



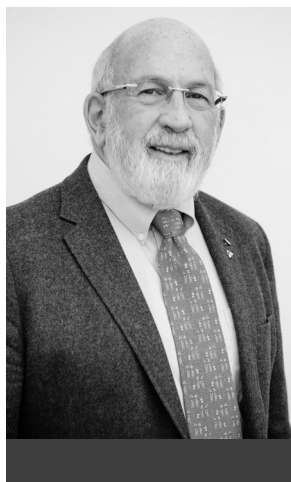
THINK SYNTHETIC BIOLOGY

Synthetic biology is the science of building simple organisms or “biological apps” to make manufacturing more green, energy production more sustainable, agriculture more robust, and medicine more powerful and precise. The US and UK are nurturing synthetic biology as humanity’s next technological frontier. It will take bold and decisive action for Ontario to seize this opportunity.



Ontario Genomics

■ FOREWORD



Over the last century, we have made tremendous strides in science and technology that have improved our quality of life.

But the threats facing our world are greater than ever. Feeding the planet sustainably, combatting lethal infectious diseases, and mitigating climate change are just a few examples of the imminent challenges demanding our attention.

Imagine a technology that has the power to counter these threats.

Synthetic biology builds on genomics to design and engineer biological entities that can solve these problems. It is pushing the boundaries of biological possibility, not just in the lab, but at an industrially-meaningful scale, generating jobs and wealth. And Ontario is ripe to benefit from it. With our world-class understanding of biology, robust genomics, engineering and IT infrastructure, and strong industry sectors in need of new sustainable strategies and practices, Ontario is well positioned to capitalize on synthetic biology.

But we must act boldly and decisively.

With this report, Ontario Genomics asks academic administrators, funders and government ministries to ‘Think Synthetic Biology’ as a source of knowledge and solutions to maintain the standard of living we deserve, for years to come.

A handwritten signature in black ink, reading "Mark Poznansky".

Dr. Mark Poznansky, C.M., O.Ont., Ph.D.

President and CEO, Ontario Genomics



■ WHAT IS SYNTHETIC BIOLOGY?

Synthetic biology is the science of designing and building simple organisms or “biological apps” to perform specific industrial or therapeutic functions. This industrialization of biology renders processes faster, cheaper, and more reliable.

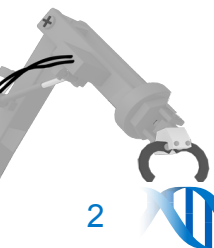
Beginning with the isolation of DNA in 1869, synthetic biology’s transformational capability stems from over a century of science exploration. In the past forty years alone, remarkable advancements in technology, instrumentation, and analytics have accelerated our understanding of genes and DNA. With ever-evolving high-tech sequencers, the cost of sequencing an entire human genome has decreased from \$2-3 billion in 2005 to less than \$1,000 today, and can now be done in a few hours instead of years. This availability of affordable DNA sequencing has enabled scientists to understand how complex biological systems perform functions that are invaluable to our society, like converting waste to energy and warding off infection.

We are now able to not only design de novo biological systems (by mixing and matching naturally-occurring genes), but actually write the code to manufacture them, much the same way that software engineers can design and build apps.

By merging this understanding with advanced digital technologies, robotics and automation, we have assembled the knowledge and tools that have enabled the capabilities collectively known as synthetic biology. We are now able to not only design de novo biological systems (by mixing and matching naturally-occurring genes), but actually write the code to manufacture them, much the same way that software engineers can design and build apps. We are able to move from the time-consuming cloning of individual genes in a lab to high-speed “design-build-test” engineering of entire biological systems and high-throughput automated manufacturing.

This has transformed biology from a science of observation, where scientists seek to characterize how living systems function, into one of building, where those systems can be designed and built for useful purposes. Genomics, no longer a niche tool, is now a data-driven, large-scale engineering program.

Synthetic biology, therefore, is more than just an interesting new discipline. It is a critical driver of the future economy and our state of well-being and a key to addressing humanity’s most pressing health, agricultural and environmental challenges. Its widescale application, immense potential, and growing accessibility positions it as the next frontier of technology to drive an industrial and social revolution, and profoundly change our world for the better.



■ THE NEED FOR SYNTHETIC BIOLOGY

The 20th century saw some of the most dramatic technological revolutions in human history. The refining of oil into a myriad of chemicals has led to immense economic growth, providing us with everything from gasoline to toothpaste, contact lenses, credit cards, golf balls, polystyrene cups and plastic bags. Key advances in agriculture such as chemical fertilizers boosted crop yields enormously, allowing us to grow the food needed to feed an exploding population. And medical advances like the discovery of antibiotics have transformed life-threatening diseases into treatable conditions.

Synthetic biology is the creation of custom biological entities that have the ability to address humanity's most pressing challenges in health, food production and the environment

While these technologies have significantly raised our standard of living, most rely on 100-year-old industrial processes that are energy intensive and unsustainable. For instance, our continued reliance on refining oil has led to air pollution, greenhouse gas emissions and wilderness destruction. Meeting the global food challenge (increasing production by 50% by 2050)¹ with the use of chemical fertilizers is simply not an option. And over 2% of global energy use can be attributed to manufacturing of agricultural supplements, which also contribute significantly to water pollution.²

Twentieth century technologies have also failed to address some of our most serious health threats - pathogens like Ebola, Zika, HIV and antibiotic-resistant bacteria remain a huge challenge. An estimated 350 million people suffer from incurable genetic diseases like muscular dystrophy³ and cancer is becoming a leading cause of premature death. These are serious problems that cannot be solved by fine-tuning existing technologies. We need an entirely new approach. Synthetic biology is the answer.

How does synthetic biology make engineering biology easier?

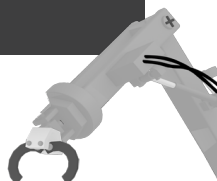
Synthetic biologists apply three simple concepts from disciplines like mechanical and electrical engineering to living systems:

1. Standardization: Libraries of standardized genetic 'parts' can be purchased off the shelf to reliably and predictably perform a certain function in a cell, regardless of the lab they are used in.

2. Decoupling design and fabrication: To maximize efficiency, productivity, and cost effectiveness experts can focus on different aspects of the engineering process from design of genetic circuits to the synthesis of DNA to assembling engineered cells.

3. Component abstraction: Complex biological systems are represented by simple modular symbols that allow designers to write genetic programs without needing to understand the scientific details of how the parts function.

Advances such as better design through bioinformatics, inexpensive DNA synthesis (as low as \$0.03/base), and increasing use of robotics and automation in the assembly of engineered cells is enabling synthetic biologists to design, build, and test engineered biological systems in a fraction of the time—with predictability and reliability. This means discoveries are made more quickly and new products reach the market faster and for less cost.



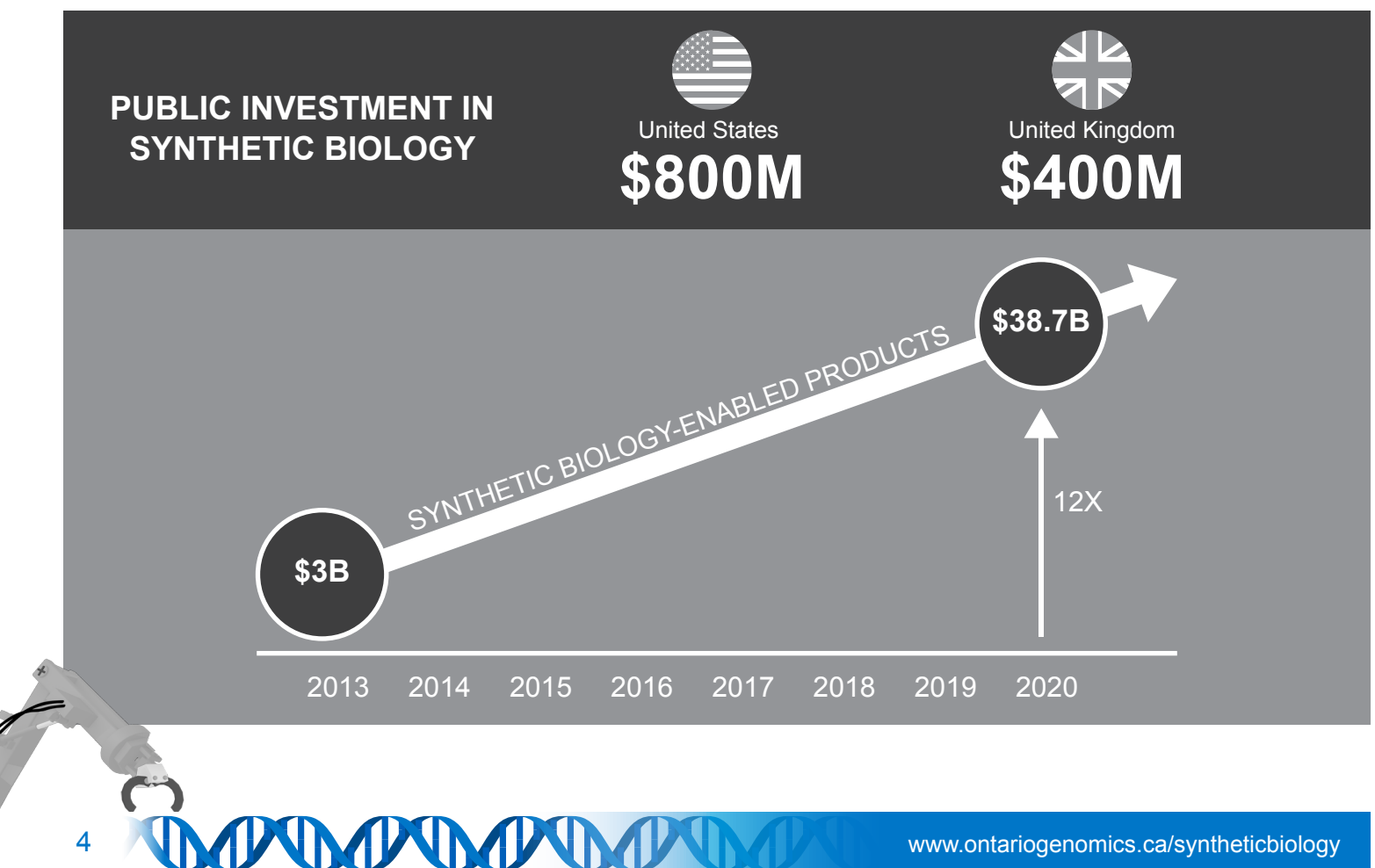
■ WHAT DOES THE MARKET THINK?

Since its inception in the early 2000s, synthetic biology has rapidly grown around the world, attracting a community of engineers, scientists, entrepreneurs, investors, sociologists and policymakers. An enduring hallmark of this community has been a focus on ensuring safe research practices and multi-tier stakeholder engagement, from government regulators to the public.

Recognized by McKinsey as one of 12 disruptive technologies that will “transform life, business, and the global economy,”⁴ synthetic biology is in a period of rapid growth and adoption. President Obama’s Bioeconomy Blueprint highlighted synthetic biology as a critical platform technology, and the UK government has identified it as one of the eight great technologies poised to propel growth in the UK.^{5,6} Both governments have made significant investments to support synthetic biology research and

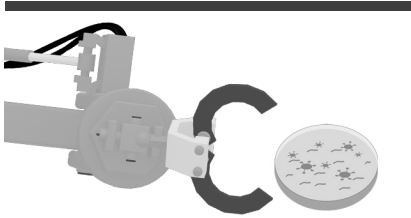
development, with over \$800M USD invested in the United States through agencies such as Defense Advanced Research Projects Agency (DARPA), and \$400M USD invested in the UK.^{7,8}

Synthetic biology has also reaped significant technical and commercial success over recent years. Valued at \$3B USD in 2013, the market for synthetic biology-enabled products is expected to grow to \$38.7B USD by 2020, with over \$1B USD in venture capital investment in startups in 2016 alone.^{9,10} Established multi-nationals in diverse sectors such as agriculture, energy, chemicals, and IT are also investing heavily in synthetic biology-driven products and processes. A notable example is Exxon Mobil’s recent investment of \$300M USD in algal biofuel manufacturing through a partnership with Synthetic Genomics.¹¹



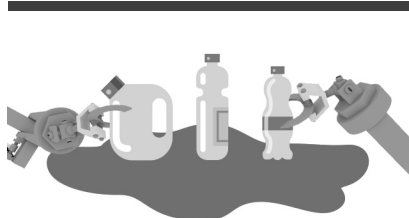
■ SYNTHETIC BIOLOGY IS SHAPING THE FUTURE

Synthetic biology is already solving real world problems across a wide range of application areas. To see it's compelling applications to Ontario today, visit www.ontariogenomics.ca/syntheticbiology



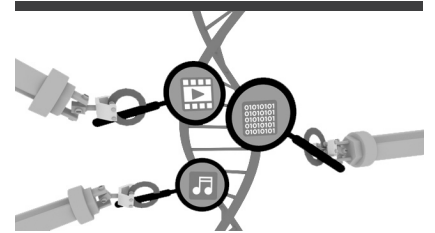
Synthetic Life

In 2016, scientists at the J. Craig Venter Institute created a new species of bacteria with a completely synthetic genome, coding only genes that are essential for life. This 'blank slate' organism can be used as the basis for specialized bacteria to make vaccines, drugs, and biochemicals more efficiently.¹²



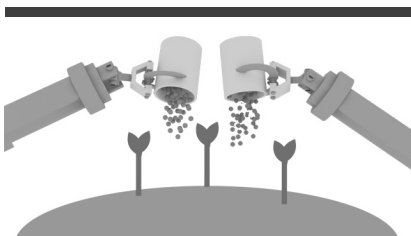
Plastics and Fuels

DuPont's Bio-PDO™ and Amyris' Biofene® are made from plant sugar by synthetic micro-organisms and used in plastics and cosmetics manufacturing. The commercial scale manufacture of biofuel from corn cob and straw waste across the United States uses a similar approach.¹⁴



DNA Data Storage

Data generation is far outpacing our capability to store it. Microsoft has invested in DNA as the densest archival storage media known, and demonstrated that 200MB of data, including a music video and the Universal Declaration of Human Rights, can be stored and retrieved from a synthetic DNA sequence.¹³



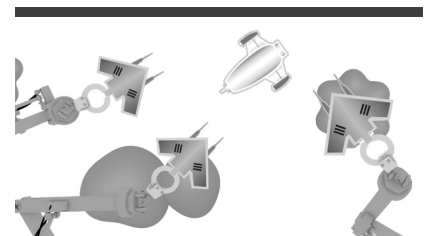
Agriculture

UK-based Azotic Technologies is commercializing a bacteria that produces fertilizer from air. This has the potential to reduce harmful chemical fertilizer use by more than 50% without sacrificing high yields.¹⁶



Rare Diseases

A 2017 clinical trial led by Editas Medicine will use molecular scissors known as CRISPR to cut out and repair a rare faulty gene in the eye that causes blindness. CRISPR methodology is also being tested in the treatment of muscular dystrophy and cystic fibrosis.¹⁵



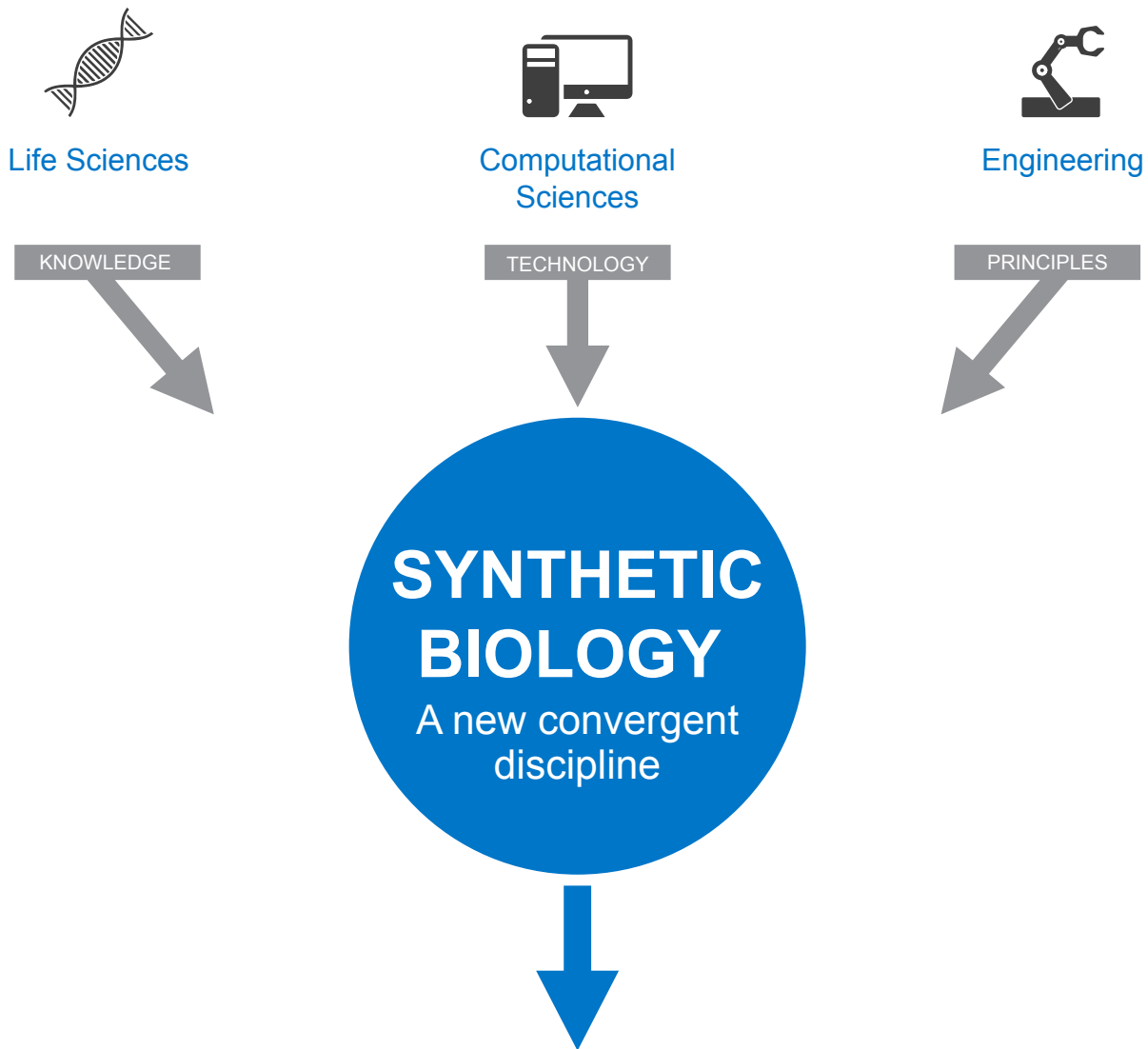
Bacterial Armies

Seres Therapeutics is leading a clinical trial that engineers gut bacteria to fight antibiotic resistant *C. difficile*. The technology has been designated a breakthrough therapy by the FDA.¹⁷

■ SYNTHETIC BIOLOGY: A NEW COVERGENT DISCIPLINE

Synthetic biology is uniquely positioned to draw on Ontario's strengths and bolster a range of application areas, allowing more value to be extracted from our existing investments in research and innovation. Through the development of platform tools - from the design of complex genetic circuits to robotic automation - synthetic biology will help address common engineering challenges, including scale up, cost, and reliability, that often prevent our laboratory discoveries from reaching the market.

Three Foundational Scientific Pillars



Enable Ontario's Major Economic Contributors



■ THE OPPORTUNITY FOR ONTARIO

As showcased, synthetic biology technologies are already reaching the market and disrupting a range of industries across the globe. It goes without saying that Ontario will need to import some of these solutions over the coming years to remain competitive and address its local challenges. But the opportunity is much greater than being a mere consumer of technology. We argue that Ontario is well-positioned to launch a home-grown synthetic biology sector that will become an exporter of game-changing technologies and products to the world.

Two key strengths needed to realize this opportunity are already in place:

1. Synthetic biology's three foundational scientific pillars—life sciences, computational science and engineering—are well-established in Ontario

Life Sciences

Ontario scientists have made seminal contributions to the field of life sciences, such as discovery of cystic fibrosis genes, insulin, and stem cells. Since 2005, over \$1B has been invested in new research facilities including state of the art genomics sequencing, imaging and cell robotics platforms.¹⁸

Computational Sciences

Ontario is home to over 3,000 software small-medium enterprises (SMEs) with booming R&D hubs in Waterloo and Ottawa anchored by firms such as Google, BlackBerry, OpenText and Cisco.¹⁸

Engineering

Ontario's engineering education and research institutions rank among the top 25 in the world.¹⁹ Over 350 automation and robotics-related companies, including leaders like Autodesk, Siemens, Toshiba, and ABB operate in Ontario.¹⁸

2. Ontario's major industries—automotive, agri-food, mining, chemicals and plastics, and health—are poised to adopt innovative and sustainable synthetic biology technologies

Mining

Ontario's \$11B mining industry is being threatened by low commodity prices and stringent environmental guidelines.¹⁸ Synthetic biology can help boost revenues and decrease the environmental footprint of mining, for instance, by helping to extract residual metals from old sites.

Agri-Food

Ontario's \$34B agri-food industry is a major economic driver, but almost half of its farms are small operations that struggle to survive.¹⁸ Synthetic biology can increase productivity and profitability through, for instance, the introduction of new high value crops tailored to Ontario's climate.

Automotive

Ontario's \$83B automotive sector is being threatened by jurisdictions with low cost manufacturing abilities.²⁰ Synthetic biology technologies will allow Ontario to compete in the global market with innovative products like lightweight bio-based car parts.

Chemicals

Ontario's \$35B chemicals and plastics industry is grappling with evolving consumer preferences for renewable and natural products.²⁰ Synthetic biology can help establish local supply chains and infrastructure for crop-based manufacturing of plastics.

Health

Ontario offers world-class health-care, but lags behind other knowledge-based economies in commercializing drugs. Synthetic biology can invigorate a local R&D-based pharmaceutical sector, while also making game-changing therapeutics available to Canadian patients faster.



■ PROGRESS TO DATE

Countries around the world are already leveraging the power of synthetic biology, and reaping the commercial and scientific benefits. Ontario has also begun taking steps in this exciting direction. Here are just a few examples:

- ✓ Researchers at [The Hospital for Sick Children](#) are using CRISPR to develop treatments for rare diseases like muscular dystrophy.
- ✓ Global success story [BioAmber](#) has set up the world's largest bio-succinic acid plant in Sarnia using custom designed micro-organisms licensed from the U.S.
- ✓ The [University of Toronto BioZone](#) has brought together a multidisciplinary team including synthetic biologists to develop improved microbes and microbial communities to tackle problems like environmental remediation and biochemical production.
- ✓ The [Medicine by Design](#) initiative at the University of Toronto has recognized the need for synthetic biology to more reliably engineer stem cells for better regenerative medicine and aims to boost provincial expertise in synthetic biology.
- ✓ Ontario has six undergraduate teams competing in the highly successful global [iGem](#) synthetic biology competition, teaching students synthetic biology lab skills and encouraging entrepreneurship and problem solving.
- ✓ Synthetic biology startups are cropping up across the province. [Designer Microbes](#) is developing custom micro-organisms for a variety of applications from agriculture to manufacturing; [Amino Labs](#) is creating new and innovative teaching tools; and [Ardra Bio](#) is focused on renewable bio-based chemicals. Software leaders like [Autodesk](#), with research headquarters in Toronto, are investing in the development of new software tools to design biological systems.

International Benchmarks



United States

Recognized as a critical platform technology in President Obama's National Bioeconomy Blueprint, the synthetic biology field has received substantial funding from agencies like DARPA, NSF, and NIH, to the tune of over \$800M USD since 2008.⁷ Synberc, a national institute dedicated to synthetic biology, has also played a crucial role in coordinating the community and engaging the public. Numerous dedicated departments and institutes have been established at top schools such as Berkeley, Harvard, MIT, Stanford, UCSF, as well as the J. Craig Venter Institute. The U.S. is also host to the enormously successful undergraduate synthetic biology competition, iGem, with over 280 teams across 30 countries.



United Kingdom

The Synthetic Biology Leadership Council, co-chaired by the Minister for Life Sciences, leads synthetic biology in the UK. The group has published two national strategies since 2012 and helped secure investments of over \$400M USD, helping to drive the rapid growth of synthetic biology.⁸ A network of seven university institutes working in diverse application areas from chemicals to agriculture to stem cells, as well as a national centre focused on the commercialization of synthetic biology technologies, have helped the UK quickly rise to one of the world leaders in synthetic biology.

■ WHAT MUST ONTARIO DO NOW?

Synthetic biology is not just an interesting new discipline, it is the next frontier of technology where IT, genomics and engineering unite to drive the next industrial and social revolution. We must take bold and decisive action to seize this opportunity. Here are six broad recommendations:



Increase Research Capacity

We must attract a critical mass of researchers focused solely on synthetic biology and create the foundational platforms to enable their work.



Expand Funding

While synthetic biology application-driven research is generally supported, we must dedicate resources for the development of software, robotics and molecular tools that are core to the practice and application of this discipline.



Innovate Responsibly

Ontario and Canada have strong existing regulations in place for biotechnology products, but synthetic biology is seeing rapid technological progress. We must continually evaluate existing systems, expertise, and policies to ensure research and commercialization are done safely and that the public is engaged and educated.



Strengthen Collaboration

Synthetic biology benefits greatly from the convergence of expertise. Opportunities for inter-disciplinary collaboration between synthetic biologists, policy makers, researchers and industry end users should be facilitated.



Look Globally

Ontario is not on the international synthetic biology radar, limiting our ability to attract talent and investment. Partnerships with global leaders in synthetic biology should be established to integrate into the international community and leverage their strengths for mutual benefit.



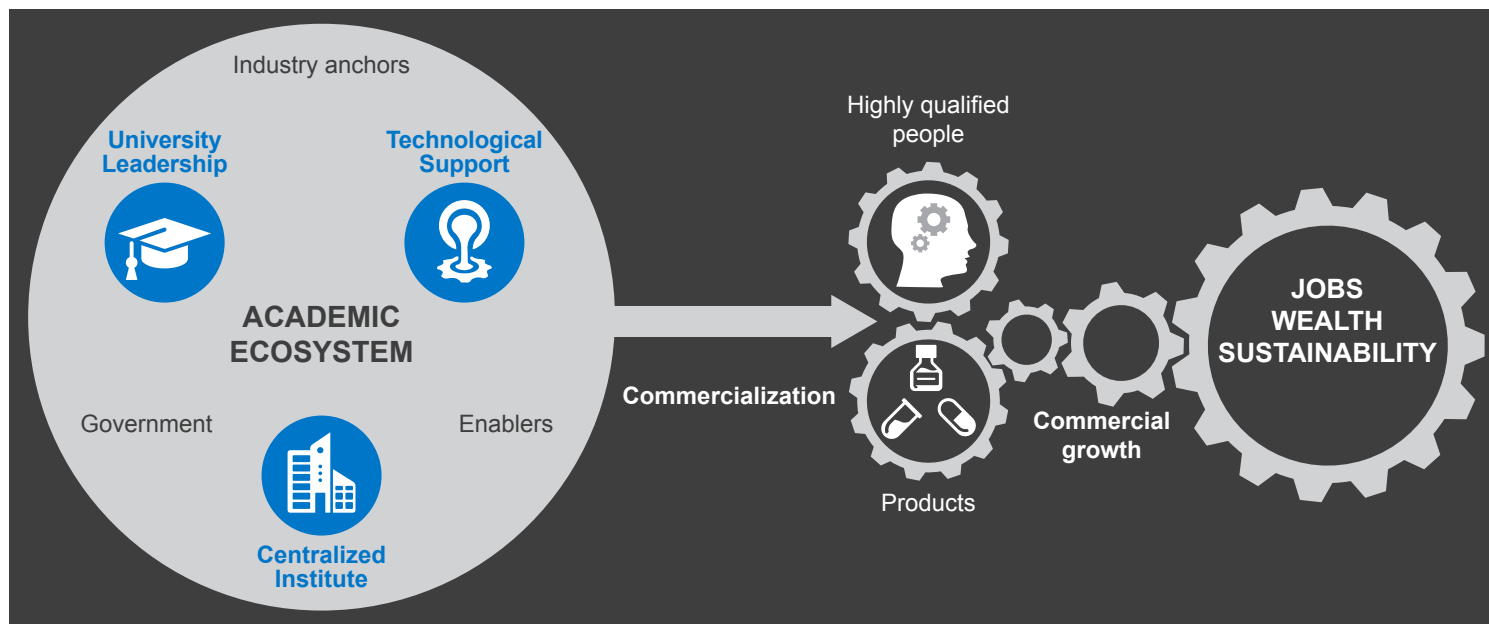
Enhance Education

Ontario has world-class education and is increasingly offering multidisciplinary programs, but training in synthetic biology as a unique discipline must be bolstered.



■ HOW CAN WE MOVE FORWARD?

There are many ways to act on these recommendations. Looking to global benchmarks, we can devise several possible and potentially synergistic paths to foster synthetic biology in Ontario.



University Leadership

In this model, leading Ontario universities would instigate the creation of entirely new departments or research institutes focused solely on the discipline of synthetic biology. This would entail building a critical capacity of expert researchers and educators, and dedicating resources for specialized infrastructure and platforms. The success of this model is showcased by the dedicated departments and institutes created at MIT, Stanford, and Imperial College London.

Technological Support

In this model, a synthetic biology service provider would offer the research community access to key enabling technologies like computational design, DNA synthesis, and rapid prototyping. Universities such as MIT, Imperial College London, Berkeley and Concordia—which have made synthetic biology a strategic priority—have all established such “foundries”.

Centralized Institute

In this model, a centralized synthetic biology institute representing key partners from across the province would be established to provide shared access to research infrastructure and a physical location for collaboration. This body would also coordinate research programs across the province, allocate research funds, and recruit new talent. The success of this model is showcased by Synberc, a nation-wide institute dedicated to synthetic biology in the United States.

■ WHAT WILL SYNTHETIC BIOLOGY MEAN FOR ONTARIO?

We believe that by implementing these recommendations, and committing to make Ontario a global leader in synthetic biology, the province's economy and its citizens will reap significant benefits. These include:



An Entirely New Economic Sector

There will exist a whole new sector of synthetic biology companies (offering anything from 3D printing of tissues and organs to microbial cocktails for cleaning up mining sites) contributing to the province's economic well-being.

Public Engagement with Science

Public engagement with science and innovation will encourage and normalize commitment to the furtherment of science, and facilitate an understanding of the impact of synthetic biology on the daily lives of Ontarians.

Stream of Private Sector Investments

Ontario start-up companies will attract increased venture capital financing from investors looking at synthetic biology as the new “yet to peak” IT sector.

A New Research Culture

Scientists will build scalability into their thinking and approach in the lab, increasing their ability to turn discoveries into viable businesses.

Food Production for the World

Ontario farmers will have access to new technologies like biological fertilizers to meet the Premier's Agri-Food Challenge, doubling the industry's annual growth rate and creating 120,000 new jobs by 2020 in an environmentally sustainable manner.

Leadership in Regenerative Medicine

Ontario will maintain its world-leading stance in medicine by incorporating the ability to reliably and rapidly program stem cells into new tissues and therapeutics.

Rejuvenation of the Chemical Industry

Ontario will house expertise to develop and rapidly screen custom industrial microbes, becoming a global destination for manufacturing of biochemicals and biofuels from waste biomass.

Access to Game-Changing Medicines

Patients will have access to cutting edge therapies developed here in the province, from rare disease treatments to new antibiotics.



■ APPENDIX 1

Stakeholders Consulted by Ontario Genomics

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Andrew Doxey, University of Waterloo
Andy Boyce, UK Knowledge Transfer Network
Benjamin Couillard, iGem University of Toronto
Bogumil Karas, Designer Microbes Inc.
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Brian Ingalls, University of Waterloo
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David Rose, University of Waterloo
Drew Endy, Stanford University
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Julie Legault, Amino Labs
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Krishna Mahadevan, University of Toronto
Lionel Clarke, UK Synthetic Biology Leadership Council
Mads Kaern, University of Ottawa
Marc Aucoin, University of Waterloo
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Megan J. Palmer, Stanford University
Murray McLaughlin, Bioindustrial Innovation Canada
Pamela Silver, Harvard University
Peter Zandstra, University of Toronto
Pratish Gawand, Ardra Bio
Ronnie Cohn, The Hospital for Sick Children
Sachdev Sidhu, University of Toronto
Sean Caffrey, University of Toronto BioZone
Trevor Charles, University of Waterloo
Tyler Whale, Ontario Agri-Food Technologies
Vincent Martin, Concordia University

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16. Azotic Technologies. www.azotictechnologies.com
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19. QS World University Rankings. www.topuniversities.com
20. Statistics Canada. www.statcan.gc.ca

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