noticed an odd squiggle creeping across his computer screen.

It was the first sign of a gravitational wave — the result of two black holes colliding 1.3 billion light years away, releasing 50 times the energy of all the stars in the observable universe.

The collision forced the black holes to merge into one entity 62 times as massive as the sun. Powerful ripples warped the fabric of spacetime and billowed outward, much like lake water after a stone is skipped upon it. Some 50,000 years ago, these waves entered the Milky Way.

In 1916, Albert Einstein predicted the existence of gravitational waves in his general theory of relativity. But their detection only became possible in 2002, when construction of the U.S.-based Laser Interferometer Gravitational-Wave Observatory (LIGO) was finished. It took another 13 years and an international team of scientists — several of them affiliated with CIFAR — for that first wave to come into view.

Since then, LIGO has detected five more black hole collisions, as well as one between two neutron stars. Thanks to this discovery, scientists hope to gain insight into mysteries such as the rate at which the universe is expanding, how the universe structured itself into galaxies, what percentage of the universe is made of black holes and much more. Gravitational waves represent, in the words of CIFAR Senior Fellow (and member of the 2015 LIGO collaboration) Vicky Kalogera, "a revolution in astronomy."

*– Cynthia Macdonald*

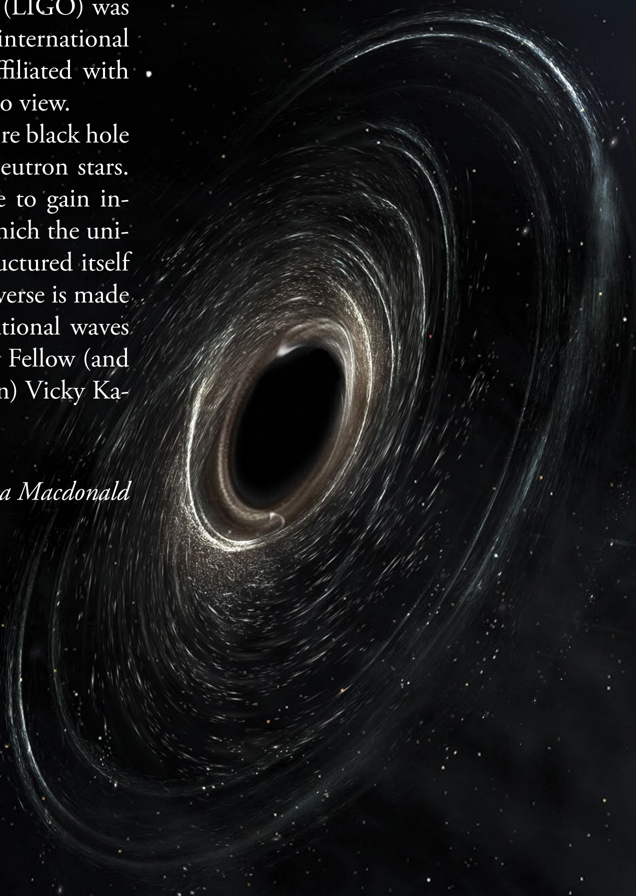


Photo Credit: LIGO/Caltech/MIT/Sonoma State (Aurore Simonnet)

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# History Note

## Remembering Stephen Hawking

### A mentor, a friend and a force of nature

Left: Stephen Hawking at the University of Alberta in 1992. Right (from left to right): CIFAR's first President Fraser Mustard, Stephen Hawking and CIFAR Distinguished Fellow Werner Israel.

**IN 1992, WORLD-RENOWNED PHYSICIST STEPHEN HAWKING** joined CIFAR as an associate fellow in the Cosmology program. The program had a focus son theoretical gravity, and one of the questions it asked was what happens to information inside of a black hole. Hawking believed it was destroyed, while particle physicists in the program argued that it must be recoverable. Associate Fellow Leonard Susskind, who would eventually show that Hawking was wrong on this point, once described Hawking as "the most infuriating person in the universe."

Later that year, program members would meet in Banff to celebrate the 60th birthday of Werner Israel, a close collaborator with Hawking on studies of general relativity. Following a celebratory discussion called "Black Holes, White Holes and Wormholes" in Banff, many members went to Edmonton for a CIFAR-sponsored lecture at the University of Alberta. Hawking discussed the future of the universe on stage with Israel and Senior Fellow Don Page. Page had studied under Hawking as did Raymond Laflamme, who is currently a senior fellow in CIFAR's Quantum Information Science program.

On March 14, 2018, Hawking passed away at the age of 76. He changed the way we look at the universe and left an indelible mark on CIFAR and its global research community.

*– Juanita Bawagan*

Photo credits: CIFAR Archives


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