Invest in Canadian Synthetic Biology to Meet Commitments to Sustainable Development and Support Economic Recovery

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Executive Summary: Canadian post-COVID-19 economic recovery efforts have been framed around values aligned with Canada's commitments to the United Nations Sustainable Development Goals (SDGs), primarily concerning environmental sustainability. The field of synthetic biology (synbio) offers many innovative ways to achieve these goals while growing the economy. Here, we discuss the opportunity for Canada to become a leader in clean technology applications of synbio. Investments in synthetic biology, which has traditionally been underfunded compared to other countries, will have beneficial impacts on the environment while driving Canada's post-pandemic economic recovery.

I. Background

Canada is a signatory to the UN Sustainable Development Goals (SDGs), which aim to address the environmental integrity of our planet and the welfare of its inhabitants (United Nations 2020). Although Canada officially recognized climate change decades ago (Maxwell et al. 1997), Canadian emissions continue to rise (Government of Canada 2020a), and global progress towards addressing the SDGs has been limited (Nature 2020). To address the economic impact of the COVID-19 pandemic, which caused Canada's GDP to drop by a record 5.1%, efforts by both the federal government and the private sector have prioritized sustainability as a guiding principle (Reuters 2021; Task Force For a Resilient Recovery 2020; Lindeman 2020; ISED 2020). In this memo, we recommend investing in synthetic biology as a technological tool to meet Canada's commitments to the UN SDGs along with stimulating economic recovery.

Synthetic biology (synbio) represents a maturation of the fields of genetic engineering and biotechnology. Synthetic biologists design and build biological systems to solve problems. The time for investing in synthetic biology is now, and this is only made more evident by the current public health crisis. Synbioenabled technologies are on the frontline of addressing the COVID-19 pandemic, ranging from novel diagnostic tests to new types of vaccines (Cumbers 2020; Kitney et al. 2021). Synbio will be critical in post-pandemic economic recovery by ushering in the "biorevolution," which is estimated to have a US\$4-trillion impact globally within twenty years (McKinsey & Company 2020). With more biomass per capita than any other country (Stephen & Wood-Bohm 2016), which can be converted into valuable chemicals using engineered microbes (French 2009), Canada is competitively positioned to take advantage of the biorevolution. Canadian regulations on biotechnology are more permissive

than in Europe, making it easier for innovators and investors to put biology to work on environmental challenges (Lassoued et al. 2018). Canada's liberal immigration policy is an opportunity for Canada to invest in the creation of skilled jobs to retain and attract competitive talent in synbio (Reiche 2019). Synthetic biology should be considered a critical technological pillar of Canada's economic recovery strategies, including those of the Industry Strategy Council and the Task Force for a Resilient Recovery. As well, synbio provides a "game-changing opportunity" to achieve various SDGs while driving economic growth (French 2019; Sworder & Zhang 2018):

SDG #6: Micropollutants in water are traditionally detected using expensive and laborious instrument-based methods. Synbio-based biosensors provide a far cheaper and simpler alternative (Ausländer et al. 2017; Bereza-Malcolm et al. 2015; FREDsense Technologies 2020; Hicks et al. 2020; Kim et al. 2018; Roggo & van der Meer 2017).

SDG #7, 11, 12, 13: Synthetic biologists are engineering organisms to manufacture vital resources, including biofuels, pigments, drug precursors, biodegradable plastics, and "smart" materials which are able to self-assemble and self-repair (Zhou et al. 2018; Darvishi et al. 2018; Le Feuvre & Scrutton 2018).

SDG #8, 9, 11: Biocatalysts can convert greenhouse gases from industrial processes into valuable products like rubber and feedstock chemicals (Newlight 2020; BIO 2013; Zhu et al. 2019). Compared with chemical catalysts, biocatalysts produce high-value chemicals at higher yields with reduced costs and waste.¹

In a survey conducted with 653 Canadian companies, half said they would invest more in clean technology if they could overcome a lack of capital budget or financing (Wichmann 2014). Synbio offers a solution to these economic barriers, with a demonstrated ability to attract funding. In 2020 alone, global private investment in synbio totalled US\$7.8B, up from US\$4B in 2018 and US\$300M in 2010 (Wisner 2021). The global market for products enabled by synbio is expected to grow from US\$2.7B (2019) to US\$9.9B (2024) at a compound annual growth rate of 30%,

three times faster than the global robotics market (BCC Publishing 2019).

In this memorandum, we outline Canada's current state of investment into synbio and clean technology, and we recommend a set of strategies for Canada to harness synbio towards meeting its commitments to the UN Sustainable Development Goals.

II. Current political and funding status

Canada is highly reliant on non-renewable resource extraction, with oil and gas making up 6% of the national GDP (Government of Canada 2019; Natural Resources Canada 2020). Consequently, in 2019, Canada had the third-highest CO_2 emissions per capita among G20 nations (Enerdata 2020). A forward-thinking national strategy is required to transition Canada towards a circular economy, which aims to extend product lifetimes and keep resources in continuous use by creating value from waste.

In 2017, the Canadian government invested US\$1.7B into technology research clean commercialization (ISED Canada 2018). While the federal government has recognized biotechnology's potential to address climate change, the funding of clean technologies has not reflected this, which has instead focused on improving traditional manufacturing, oil and gas, and renewable energy technologies (Health Canada 2017: Natural Resources Canada 2020; Government of Canada 2020b; SDTC 2020). Encouragingly, a recent investment of US\$11M to commercialize industrial applications of clean biotechnology represents a new funding direction (BIC 2020). However, before new technologies can be commercialized, fundamental research and training must be financially supported.

Unlike Australia, the USA, the UK, Germany, China, Finland, and Singapore, Canada has not yet funded a national strategy for synbio research and training (Gray 2018; Tong and Zhao 2016; Synthetic Biology Leadership Council 2016; Raffler 2018; Pei et al 2011; Penttilä 2017; NRF Singapore 2020). The National Engineering Biology Steering Committee has recently outlined such a strategy, which highlights how synbio could revolutionize many sectors of the Canadian economy, but funding has yet to be dedicated to support the strategy (Can-DESyNe 2020).

¹ Refer to Appendix I for the full list of SDGs.

Funding from the primary federal grant agencies in Canada (the "Tri-Agency": CIHR, NSERC, SSHRC), has not kept pace with the growing private sector enthusiasm for synbio (Wisner 2021). Between 2010 and 2019, median Tri-Agency funding for Canadian synbio research was US\$7.3M/year, with only US\$2.8M awarded in 2019 (Cognit.ca 2021) (Figure 1). Genome Canada funding is not included in these data (US\$137M/year), which is applied to many fields including but not limited to synbio (Genome Canada 2020). For comparison, the US aggressively funded synbio research beginning in 2008, with an average of US\$136M/year of public funding (Synthetic Biology Project 2015), while the UK has invested US\$80M/year (Synthetic Biology Leadership Council 2016). Based on 2019 GDP, the US economy is \sim 12times larger than Canada's, and the UK's is ~1.6-times larger. Australia, which has a similar sized economy to Canada and is also reliant on resource extraction. invested US\$10M towards synbio research in 2016, which expanded to a US\$31M research portfolio by 2018 (Vickers 2018).

Notably, two Canadian universities in the past five years have received federal funding for synbio laboratory infrastructure (Centre for Applied Synthetic Biology at Concordia; SynBridge at Lethbridge), and new training programs have been started at three Canadian universities (Concordia, Ottawa, and Western). The recently launched NRC Challenge program also includes funding for therapeutic applications of synbio (National Research Council Canada 2019). These examples are encouraging and buoyed by significant interest from students (Western University 2020), but they do not represent a concerted national effort to advance synbio, as seen in other countries.

III. Policy recommendations

We recommend a set of responses that will establish Canada as a leader in harnessing synbio for clean technology:

i. Strengthen the synthetic biology ecosystem in Canada

There is an urgent need to develop synbio capabilities in Canada to remain globally competitive. A significant, broad, and flexible investment is needed to retain and attract talent and spur innovation. An ecosystem-focused approach to increasing Canada's synbio capabilities, like the National Industrial

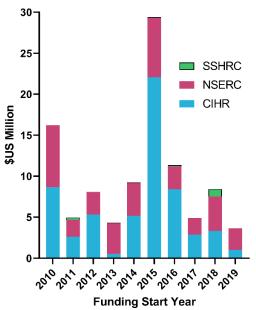


Figure 1: Tri-Agency funding of synthetic biology research in Canada. Funded research described as "synthetic biology" by the grant awardee is reported. Research that may be considered synthetic biology but was not described as such by the grant awardee is not included. SSHRC: Social Sciences and Humanities Research Council; NSERC: Natural Sciences and Engineering Research Council; CIHR: Canadian Institutes of Health Research. Data retrieved from cognit.ca January 27, 2021.

Symbiosis Programme Canada initiative, would maximize the impact of such an investment (NISP Canada 2019). This effort should include support for research and training, seed capital for Canadian synbio startups, coordination across geographic regions, and increased public engagement to improve understanding of biotechnology. A new ecosystem initiative, called Can-DESyNe, promises to develop and steer such a coordinated strategy (Can-DESyNe 2020), but its success depends on significant contributions from both the public and private sectors.

We recommend at least US\$50M/year of public funds be invested in synbio, which is based on the relative size of Canada's GDP to the UK's and the amount the UK has already invested in synbio (Synthetic Biology Leadership Council 2016).

Based on the transformative potential of synbio across many industries and sectors, initial rounds of funding should support synbio research broadly and not be limited to clean technology applications. This diversified approach will result in infrastructure and

tools that can be used for many applications, such as automated laboratories and new model organisms (Adams 2016). Vital synbio training programs will build a skilled workforce to utilize these resources. The scientific, physical, and human resources made possible by this general funding can then be strategically leveraged towards achieving the SDGs.

ii. Fund synbio clean technologies for environmental remediation (reactive response)

Based on the immediate need for new solutions to deal with the environmental impact of human activity, we recommend that the Government of Canada invest in the private-sector uptake of synbio technologies that focus on remediation.

Synbio startup companies already enable the sensing, remediating, and managing of pollutants, such as FREDsense, a Canadian-based startup that engineers bacteria to detect heavy metals in water (FREDsense Technologies 2020). There is also extensive research in using microbes for cleaning up tailings ponds resulting from the Alberta oilsands (Foght et al. 2017; Khamar et al. 2015), as well as utilizing bacteria for cleaner oil and ore extraction (Xu et al. 2011; Seifelnassr et al. 2013). Engineered microbes also hold promise for capturing and recycling carbon dioxide (Singh et al. 2019).

Prioritizing remedial solutions will accelerate Canadian innovation in synbio by capitalizing on the growing clean technology market, which is partly created by public policies aimed at meeting environmental goals (Elgie & Brownlee 2017). Incentives for meeting government regulations and corporate social responsibility, paired with the improved return on investment that synbio promises over other clean technologies (Carbon Brief 2019). will drive commercialization. According to the pioneering synbio venture capitalist, Arvind Gupta, Generation Z and Millennial consumers are increasingly willing to pay a premium for ethical business (Draper 2020). These same consumers are also increasingly open to foods produced using genetic technologies compared to Generation X and Baby Boomers (Ketchum 2019), indicating an increasingly positive public perception biotechnology which will complement increased investments in this sector.

This recommendation seeks to mitigate the environmental impacts of industrialization without fully addressing the source of the impact. Nevertheless, investing in bioremediation technologies will develop Canada's public and private capabilities to pursue more disruptive innovations.

iii. Fund transformative synbio clean technologies (proactive response)

An incredible number of biosynthetic pathways exist in the natural world that can be harnessed using synbio to generate valuable products, including industrial chemicals and food (Smanski et al. 2016). Synbio therefore holds the potential to move the Canadian economy away from its reliance on resource extraction, and thus reduce the need for environmental remediation. Further advances in synbio will accelerate the global move towards circular economies, such as using synbio-enabled technologies to convert waste and emissions into something valuable (Savini 2019).

Using engineered biological systems to reduce and recycle waste—and ultimately replace unsustainable manufacturing processes—is one of the great promises of synbio. Examples already exist, such as using yeast to produce palm oil (Kalyanaraman 2018) or engineering cyanobacteria to produce high-value chemicals from greenhouse gases (Fabris et al. 2020). Another transformative synbio technology comes from Pivot Bio, which has harnessed soil microbes to reduce the need for nitrogen fertilizers (Pivot Bio 2020). The production and application of nitrogen fertilizers cause significant greenhouse gas emissions (Carlson et al. 2016) and directly contribute to toxic algal blooms in the Great Lakes (Mezzacapo 2018). Funding the continued exploration and design of biosynthetic pathways, and non-standard microbial chassis to host these pathways, is necessary before they can be applied on economically-relevant scales (Brietling et al. 2016).

Synbio also has many applications in the food industry, including the production of animal-free meat and dairy products, and flavouring for plant-based burgers (Bomgardner 2020). Crop and livestock production account for 10% of greenhouse gas emissions in Canada (Government of Canada 2020c), thus the adoption of synbio-enabled animal-free food may help to lower these emissions. Funding the growth and adoption of similar technologies in

Canada is also an opportunity to ensure food security, as climate change has the potential to disrupt traditional food supplies globally (Wheeler & von Braun 2013).

This proactive approach aims to harness the creative potential of new synbio technologies, enabling Canada to become a leader in technologies that can help achieve the UN SDGs, while driving job creation. This recommendation can be understood as an appeal for public and private investment in higherrisk, higher-reward applications of synbio.

IV. Avoiding potential pitfalls

As many of these engineered biological systems are intended to be applied to solve real-world problems, ethics and biosafety must be incorporated in every synbio training curriculum, academic lab, and company. Environment and Climate Change Canada should also be involved in the coordination and management of synbio funding regarding environmental applications.

Biotechnology commercialization is challenging, where a "valley of death" is perceived to exist between academic results and a successful biotech company (Moran 2007). In cases where research is intended to be commercialized, business training to develop compelling market validations would help to maximize the probability of commercial success. Early-stage investment of companies is also required, which could be modelled on the USA's successful Small Business Innovation Research (SBIR) program (SBIR 2020), or joined with the efforts of Sustainable Development Technology Canada (SDTC 2020). These programs provide non-dilutive seed funding for small businesses, including research into clean technology.

Canadian private investors are known to be more risk-averse and have been hesitant to capitalize on

synbio opportunities (Goodsell 2016; Kinder & Robbins 2018). Initial government investment would reduce the financial risk and increase confidence from the private sector. Importantly, synbio presents a more favourable risk/reward ratio than previous generations of biotechnology, due to rapid advancements in the tools available (El Karoui et al. 2019). Therefore, the cost and time required to build a synbio-based company has been significantly reduced, as evidenced by the hundreds of synbio companies in the US and UK established in the past ten years (Clarke & Kitney 2020).

Canada must be cautious about investing only in remediation-focused technology, which would maintain an environmental status quo. As well, the benefit of new synbio technologies is not always immediately obvious. For example, engineering bacteria to clean a lake has a direct positive benefit, which first needs genetic tools to control complex microbiomes. The latter requires more investment in the fundamental research stage, which would involve a longer delay before the technologies become marketable. As such, to achieve the third recommendation, a significant portion of the funding committed to synbio clean technology should go towards fundamental research, and not only to immediately marketable technologies.

Synbio has the potential to transform many sectors and provide solutions to environmental and climate change challenges. We recommend an ecosystem-focused federal investment, with support for using synbio to remediate the environment (reactive) as well as improve or replace wasteful industries (proactive). In doing so, Canada will position itself as a leader in synbio, meeting its commitments to the UN Sustainable Development Goals while accelerating its post-pandemic economic recovery.

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Appendix

The following lists the 17 Sustainable Development Goals (SDGs) put forth by the United Nations Department of Economic and Social Affairs to be achieved by 2030 (United Nations 2020). Reprinted with permission.



Brendan Grue is currently a medical student at Dalhousie University. Prior to medical school he completed his PhD in Biomedical Engineering at Saint Mary's University. His doctoral research focused on the development of a novel mineralized collagen scaffold for bone repair and regeneration. He has an active interest in scientific policy, communication, and knowledge translation.

Samir Hamadache has an Honors Bachelor of Science in Genetics & Biochemistry from Western University. As a biochemistry graduate student, his research at the intersection of synthetic biology and automation is aimed at developing new tools for agricultural biotechnology. In addition to being the Vice President of SynBio Canada, Samir is the Founder and President of Forest City SynBio, a startup that is building a Canadian centre of excellence for synthetic biology entrepreneurship and innovation.

Dhanyasri Maddiboina is a PhD student from McMaster University and her research is at the intersection of engineering and biology. She is investigating the use of bacteriophages (viruses that kill bacteria) for treating infections. Complementary to research, Dhanyasri is heavily involved in mentorship of undergraduate students and in training graduate students in science communication.

Benjamin Scott recently joined the Concordia University Genome Foundry as a Business Development & Partnerships Engagement Advisor. His post-doctoral and PhD research focused on engineering cellular signaling to develop biosensors for industrially relevant compounds, and to create cell-based therapies. He founded SynBio Canada to strengthen the national research community, to advocate for trainee needs, and highlight their accomplishments.

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