Nature Co-Design: A Revolution in the Making

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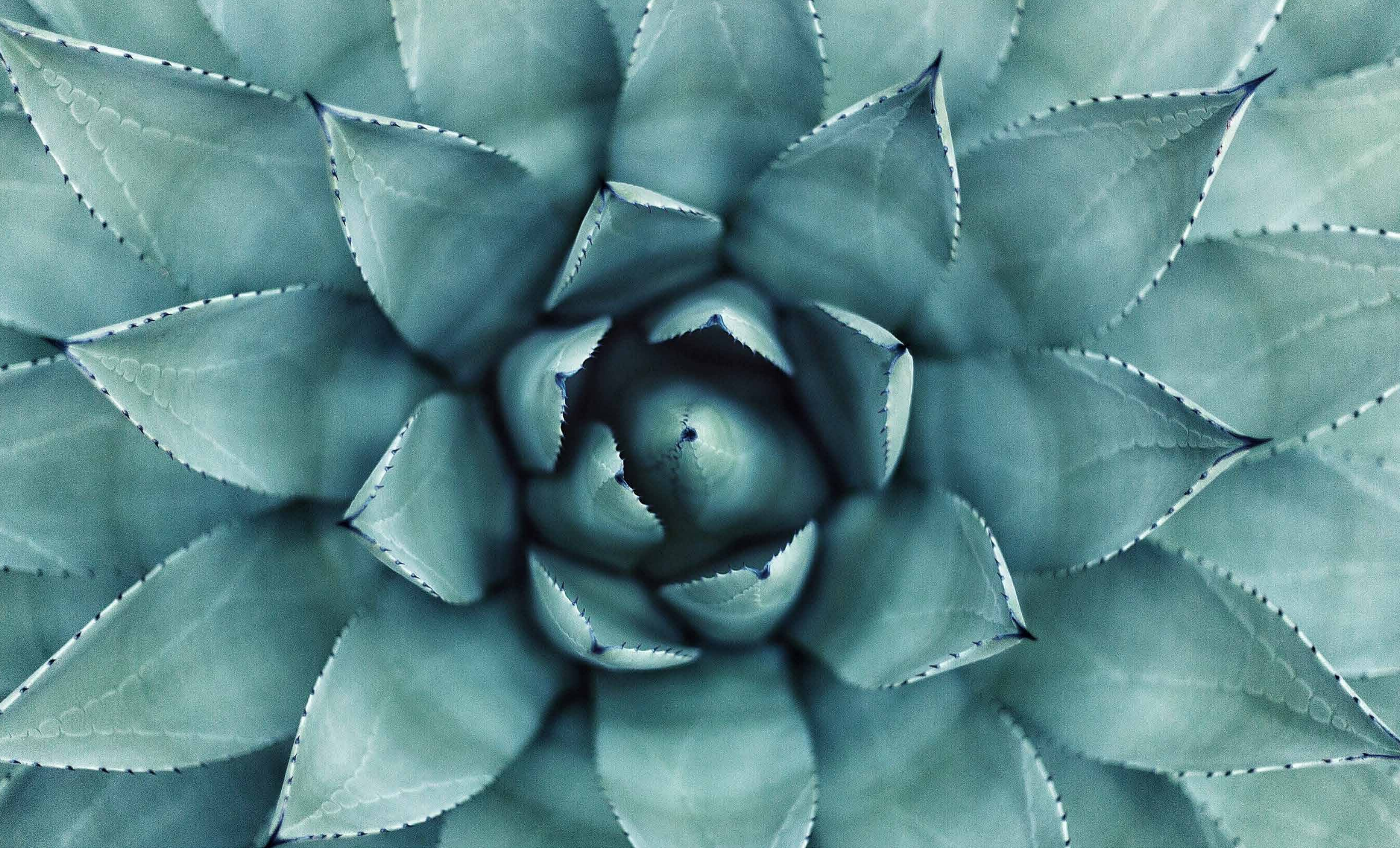

Nature Co-Design: A Revolution in the Making

This paper is the second of a series of reports on deep tech. It focuses on nature co-design, the most foundational development powered by deep tech. The first report provides the overarching reference framework for deep tech.

In this second report, we outline the importance and the impact of nature co-design, which has the potential to lead to a new industrial era. We will explain what it is, how it works, and how it can be harnessed for competitive advantage.

We will address the "why now" question and the strategic imperatives that business leaders must understand in order to compete and thrive in the nature co-design era.

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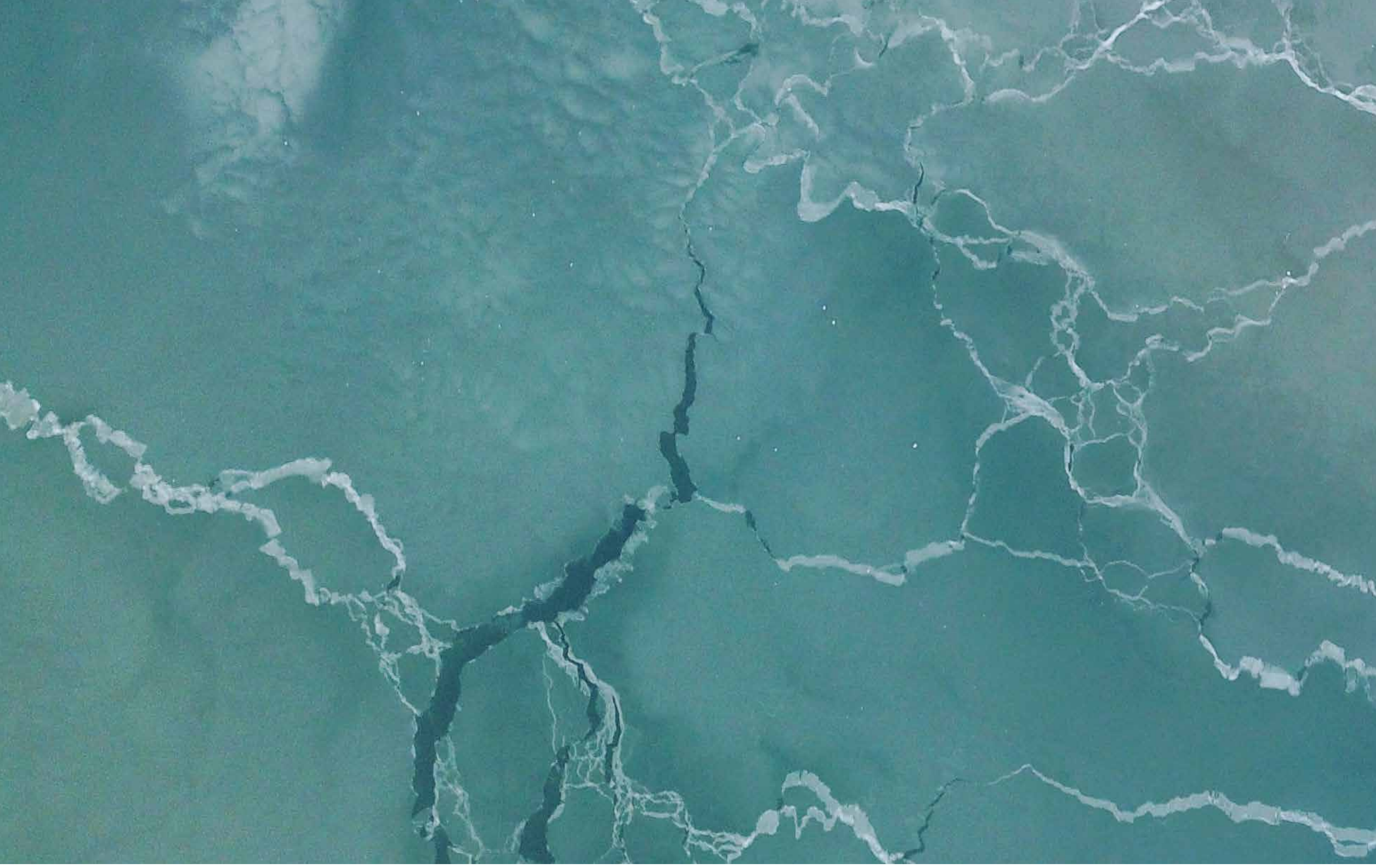
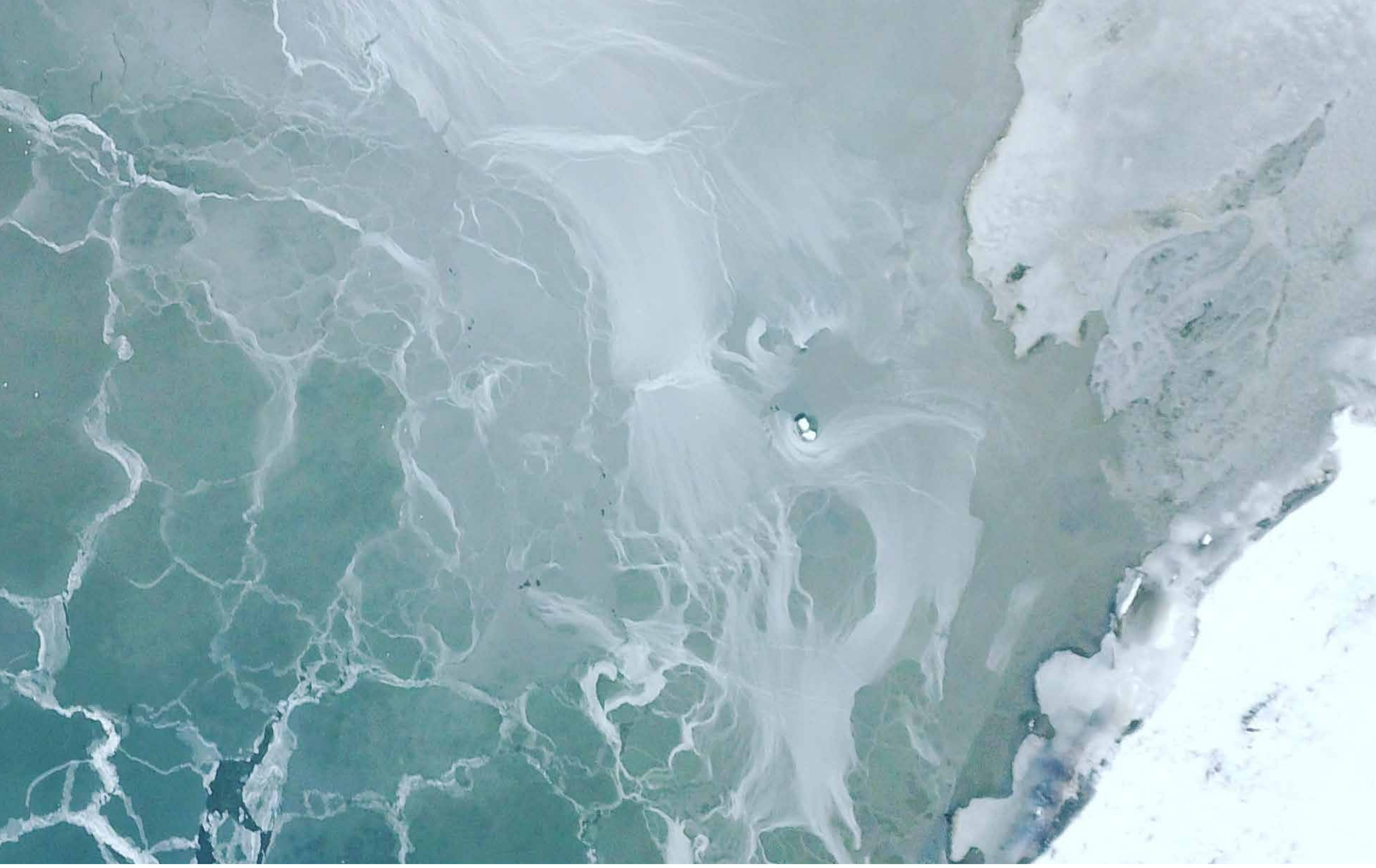


Executive Summary

The fourth industrial revolution, brought in on a wave of advanced technologies and machine learning, is already redefining supply chains, value pools, and business processes. But much less publicized, and yet much more disruptive, is the other side of this fourth industrial era - that of nature co-design. This is where biology, material science, and nanotechnology meet to leverage nature's design principles and manufacturing capabilities at the atomic level. Nature co-design opens entirely new economic lanes of growth while also addressing the challenges entailed by diminishing finite resources and climate change.

Nature co-design signals a shift from exploitative, by consuming natural resources to using deep tech's design-build-test-learn cycle, to generative, by building precisely and ordering at the atomic scale. Nature co-design obviates the need for energy-intensive processing of raw materials and builds solutions under atmospheric pressure conditions and in relatively low temperature environments instead. By working with nature at nano level, rather than pillaging it for resources and then deploying even more resources to fuel processing energy, nature co-design introduces a new era of economic potential through decarbonization. Nature co-design can be compared to Lego: it creates a range of precise, colored bricks of different shapes, from which almost infinite constructions can be made, disassembled and repurposed.



This isn't science fiction: this is here and now. Nature co-design's impact on value chains can be understood along four intertwined dimensions:

- Nature co-design enlarges the option space, shifting value pools to create new value.
- Nature co-design forces to rethink from value chain to value net by transforming waste into resources.
- Nature co-design will redefine economics to reflect the precision and selectivity of designing and manufacturing with nature.
- Nature co-design requires an increase in scientific knowledge and imagination.

Nature co-design has profound implications for business, but also for the health of the planet. It disrupts every industry, from agriculture and consumer goods to construction and pharmaceuticals. Working with nature has the potential to create a new economic model that is intrinsically more sustainable and allows for faster, leaner innovation.

The market opportunity is in the trillion dollar range. According to a report by WEF, nature-positive solutions can generate some $10 trillion by the end of 2030. And while we don't know how much economic wealth can be generated in the longer term, we predict that $30 trillion will be impacted over the next 30 years, the equivalent of 40% of global Gross Domestic Product.

Nature co-design is no incremental step: it requires an entirely different way of thinking, adopting a non-reductionist approach to nature, establishing a robust ethical framework to navigate future ambiguity, and managing risks. The scientific and business communities need to work together to combat fears and disinformation that may threaten public acceptance of these transformative moves.

Nature co-design is coming fast and will impact every industry, in every economy. Businesses that adopt nature co-design as a foundational element will leapfrog their competition, catalyze the transformation to a sustainable future, and reap the rewards.

> "I think the biggest innovations of the 21st century will be at the intersection of biology and technology. A new era is beginning."
>
> **Steve Jobs, 2011**

Nature Co-Design: A Revolution in the Making

In recent years, deep tech ventures have begun demonstrating how to take a fundamentally different approach and radically rethink how to address today's biggest challenges. This new approach leverages not only biology but nature more broadly. By harnessing nature's design principles and leveraging its manufacturing capacity, we enter the era of nature co-design.

The broad scope of challenges addressed with nature co-design proves its impact on all industries, as these examples demonstrate.

Reducing dependence on artificial fertilizers

To take one example, increasing food production to sustain a world that will soon have 8 billion people is a well-known challenge. Artificial fertilizers that depend upon the Haber-Bosch synthesis may have enabled increases in food production to keep up with a doubling of the global population since 1970, but this process has many downsides (Exhibit 1):

- It requires massive amounts of energy to convert atmospheric nitrogen into ammonia
- It is energy-intensive, consuming 3% to 5% of the world's natural gas supply and around 1% to 2% of the world's energy supply, and is also responsible for more than 1% of all CO_2 emissions. Apart from energy intensity, N_2O emissions result from the inefficient use of nitrogen fertilizer. N_2O is 250 to 300 times more potent than CO_2 in global warming
- It disrupts ecosystems since the efficiency of nitrogen use by plants is below 50%, and the rest of the ammonia is washed off the crops, contaminating water sources.

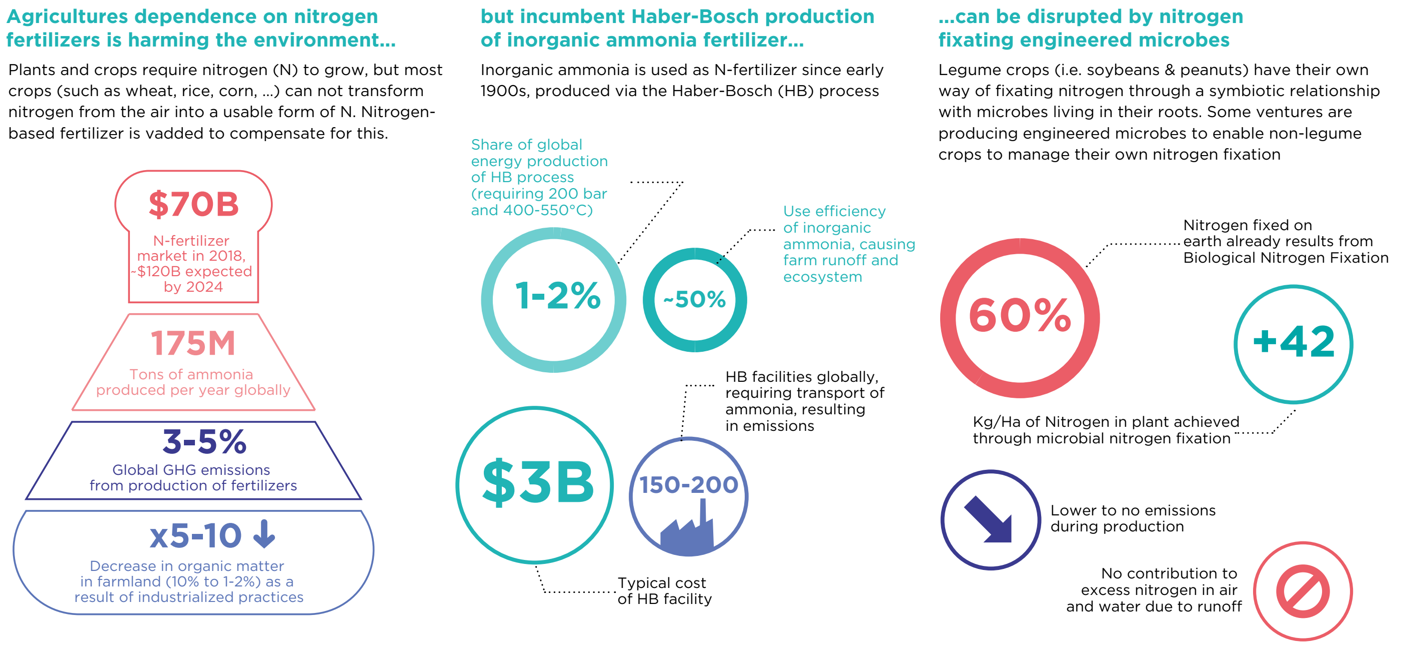
The ammonia produced via the Haber-Bosch process is the "most energy-intensive commodity chemical" and plays a major role in agriculture's contribution to climate change.

Two separate companies—Pivot Bio and Joyn Bio (a Ginkgo Bioworks-Bayer joint venture)—decided to leverage nature co-design using gene-editing techniques. Iterating through multiple design-test-build-learn cycles, they identified the bacterial strains capable of fixing nitrogen directly on plant roots.

Beyond providing huge environmental benefits, both will disrupt the global ammonia market, valued at $48 billion in 2016 and estimated to reach $77 billion by 2025[1]. Finally, moving to a biological process allows descaling and increases access to ammonia since building a Haber-Bosch facility costs some $3 billion and requires a natural gas infrastructure.

And disruption in agriculture is not limited to ammonia replacement. Examples range from reducing livestock's carbon footprint by increasing protein content in plants (Plant Sensory Systems) to improving a plant's ability to sequester carbon in the soil (Soil Carbon), or creating population-controlled insects to avoid crop destruction (Oxitech).

Exhibit 1: Nature co-design disrupts century old chemical process



Source: IEA; Mordor intelligence, 2020; Berkeley Lab; Joyn Bio; Pivo Bio, Nitricity; A. Soumare, A. G. Diedhiou, M. Thuita, M. Hafidi, Y. Ouhdouch, S. Gopalakrishnan, L. Kouisni - Exploiting Biological Nitrogen Fixation: A Route Towards a Sustainable Agriculture (2020); BCG and Hello Tomorrow analysis.

1. Grand View Research

Food, waste processing, and advanced materials

The list of promising solutions in development that deploy nature co-design principles is long and already impacting a broad range of industries from energy generation to medicine to materials

- Engineering of yeast into a molecular assembly line to produce medicinal molecules (Antheia), plant-based milk and cultivated meat (Perfect Day, Memphis Meats), and programmable materials based on spider silk and cow leather (Bolt Threads, Spiber, Modern Meadow)

- Recycling and upcycling waste streams from industrial processes to "brew" fuel (LanzaTech), proteins (Kiverdi, NovoNutrients), fibers and materials (Mango Materials, Polybion)

- Modeling of living systems with computer-aided design tools to advance therapeutic applications (Asimov), improve protein design (Arzeda), create novel sensors (Koniku), and solve the 50-year-old challenge to predict protein folding (AlphaFold2)

- Leveraging of AI and automation for the discovery of advanced chemicals and materials (Kebotix, IBM RoboRXN, Citrine) as well as the reduction of the development time for advanced materials from 20 years to less than 2 years by unlocking the potential of nanoparticles (VSPARTICLE)

- Engineering and manufacturing of advanced materials drawing lessons from nature and applying them to electronic films (Zymergen), construction (Biomason, Ecovativ), advanced materials (Niron Magnetics and Sila Nanotechnologies), advanced manufacturing (Terapore), and even luxury (Heyaru).

These examples show nature co-design in action. Instead of exploiting natural resources, nature co-design works with natural laws to manufacture new products and solutions. As a result, nature becomes humanity's primary partner.

Nature co-design isn't just clever science: it has the potential to be a primary economic driver. According to IndieBio, it could add some $100 trillion to global economy by 2040.

The Evolution of Nature Co-Design

Nature has been at the center of the first two industrial revolutions: the first one in England when coal-fired steam was harnessed to power machines and drive trains; the second one led by the United States when electricity, gas, and oil were established as new energy sources, enabling the rise of the steel and chemical industries. Each of these economic leaps brought waves of new sources of wealth to those who led them, and employment to those who worked in these new industries. The third industrial revolution, based on semi-conductors, computing, and the Internet, enabled the digital age and with it, a generation of companies whose revenues equal the GDP of many advanced economies, for the first time in history, we are in a position to move away from exploiting nature by brute force and start harnessing its design principles and leveraging it as a manufacturing platform instead—this is nature co-design.

Made possible by advances in science and technology, nature co-design is defined by four characteristics outlined below and illustrated in Exhibit 2:

- Nature co-design adopts the deep tech approach including the design-build-test-learn cycle
- Nature co-design draws on organic and inorganic matter at the atomic level to create new solutions
- Nature co-design leverages nature's design principles and manufacturing capabilities
- Nature co-design is a transformational business opportunity with significant sustainability potential

Exhibit 2: Nature co-design is made possible by science and technology advancements and is defined by four characteristics:

It adopts the deep tech approach including the **Design-Build-Test-Learn** cycle	It draws on **organic and inorganic matter** at the atomic level to create new solutions	It leverages **nature's design principles** and manufacturing capabilities	It is a transformational **business opportunity** with significant sustainability potential

Source: BCG and Hello Tomorrow analysis

Nature Co-Design Adopts the Deep Tech Approach

Nature co-design operates in the space between science, engineering, and design to produce new services, solutions, and products that profit from widespread access to innovation tools.

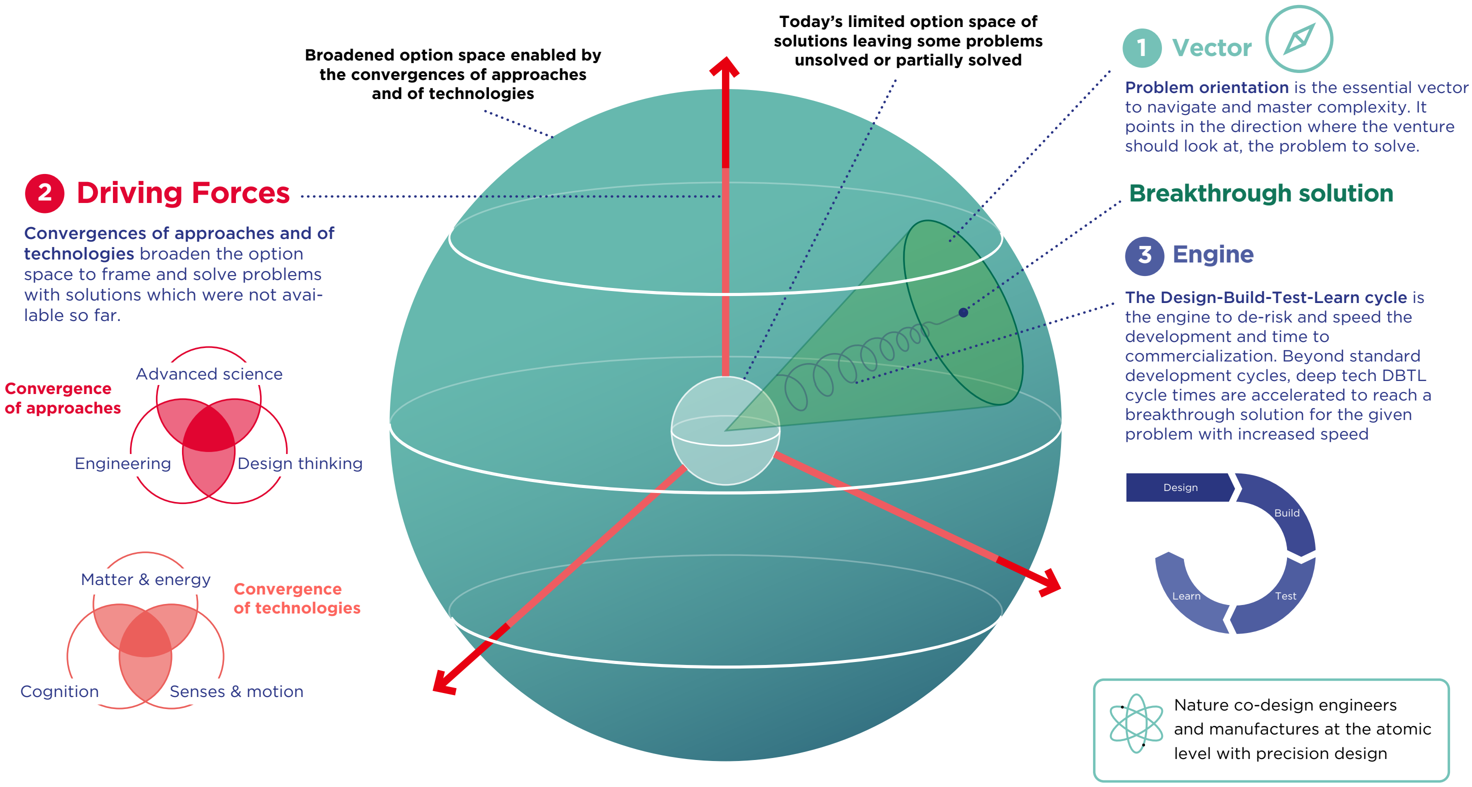
Nature co-design leverages the convergence of established and emerging technologies like innovation tools, including DNA sequencing and synthesis, the gene-editing tool CRISPR and its related cousins, especially base-editing, precision fermentation and bioprocessing, artificial intelligence/machine learning, nanotechnology, or any relevant emerging technology. These technologies are increasingly accessible with prices dropping exponentially. Nature co-design modifies RNA and DNA, but also leverages small molecules in novel ways to enable existing proteins in cells to perform activities that will lead to desired outcomes.

Nature co-design adopts the deep tech approach (see The Great Wave of Innovation[1]) by being initially problem-oriented and powered by the convergences of approaches and technologies. It continuously iterates through the design-build-test-learn (DBTL) cycle to produce better, previously unimaginable, solutions (Exhibit 3). Nature co-design leverages the improved capability and increased speed of building and testing defined solutions. The power of AI is then applied to make sense of the data generated during the build and test phase and to learn and improve designs, with constant iteration at speed throughout the cycle until a working solution is discovered.

While the two first industrial revolutions were built on exploiting nature by brute force, the era of nature co-design exploits the design process instead—quickly iterating through the design-build-test-learn cycle, and producing huge amounts of data to devise the right solution that leverages nature to design and produce what we want. Beyond the deep tech approach, it operates at the atomic level to expand the option space of possible solution and ensure ultimately customized solutions.

1. https://hello-tomorrow.org/bcg-deep-tech-the-great-wave-of-innovation/

Exhibit 3: Nature co-design adopts the deep tech approach, including the DBTL cycle, and precision design



Source: BCG and Hello Tomorrow Analysis

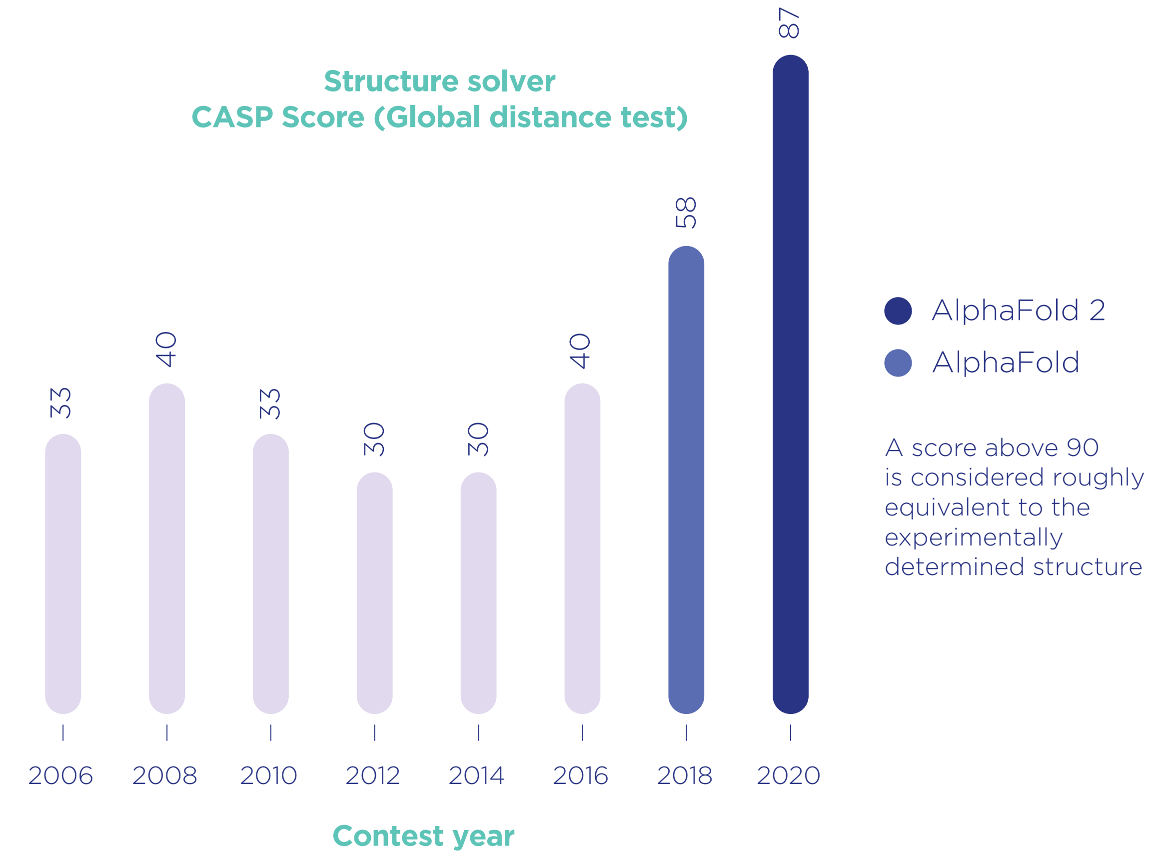
Accelerating the DBTL-Cycle by solving a 50-year-old problem

This is reflected in the recent announcement that the protein folding problem, a 50-year-old grand challenge in biology, has been solved by DeepMind's AlphaFold, a deep learning algorithm. The scale of this breakthrough cannot be understated: proteins play a fundamental role in our lives, from developing treatments for diseases, being able to feed the world, to creating new materials and processes, and breaking down industrial waste. But what a protein does largely depends on its unique 3D structure, and predicting a protein's structure has remained an elusive challenge, meaning that the only way to know a protein's structure was through experimental determination – a slow and costly process. This explains why, while 180 million protein sequences are known, only around 170,000 protein structures have been codified to date.

DeepMind's AlphaFold2 has been able to solve the protein folding challenge. The novelty of their model lies in its attention-based deep learning architecture, which extracts much richer information from data and determines highly accurate structures in a matter of days. This breakthrough hugely accelerates the DBTL cycle for innovations tied to proteins, where AI will be able to support researchers in codifying the structure for the millions of proteins whose sequence is already known.

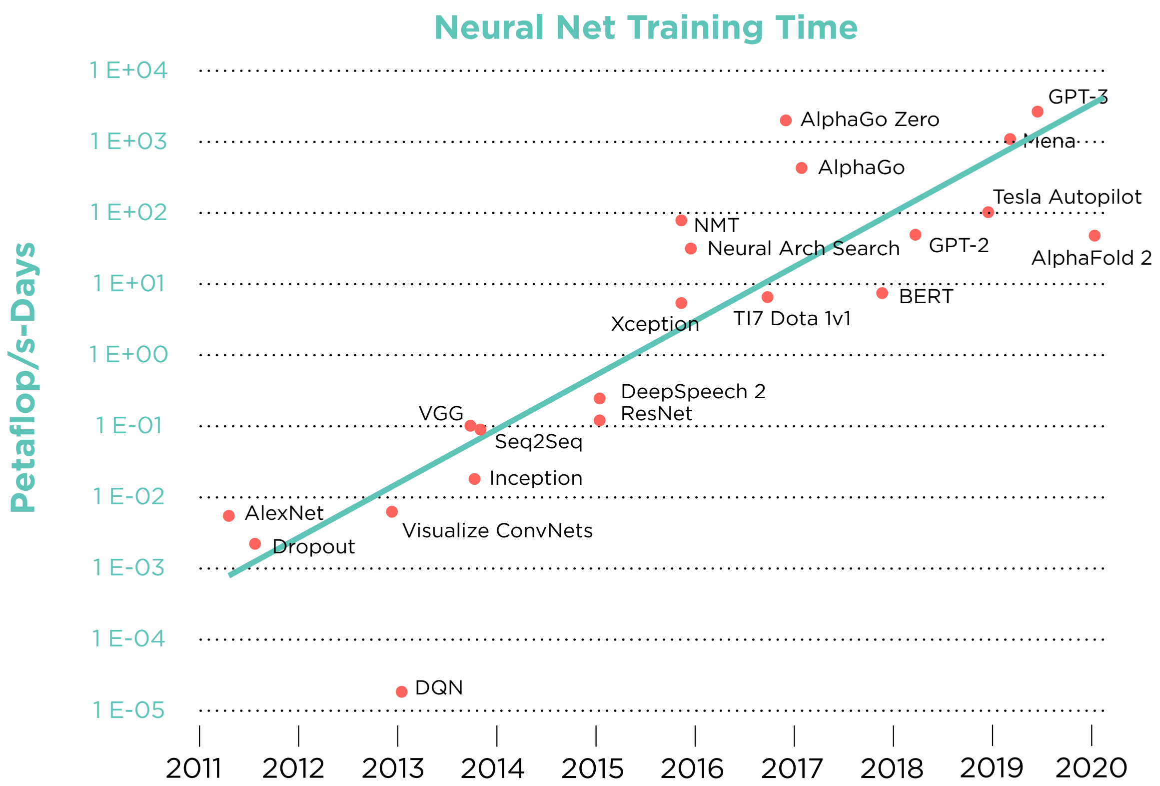
Protein structure prediction had been at similar levels of precision for years (Exhibit 4) and then AlphaFold radically changed the game in only two iterations, decades before what many experts in the field would have predicted. Not only was the breakthrough extraordinary in its speed but also in its cost. The architecture used for the AI system enabled more efficient training, requiring less computing time and therefore lower costs than usual (Exhibit 5). This is just a preview of the power of leveraging the DBTL cycle, and we can expect to see many other apparently unsolvable problems being suddenly unlocked.

Exhibit 4: AlphaFold reaches in two iterations breakthrough precision levels



Source: Nature, Deepmind

Exhibit 5: AlphaFold 2 requires less computing time than its 2019-2020 peers



Source: ArkInvest, OpenAI

Nature Co-Design Draws on Organic and Inorganic Matter at the Atomic Level to Create New Solutions

Nature co-design goes beyond biology, incorporating fields of non-living matter—chemistry, nanotechnology, and the material sciences—to create the foundation of a new manufacturing paradigm.

Biology is a three-billion-year-old research & development and manufacturing lab. It offers DNA as the most efficient information storage – amino acids assembled into workhorse proteins – and replication and selection as problem-solving mechanisms. Biology produces atomically precise structures on the microscopic (viruses) and mega (Redwoods) scales. It works with both organic and inorganic compounds. We can engineer biology—combine it with the fields of chemistry and nanotechnology, and leverage quantum properties and material sciences to solve societal and planetary challenges—while creating myriads of business opportunities.

While arguably less advanced, the revolution in biology is now coming to materials, to encompass all living and non-living matter. The molecules, DNA, and organisms that comprise biology translate into atoms, material microstructures, and macroscopic properties in material sciences. Nanotechnology offers the ability to leverage the forces present at the atomic level and create materials with properties that can't be found in nature. Nature forms nanomaterials and assembles them into more complex structures in a constant process, and the developments in advanced materials enable us to get free from the exhausted brute force model. While nanotechnology field is already decades old, the ability to leverage the DBTL cycle to systematically design and manufacture nanoparticles with the desired properties has the potential to disrupt countless industries.

Rather than thinking of biology and chemistry as a given set of constraints with a predefined dictionary of design principles and technologies, nature co-design applies engineering principles to organic and inorganic matter to design organisms and materials with the desired properties to deliver specific outputs (molecules) or behave according to predetermined (or predesigned) programs.

In the first and second industrial revolutions, we relied upon raw materials extracted from the earth to generate energy and build new materials. In the era of nature co-design, we consider the feedstock and engineer the organisms that will consume it to manufacture the products we desire with precision, or we take the properties required from a material and work at the nanoscale to create them. This approach starts from the problem and drills down to the atomic level to build a solution from the nano scale up. There is no “inspired” trial-and-error in the nature co-design model.

Synthetic Biology, Advanced Materials and the Origins of Nature Co-Design

From Biotech's Origins to Synthetic Biology and Advanced Materials

The foundations of nature co-design were laid in the 1970s with the rise of the biotechnology industry. The ability to genetically engineer living organisms led to the emergence of the first biotech start-ups and the transformation of the pharmaceutical industry from a focus on small molecules produced by internal R&D to large protein molecules produced through partnerships and outsourced research.

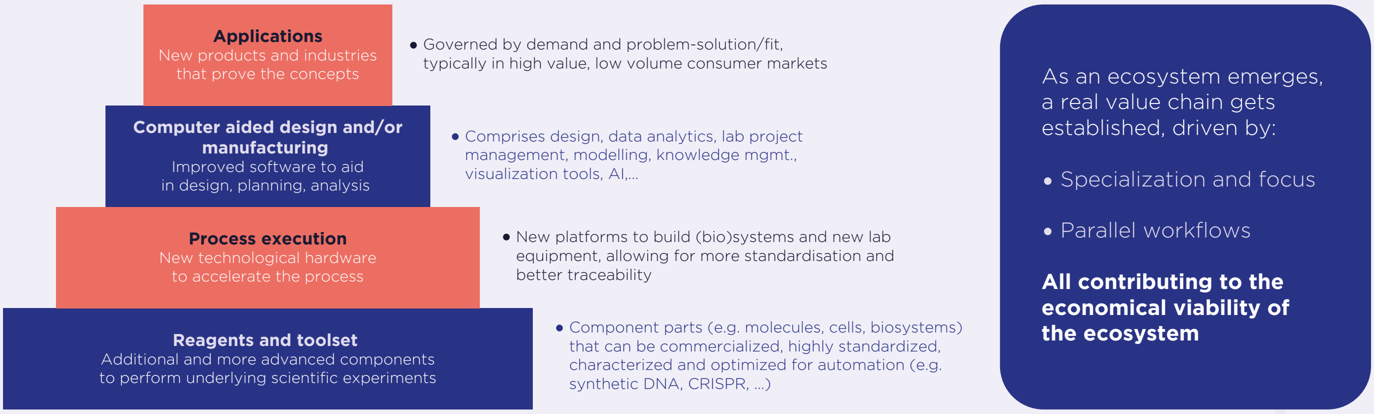
Organic Matter: Synthetic Biology

Synthetic biology is the most advanced nature co-design field, leveraging the design-build-test-learn cycle and introducing engineering principles in biology.

Synthetic biology owes its growth and acceleration to the convergence of multiple technologies. Foundational technologies such as reading and writing DNA and gene-editing tools like CRISPR are the core of synthetic biology, while a growing 'stack' of new technologies enables companies to specialize and enter the market faster (Exhibit 6). These technologies include gene synthesis and editing, computational tools, organism engineering platforms, cell-free systems (that require no organism to manufacture end-products), 3D bioprinting, and precision fermentation, among others.

Like the ICT revolution of the 1970s, there is an open ethos and a collaborative culture among researchers and the business community driving innovation. In the last 10 years, one of the most recent Nobel Prize winners in Chemistry has been awarded for advancing battery technology while, during this time period, eight have been awarded to discoveries that enable nature co-design. This represents an unprecedented shift in chemistry even bigger than the advent of organic chemistry born out of tar-based dyestuff industries.

Exhibit 6: Growing 'stack' of new technologies enables and accelerates innovation through specialization



Source: Freemont P., Synthetic biology industry: data-driven design is creating new opportunities in biotechnology, Portland Press 2019; BCG and Hello Tomorrow analysis

Investments in biofoundries—integrated facilities where genetic constructs can be designed, built, and tested—and platform technologies have community-wide benefits. Benchtop mini-foundries, cloud laboratories, and outsourced fermentation make otherwise expensive facilities and capabilities widely accessible. Moreover, with the top-ranking 100 global R&D companies spending more than €300 billion in R&D, a change in their way of investing and innovating could fuel nature co-design with capital.

Increasing computational power is accelerating the digitization of biology, which in turn is driving further increases in computational power.

Investments in synthetic biology are steady and growing, with more than $95 billion[1] invested over the 2016 – 2020 period. The field boasts the rise of nature co-design unicorns such as Ginkgo Bioworks (which has raised nearly $800 million at a $5 billion valuation as of May 2020) and publicly-traded companies such as Berkeley Lights, Checkerspot, and Twist Bioscience.

The change from biotech to synthetic biology is highlighted by the breaking of Eroom's law (Moore's law in reverse), which is the observation that drug discovery is becoming slower and exponentially more expensive over time. In the last 10 years, Eroom's law was broken with successes in biopharma, attributed to better knowledge of human biology and genetics, more efficient drug discovery processes, and an increase in synthetic biology tools.

1. Preliminary estimates including disclosed private investments, minority stakes, initial public offerings and merger and acquisitions

The coronavirus pandemic has accelerated vaccine development and adoption by shortening traditional timelines (such as FDA approval), building global infrastructure (vaccine production facilities), and favoring worldwide ecosystem collaboration and knowledge sharing. For example, the SARS-CoV-2 genome was shared openly a few weeks after the first infections, and the structural determination of the virus and key proteins shared within months, while the global effort to develop a vaccine highlighted the importance of the field. The ultimate proof of the power of synthetic biology came with the success of the two mRNA-based vaccines by BioNTech and Moderna.

The Biofuels Bust

A very important step in the evolution of synthetic biology was the biofuel bust. In the early 2000s, entrepreneurs raised billions of dollars from venture capitalists and governments to turn corn into ethanol and extract oil from algae. At the time, oil prices were at their highs. The promise of biofuels was that synthetic biology—advanced genetic engineering techniques that radically change the way an organism functions—could be used to make new strains of bacteria and yeast that would produce common biofuels (ethanol and biodiesel) and hydrocarbon fuels identical to gasoline, diesel, and jet fuel.

But after years of rapid growth, strong government support, and millions invested, the biofuel industry was decimated by falling oil prices, rising production costs, inadequate infrastructure, and the global economic crisis of 2009, creating substantial losses for the venture capitalists who invested in it.

The "biofuels bust" set the stage for the rise of synthetic biology. The tools developed for metabolic engineers to construct organisms to produce fuels were leveraged (and further advanced) for nature co-design, and the learnings drawn continue to shape the nature co-design approach for the better.

Inorganic Matter: Advanced Materials

Historically, the adaptation of nature co-design principles for advanced materials has lagged behind progress in synthetic biology. However, momentum is building.

The "inspired" trial-and-error era is substituted by the design-cycle, enabled by simulation and modelling with unprecedented precision. Where Thomas Edison had to test 1600 different materials for the filament of the first light bulb, we can leverage AI to discover new materials with precision, and robotics to build and test them at unprecedented speed. We're entering a new paradigm, where breaking up bulk materials into very small particles enables us to change their physical properties leveraging quantum mechanics.

Recent examples showing a change of attitude in the field include: Kebotix, a company that uses a combination of robotics and AI to design new advanced materials; IBM RoboRXN, a cloud-based, AI-driven chemistry lab synthesizing new materials faster and more efficiently; and Riken, a 100-year-old Japanese company that recently announced a new algorithm designed to identify new materials.

And there is more to come. The wave of disruption we currently see in advanced materials and chemistry comes from boosting the speed at which we can select a promising compound, test it, and ultimately produce it. Nanotechnology goes even further by changing the properties of materials at the atom level, obtaining properties that did not previously exist in nature.

Instead of starting with a set of known materials and look for the one with the most suitable properties, nature co-design ventures can start from the desired properties and identify the nanoparticle (maybe undiscovered so far) that meets them, to then produce the required component through Additive Manufacturing.

A promising example is VSPARTICLE, a venture that links nanoparticle research and material informatics with additive manufacturing, to enable property-based engineering. The pace of growth in advanced materials has some clear parallels with the revolution in synthetic biology. A key enabler is the convergence of technologies that is both accelerating growth and expanding what we are able to do in the advanced materials space. Falling barriers including decreasing costs and increasing computation speed are broadening the spectrum of what is possible. And the speed of change may be even faster than we believe. While we are expecting a double-digit growth for additive manufacturing[2](26%) and advanced materials such as nano-coatings[3] (21%) or metamaterials[4] (21%), the convergence of these technologies has the potential to accelerate exponentially beyond current projections.

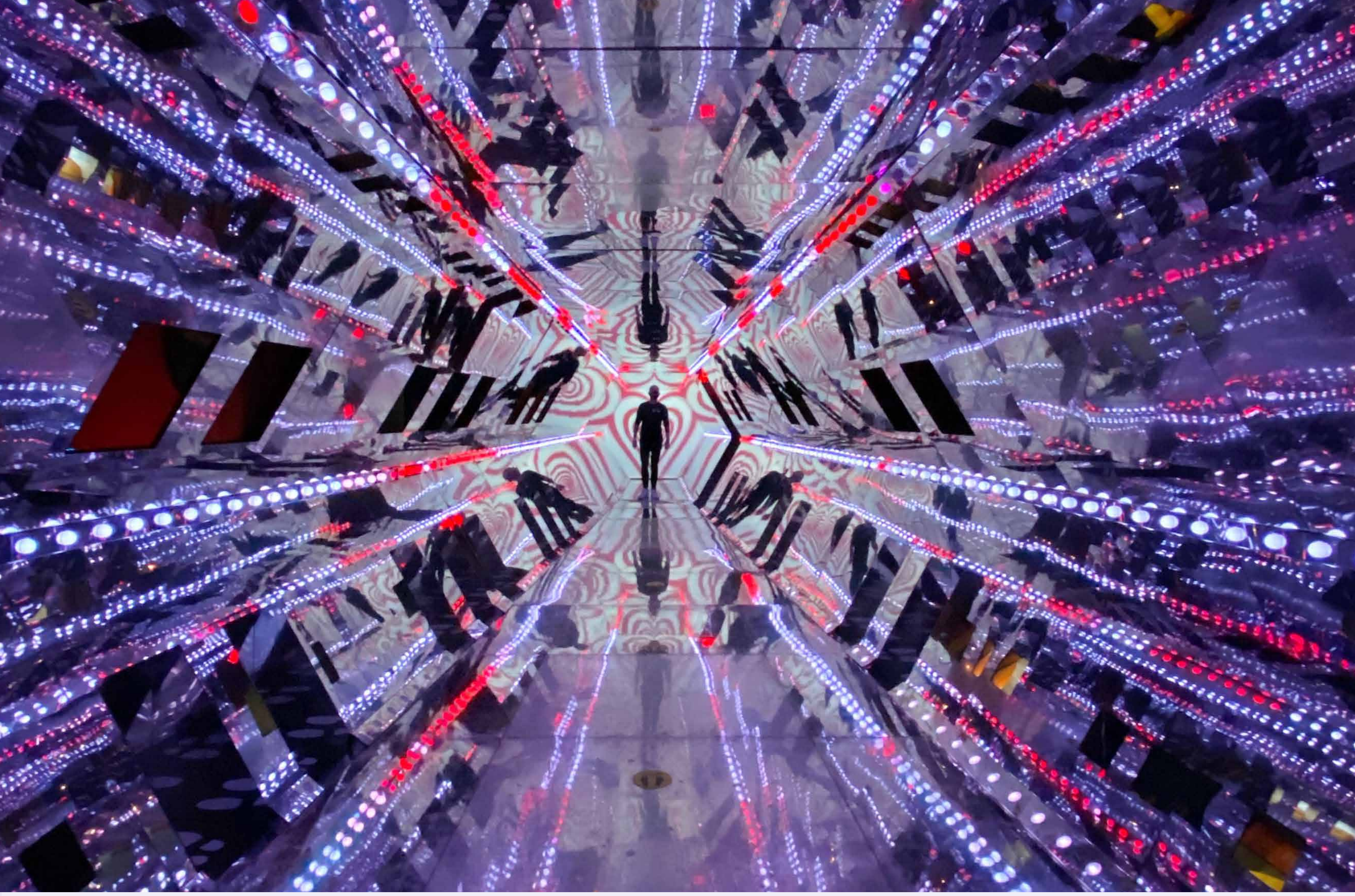
As with synthetic biology, an open ethos in advanced materials research and development is driving innovation. For example, the Materials Project provides open web-based access to computed information on known and predicted materials as well as analytics tools to inspire and design novel materials. Just as a growing stack of new technologies made synbio flourish, we now see this emerge for advanced materials.

Investors' interest has grown as advanced materials research accelerates, with many emerging technologies joining the bench. Between 2016 and 2020, our preliminary estimates identify $13 billion of disclosed private investments in advanced materials deep tech ventures. Specialist funds operating in this space include Pangaea Ventures, dedicated solely to advanced materials that solve fundamental challenges impacting the world.

Advanced materials can have a profound impact on energy generation, transmission, and storage. Another area of growing interest is that of metamaterials, synthetic composite materials whose properties are not typical of natural materials. These materials are already being used in aerospace and defense applications. Looking further into the future, new 3D printing techniques might push back the frontiers of material solidity, cost, and complexity.

To understand why advanced material R&D is at an earlier stage than synthetic biology, it's useful to know the hurdles that synthetic biology has already overcome, but which still play a role in advanced materials. The DBTL cycle is now a well-established development model in synthetic biology, while in advanced materials a set of enablers need to be put

2. Mordor Intelligence
3. Allied Market Research
4. How metamaterials could one day bring the impossible to life, Tech Radar / Science Daily



in place. The field of Materials Informatics must mature, providing the ability to codify knowledge and translate it into digital. Access to cross-disciplinary talent has lagged in material science, while the combination of materials and chemistry backgrounds with data scientists, computer scientists, and mathematicians is fundamental to create sound algorithms based on the understanding of the science behind them. Therefore, ML/AI applied to material science is still at a less mature stage than synthetic biology.

Another set of barriers has more to do with resources, talent, and culture. Where biotech and later synbio benefited from pharma's deep pockets, paving the way to business success (including acquisition), advanced materials did not have the same advantages. Moreover, advanced materials continue to be a very academic field, with research rooted in theoretical science. Some resistance to the acceptance of results that cannot be theoretically proven, is an obstacle to progress, particularly, for example, in Deep Learning.

Finally, by encompassing organic and inorganic matter, nature co-design can also leverage the developments in advanced chemistry. For the past hundred years, chemists have predominantly focused on thermocatalysis and the petrochemical industry breaking petrol down and refining it to produce molecules for many industries. Advances in catalysts, solvents, and in the understanding of chemical reactions are enabling a wave of innovation inspired by nature. Polystyvert, for example, is using p-cymene, a solvent found in cumin essential oils, among other sources, to dissolve postconsumer polystyrene for recycling. Since the process can be completed at low temperatures, it keeps the operating costs low and it also reduces emissions by more than 80% compared to making virgin materials from fossil fuels.

While still nascent compared to synthetic biology, the potential of nature co-design in inorganic matter is no less significant. Companies should pay careful attention to developments in this area, since they are likely to be instrumental to the second wave of nature co-design, after incorporating advancements in quantum computing. While the emphasis of the field lies less on the shift from value chain to value net, all four principles of nature co-design apply.

Nature Co-Design Leverages and Expands Nature's Design Principles and Manufacturing Capabilities

Nature co-design leverages and expands the design principles and manufacturing capabilities that nature already possesses, making them more efficient and adapting them to our purposes.

A better understanding of natural laws and mechanisms enables us to co-design with nature, using microbes and nano-scale forces to manipulate single atoms and build molecules with desired properties from scratch, using minimal energy.

Evolutionary pressure has forced microorganisms to become incredibly energy efficient. By engineering alternative selection pressures in the lab, we can accelerate natural selection to discover the best solution to manufacturing challenges.

However, nature co-design goes beyond engineering life forms to use them as a manufacturing platform. By understanding the phenomena that are intrinsic to the nanoscale, we can harness natural laws and mechanisms to create materials with unprecedented properties.

Applying the assembly principles found in nature, we can store more information in molecules than we ever could on solid or tape hard drives. We can create materials more flexible than Kevlar fiber and stronger than steel. We can create magnets with more powerful electromagnetic fields. We can manufacture nanoscale machines and self-assembling or self-healing items. Many of the materials created with nature co-design will be recyclable, marking the era as inherently sustainable and answering the call to circularity.

In the first and second industrial revolutions, we could only build new materials from those extracted from the earth. In the era of nature co-design, we start designing and building at the atomic level, knowing that all forms of life on the planet are made of carbon and carbon binds to every other element. This gives us the opportunity to build not only from carbon but from nearly every inorganic compound.

Nature Co-Design Is a Transformational Business Opportunity with Significant Sustainability Potential

Nature co-design should be seen, first and foremost, as an extraordinary business opportunity that will catalyze the transformation toward a sustainable future.

If we consider all non-service sectors, nature co-design has the potential to impact more than 40% of the global gross domestic product, equivalent to more than $30 trillion as projected by the OECD and the World Bank. It is a huge business opportunity and an inescapable economic imperative. Business leaders from all sectors need to take notice.

Nature co-design is led by purpose and problem-driven entrepreneurship, but economics and performance remain keys to success. And the need for nature co-design cannot be more urgent. If we want to operate within planetary boundaries, replacing the same energy needs by switching from fossil fuels to renewable energy will not be enough. Nature co-design leverages nature's manufacturing and engineering principles and can operate within reasonable temperature and pressure spectrums, requiring much less energy.

Nature: The Forgotten Half of the Fourth Industrial Revolution

The underlying paradigm of the first and second industrial revolutions was the application of brute force to natural raw materials. Raw materials, such as oil and metals, but also food, fiber, and fuel produced by today's agriculture were extracted from the earth, burned to generate energy, and transformed into more valuable products. The third industrial revolution—the information age—continued to rely on that extractive paradigm. In the fourth industrial revolution, nature was initially part of the original description, but as we moved into it, the narrative shifted away from nature, focusing more on digital and automation and turning nature into the forgotten half of the fourth industrial revolution[1] (Exhibit 7). In fact, as of July 2020, nature co-design related fields were mentioned in only 10% of the stories published around the fourth industrial revolution (See Exhibit 8). It is now clear that nature co-design marks the start of a new era that puts nature first. We all need to prepare.

1. Klaus Schwab, "The Fourth Industrial Revolution," Foreign Affairs, January 2016.

Exhibit 7: Nature has become the forgotten half of the fourth industrial revolution

1st

End of 18th - Begin of 19th century

- Mechanization to replace agriculture with **industry** as backbone of society
- Massive **coal extraction** to drive steam engines

2nd

End of 19th century

- **Electricity, gas and oil** as new sources of energy
- Rise of the **steel** and **chemical industry**

3rd

Second half of 20th century

- Nuclear energy
- Telecomms, electronics & computers
- Automation driven by PLCs and robots

4th

Ignited by the 3rd wave

Merging digital, physical and biological worlds – initially with a place for nature, but strong focus on computing and robotics afterwards

Initial thought leadership on the fourth industrial revolution **included a focus on nature**, as seen in the Industry Emerging technology breakthroughs listed by the WEF in 2015:

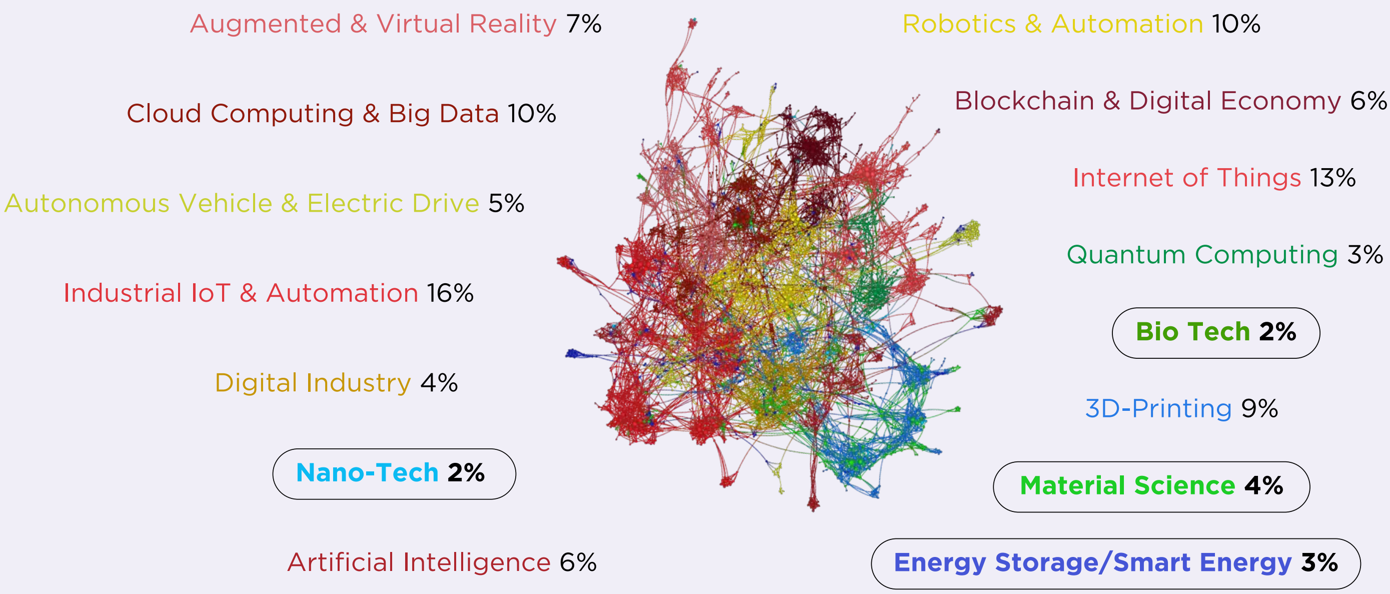
- Artificial intelligence
- Robotics
- Internet of Things
- Autonomous vehicles
- 3D-printing
- **Nanotechnology**
- **Biotechnology**
- **Materials science**
- **Energy storage**
- Quantum computing

However, **overtime the narrative converged to focus on IoT, automation & robotics topics**, giving Nature diminishing attention

Taking the content published on Industry 4.0 since the start of 2020 as a proxy, **nature-related topics are only recurring in 10% of content pieces**

Source: The Fourth Industrial Revolution – What it means and how to respond, Klaus Schwab (2015); BCG and Hello Tomorrow analysis

Exhibit 8: IoT, automation & robotics dominate the narrative of the 4th Industrial Revolution; nature-related topics are only recurring in one out of 10 cases

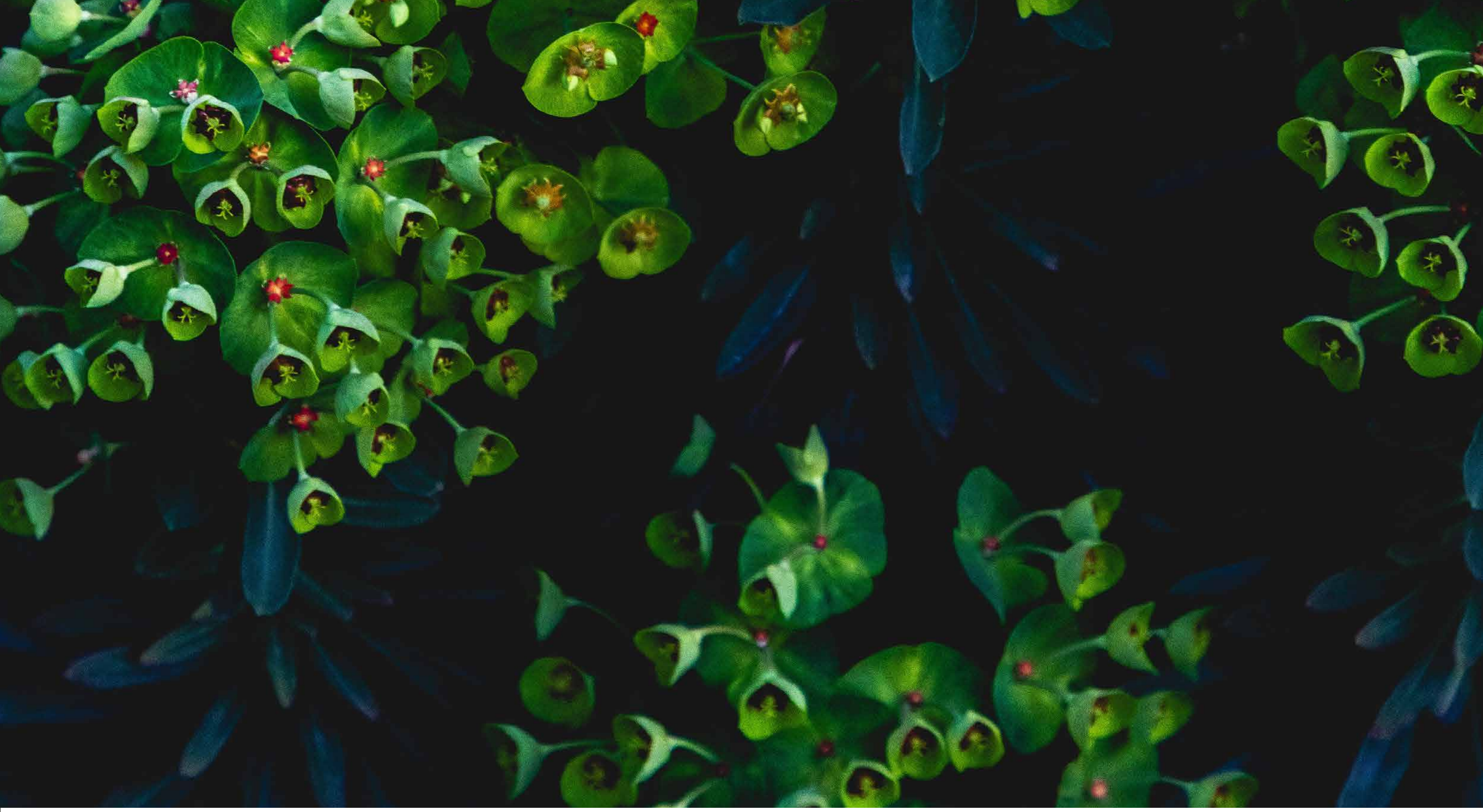


% Share of stories in each cluster. Note: Each node represents one individual story and the nodes are sized by publication count ~4k Stories related to 'Industry 4.0 & related technologies that have been published from January 2020 onwards were discovered with Quid and are clustered based on ther titles and texte bodies. ~15% of the stories could not be clustered.
Source: Quid, BCG Center for Growth & Innovation Analytics; BCG and Hello Tomorrow analysis

“We believe that we’re in the early stages of a sustainability revolution, one that will be larger than the Industrial Revolution with the speed of the digital revolution. We believe it’s the biggest investing opportunity in the history of the world, and the biggest business opportunity in the history of the world.”

Al Gore, June 2020[1]

1. https://www.wired.com/story/global-warming-inequality-covid-19-and-al-gore-is-optimistic/



A Revolution Is Taking Place: Rethinking Value Chains

Nature co-design forces a fundamental shift in the innovation equation. While information technologies including the internet, AI, blockchain, and robotics garner the bulk of business attention, the addition of nature in the form of organic and inorganic matter to the innovation equation leads to a wealth of opportunities that were not addressable before.

Nature co-design builds upon and leverages the ongoing digital transformation of our economy to create a very different level of optionality.

Calling nature co-design a revolution is for once not hyperbolic for two critical reasons:

- Value chains will be redesigned to improve economics and sustainability, changing the fundamentals of previous revolutions. No sector or industry will be spared the impact of nature co-design

- Triggered by the convergence of technologies and underlying exponential acceleration, change will come fast—faster than many people think.

As nature co-design and the technologies behind it reach the market, the decades-old value chains of industries such as agriculture and food, chemicals and materials, energy and utilities, and consumer goods will be disrupted.

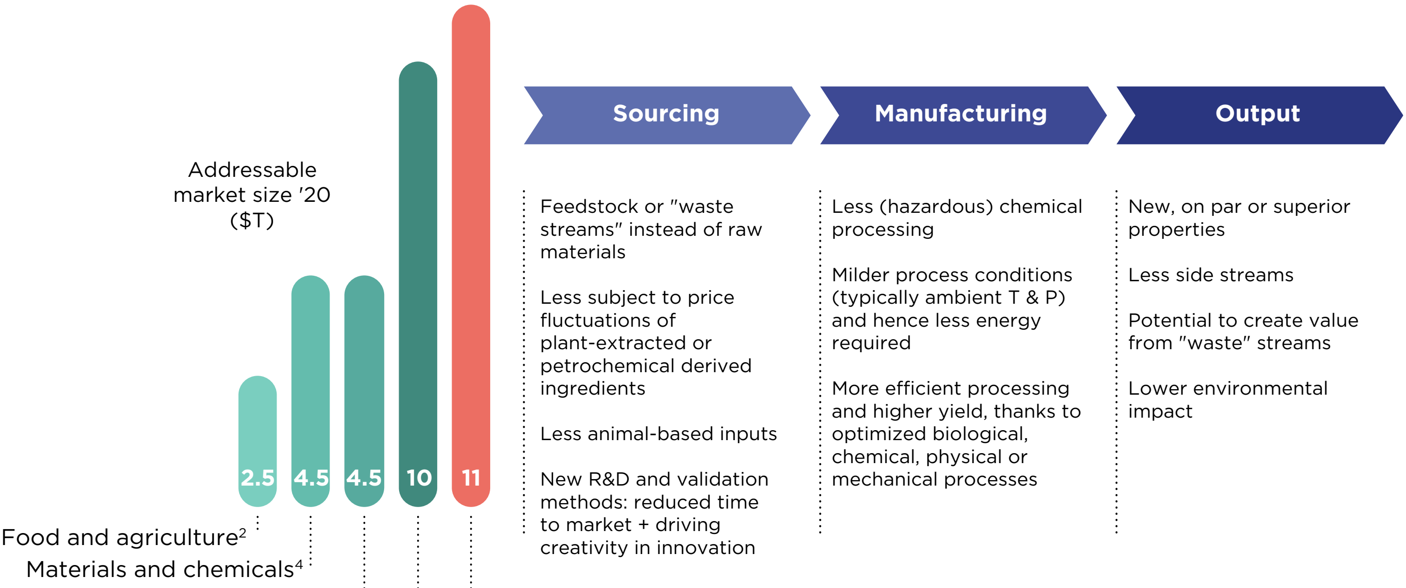
While estimating specific market opportunities is tempting, this would distract from the fundamental message.

Nature co-design represents a fundamental and radical shift in the way value chains are structured and established.

Nature co-design represents an opportunity to rethink value chains and create true competitive advantage together with real economic value that corporations cannot afford to miss. Imagine we are in the early 1990s and this thing called the Internet is beginning to emerge...

The takeaway for every business leader is that the market opportunity is huge—in the trillion dollar range (Exhibit 9) —with many open variables and unexplored (and even unfathomed) possibilities. But nature co-design also requires new and different approaches.

Exhibit 9: Nature co-design has the potential to disrupt to reimagine whole value chains, potentially impacting 40%of the global GDP, equivalent to more than $30T



1. Research and markets, Utilities Global Market Report 2020-30; 2. Global Agricultural Products, Market line 2020; 3. Global Healthcare Focus Report, Knowledge Center 2020; 4. Oxford Economics 2020; 5. Euromonitor, consumer goods excl. drinks and food and 'retailing' 2020

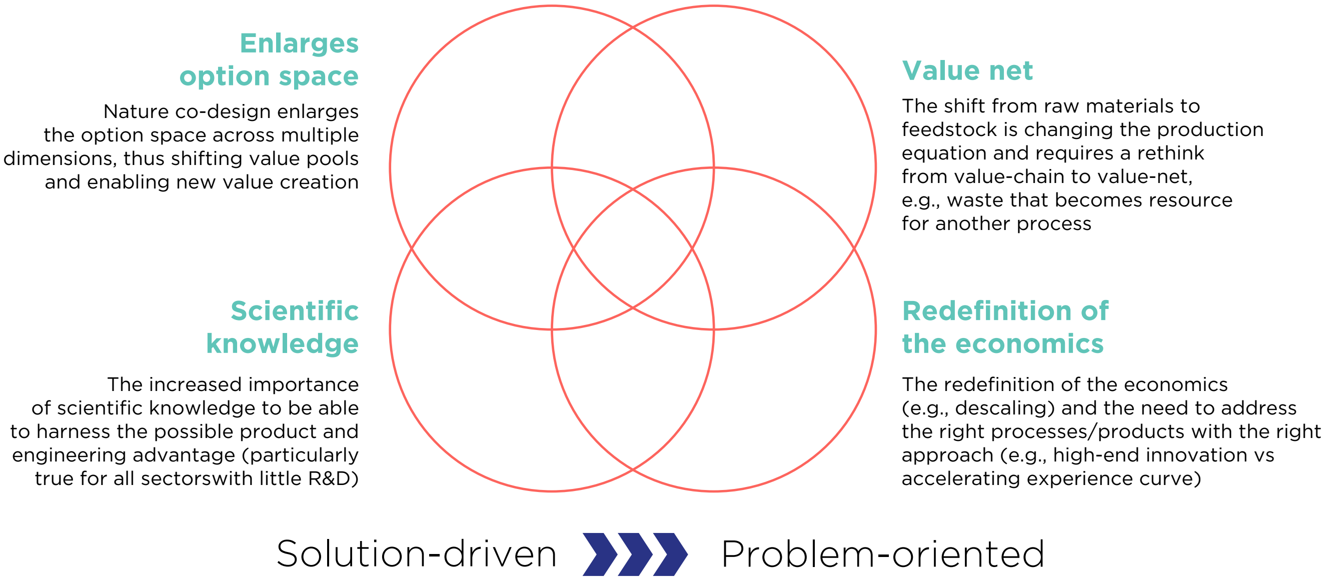
Source: OECD, World Bank, BCG and Hello Tomorrow analysis

Nature co-design's impact on value chains will have impacts along four intertwined dimensions (Exhibit 10):

- Nature co-design expands the option space, shifting values pools and enabling new value creation
- Nature co-design requires to rethink from value chain to value net as the material needs of society will be met by a move from extraction and raw materials to feedstock, changing the production equation—for example, waste becoming a resource for another process
- Nature co-design will redefine economics and the need to address the right processes/products with the right approach—for example, high-end innovation versus accelerating the experience curve
- Nature co-design will increase the importance of scientific knowledge and the need for trust in science, relying on imagination to harness possible product and engineering advantages and imagine new possibilities, especially in sectors with little R&D

To grasp the opportunities of these new value chains, mindsets need to shift from solution-driven to problem-oriented and existing frameworks must be reimagined. Below, we explore each of the four dimensions in detail.

Exhibit 10: The impact on the value chains will happen along four main dimensions, which are very much intertwined:



Source: BCG and Hello Tomorrow analysis.

Value Creation Through an Expanded Option Space

Nature co-design is not one single innovation but rather a set of principles unlocked through advances in science and engineering that together increase the option space.

Consequently, nature co-design allows us to overcome several century-old boundaries in manufacturing, making the unthinkable possible by following three main principles.

First, instead of breaking raw materials down into smaller building blocks and then recombining them, **nature co-design enables us to build materials from scratch atom by atom**, allowing for unprecedented precision in manufacturing.

Second, because biology is highly selective and can deal with a mixture of inputs, **nature co-design allows manufacturing from impure sources**. This enables to manufacture products from inseparable mixtures of input materials.

Third, based on the two previous principles, nature co-design shifts the energy equation, making processes that were previously uneconomic due to high energy demand affordable.

Examples of companies creating value by expanding the option space and shifting the value pool include Pivot Bio, Joyn Bio, Zymergen, and Niron Magnetics. Pivot Bio and Joyn Bio are replacing the Haber-Bosch synthesis, a century-old, energy-intensive process to produce ammonia fertilizer with engineered, nitrogen-fixing bacteria. Zymergen is replacing the petroleum-based incumbent products with a novel, designed-from-scratch, biofabricated product (Hyaline). Niron Magnetics leverages the assembly principles of nature to form a better, cheaper product from abundant, sustainable sources.

What unites these companies is that they replace decades-old commoditized products and processes that have perfected value chains and rely on huge economies of scale. For these companies, trying to compete on price alone would be self-destructive, as illustrated by the "biofuels bust". Rather, these companies are creating an additional form of value that justifies the leap to the new technology or ingredient. Understanding that they do not compete on price is critical .

Deep tech ventures leverage at least one of the three principles described above that come with nature co-design to create processes and products that generate a new form of value. For biology, this may translate into the precision of producing a designed molecule; for advanced materials, this may include assembling the desired form at the atomic scale using nanoscale forces.

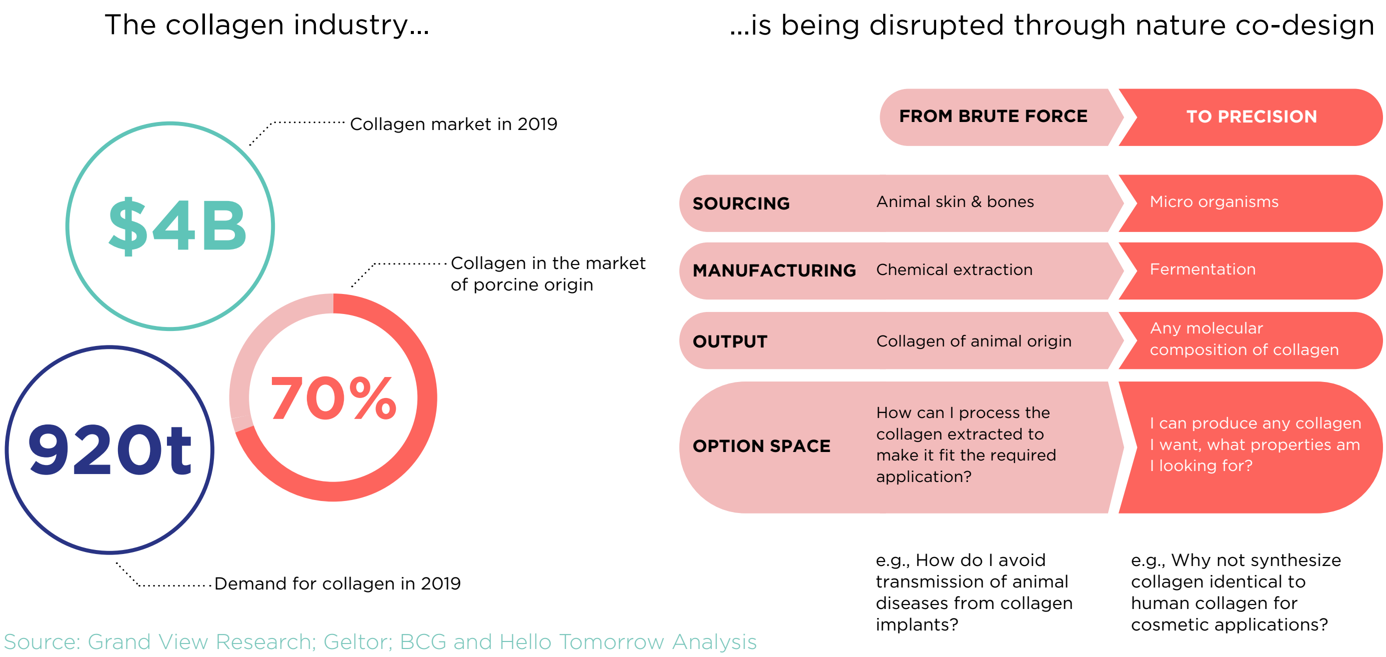
Equally important, value creation through an expanded option space is not necessarily limited to parts of the value chain—it can replace the whole value chain (meat and dairy) or substantial parts of it (textile).

Two companies that are replacing or are poised to replace entire value chains are Geltor and C16 Biosciences.

Collagen alternatives

Geltor leverages nature co-design to produce bio-designed proteins such as collagen, an estimated $4 billion market in 2019 according to Grand View Research. Collagen is the most abundant protein in the animal kingdom and is one of the most abundant proteins in the human body. Today, the majority of collagen produced for cosmetics and supplements is separated from animal tissues. Beauty industry chemists, for example, spent years attempting to make fish-derived collagen skin-colored and odorless. Geltor created a platform to produce bio-identical human collagen from scratch using a fermentation process not unlike brewing. Further, the company has introduced a service that develops "Ingredients-as-a-Service™". According to the Geltor website, the "Ingredients-as-a-Service™ team offers customized services to brands and manufacturers seeking to develop tailored ingredients for products that are truly distinguished in the marketplace. Geltor's biodesign experts will work with you to personalize new proteins, using our proprietary computational biology platform."

Exhibit 11: Nature co-design is radically enlarging the option space for the collagen industry



Source: Grand View Research; Geltor; BCG and Hello Tomorrow Analysis

Palm oil alternatives

C16 Biosciences is a start-up leveraging nature co-design to produce an alternative to palm oil using fermentation. Palm oil is a ubiquitous ingredient found in nearly 50% of all packaged products, including pizza, doughnuts, chocolate, deodorant, shampoo, and toothpaste, to name a few. The glob-al market for palm oil is estimated at $61 billion[6]. Palm oil has been and continues to be a major driver of rainforest deforestation. C16 Biosciences has created a platform to produce sustainable alternatives to palm oil, producing a product with better performance and cost-competitive.

Nature co-design's ability to expand the option space and create value with better products that will shift value pools is not limited to biology. Similar examples can also be found in advanced materials with TeraPore and Sila Nanotechnologies.

Smart filtration membranes

TeraPore is a start-up using nanotechnology to disrupt the market for filtration membranes in virus filtration—an important step in the manufacture of biologics, a market expected to reach $400 billion by 2025[7]. TeraPore is using advanced nanotechnologies to produce filtration membranes with superior properties compared to incumbent products.

6. AZO Cleantech

7. Coherent Market Insights

TeraPore is expanding the option space by replacing the commodity polymers used by competitors with new engineered polymers capable of self-assembly at nanoscale. After 25 years of research and development, TeraPore's main competitor generated three virus filtration membrane product designs. In contrast, in just four years, TeraPore generated more than 25 designs, representing precise, tunable filtration products.

Alternative anodes for Lithium-ion batteries

Start-up Sila Nanotechnologies uses nature co-design to develop better materials for batteries. Co-founded by Tesla employee number seven, Sila replaces the graphite anode of batteries with silicon—a cheaper, more abundant material. To widen the option space with a new material, the Sila Nanotechnologies team spent its first three years iterating. Their first breakthrough increases battery density by at least 20% and provides a boost to the exhausted chemical potential of Lithium-based batteries. Value is a key driver of Sila's strategy. The company started addressing the mobile phone batteries market, where value delivered is high relative to cost. The company is now entering the electric vehicle market and will eventually sell into the energy storage market.

Property-based design of nanoparticles

However, where advanced materials really leverage the full potential of nature co-design is where we can go to the atomic level and leverage nanoscale forces to achieve properties that are not present in nature. It opens a new paradigm, in which we define the properties needed for an application and create them at the atomic level, where quantum mechanics apply.

A company pioneering this field is VSPARTICLE. VSP has developed a process to remove variability and manual effort from nanoparticle production. The incumbent wet chemical synthesis process is confined to research labs and involves months of lab work to make and analyze a single nanoparticle, incompatible with a healthy design cycle and difficult to scale. VSP's technology is able to produce nanoparticles with the required specifications, without manual work, reducing development time by an order of magnitude, from months to days.

When such capabilities become available, it is suddenly possible to deliberately leverage the DBTL cycle to accelerate innovation, instead of being hindered by slow build and test phases. We are then able to design nanoparticles through algorithms, produce them with precision, and have the test results fed back into the algorithm, improving exponentially the ability to generate better nanomaterials. Leveraging their core technology, AI, and automated laboratory VSPARTICLE is on its way to reduce advanced material development times from 20 years to 2 years. This is a change of paradigm, in which properties we could not imagine before, become possible, and the inherent constraints in material properties are removed as we can determine them.

By enlarging the option space to properties that cannot be observed in nature and shifting away from extraction and waste to build from the bottom up, the value equation is also fundamentally different. The nanoparticles produced by VSP have unique properties, are fit for high-value applications where industrial scale is neither needed nor desired.

The dominating factor is the precision in producing particles with the exact properties needed, and that grants impactful added value.

From Value Chain to Value Net

"Raw materials" and "crude oil" are the terms used to refer to the approaches of the second industrial revolution, where starting materials needed to be processed and refined using significant amounts of energy.

Nature co-design massively shifts the approach and forces to redesign the production equation. We will no longer dwell on a linear production chain that starts with raw materials and ends with waste. Instead, nature co-design brings us closer to a universal material ecosystem, where everything becomes a resource and a potential starting point for value creation, just as it is in nature.

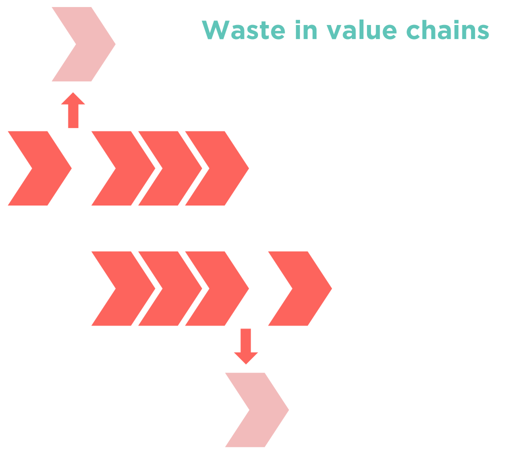
In the universal material ecosystem, the waste of one production process can become the starting point of another. Waste becomes an asset if it can be used as feedstock to feed organisms that produce a different product. This leads to a very different carbon cycle.

Waste in one process is a valuable resource for another

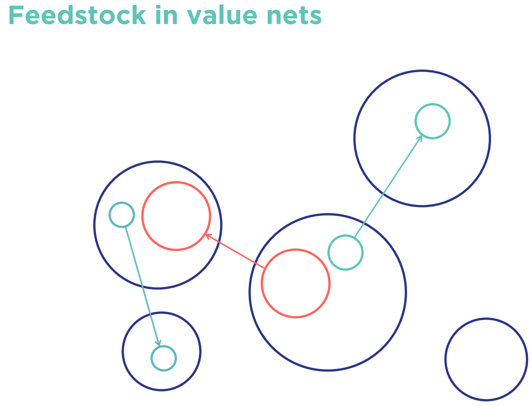
In the new nature co-design production equation, feedstocks can include sugar, corn, algae, carbon dioxide, methane, or any carbon-containing waste stream such as cotton or even plastic waste. Waste in one value chain can become a resource in another; this has an impact on economics as well as on the size and the location of production plants since proximity to waste streams can become an important variable.

For example, start-ups LanzaTech and Mango Materials both use waste as foundational materials for value creation and co-locate their production facilities where waste is produced. Nature co-design is leading to a shift from the notion of value chain to the idea of value net[8], defined as a set of value chains connected by waste streams turning into resources for other value chains (Exhibit 12).

Exhibit 12: From waste to feedstock, from value chains to value nets



In the second industrial revolution, material input is extracted, processed and refined using massive amounts of energy. Brute force is applied to break down the raw material and extract what is valuable,while rejecting the rest as waste



Nature Co-Design shifts the paradigm, starts from the precision to design at the nano-scale, paralleling Nature's efficiency and transforming traditional waste into an asset as it can be used as feedstock

Source: BCG and Hello Tomorrow analysis

The list of companies using waste from other processes as main feedstock is already long. It includes NovoNutrients and Kiverdi, both using industrial carbon dioxide emissions to produce proteins for human and animal nutrition; LanzaTech using industrial off-gases to produce fuels and chemicals; Mango Materials using methane to produce biodegradable plastic that can be used to develop fabrics; Carbios leveraging an enzymatic process that converts plastic waste into fully biodegradable plastics; and Evrnu, a start-up producing new renewable fibers from cotton textile waste via repolymerization.

Waste streams can also be upcycled without turning them into feedstock for microbes. For instance, CO_2 from flue gas powers Agora Energy Technology's redox flow battery and serves as a key resource to design nanomaterials at Carbon Upcycling Technologies.

For managers, value chains must be redefined based on a critical assessment of the most advantageous resources, with the resources themselves reexamined as possible assets or constraints.

8. Value net should not be confused with value network, a concept related to disruptive innovation.

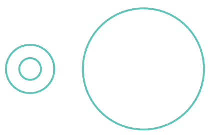
Redefining Economics in the Era of Nature Co-Design

Nature co-design implies a radical shift in the approach to engineering and manufacturing (Exhibit 13). The brute forcing of nature is replaced with precision, selectivity, and energy-efficiency. The implications on manufacturing economics are radical.

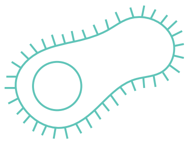
Instead of relying on processes and energy to obtain desired outcomes, nature co-design requires that economics are adapted to reflect the precision and selectivity that comes from designing and manufacturing with nature. “Scale” and what it takes to leverage it economically take on a very different meaning.

Exhibit 13: Nature co-design implies a radical shift in the approach to engineering and manufacturing.

The brute forcing of nature is replaced with precision, selectivity, and energy-efficiency.
The implications on manufacturing economics are radical.

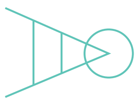


Bigger is not better

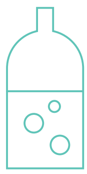


Organisms as Capex

The scaling up challenge



Design-to-cost matters



Precision fermentation is showing the way

Experience Curve and the right value strategy

In the past, the central aggregation of processing and refining promised efficiency gains. There was an implicit and intrinsic need for scale, which resulted in a “bigger is better” mindset. Consequently, plants like refineries represented huge investments, well above $1 billion, with capacities above 200,000 barrels or 30 million liters per day. Decades of practice and experience delivered optimized processes and costs, with consequent lack of flexibility. In the ‘bigger is better’ world, understanding cost structures and cost dynamics was key and deep.

When we look at the world through the nature co-design lens instead, precision becomes the dominating dimension.

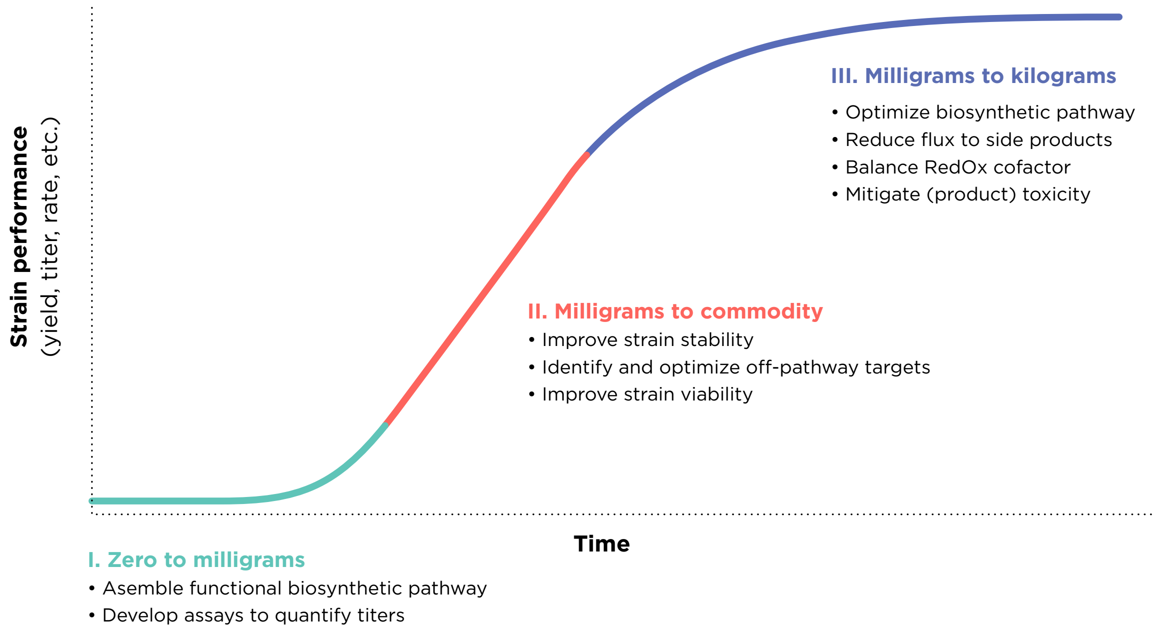
We are starting at the nanoscale, building with atomic precision. In this setting, scaling up is the challenge.

Bigger is not necessarily better or more profitable

A sizable nature co-design synthetic biology plant may cost more than $100 million to build and produce 30 million liters/year, compared with $1 billion and 11 billion liters/year for a refinery. In contrast, a normal fermenter or bioreactor can produce between 10,000 and 100,000 liters per batch and cost much less depending on its use.

Dealing with living organisms, organic feedback loops must be taken into account. Microorganisms, for many reasons, do not scale linearly. Instead, their performance follows an S-curve (Exhibit 14). As a result, there is no real improvement in performance beyond a certain scale. This means, particularly for biological manufacturing, that difficulties in scaling limit the optimal size of a nature co-design plant.

Exhibit 14: Microorganisms do not scale linearly but rather following an S-curve



Source: Best practices in fermentation bioprocess development, Culture Biosciences and Stefan De Kok, Ph. D. (2020); BCG and Hello Tomorrow Analysis

Beyond the behaviors of living organisms, the size of an optimal plant is altered by the value creation through expanded option space and the replacement of raw materials with feedstock. Each has a substantial influence on the economics of nature co-design.

Expanding the option space for parts of the value chain implies creating a multitude of new solutions that need to be manufactured, thus reducing the need for scale and increasing the need for flexibility. The overall result is a need for smaller, more modular, and intrinsically flexible facilities, since the shift from one product to another "simply" requires swapping out the "producing" organism. It may also require changing the feedstock. However, it does not require a change in the capex infrastructure. For advanced materials, the dominating factor is the (nano)composition of the compound in order to obtain the desired properties, again reducing the need for scale and increasing the need for flexibility.

Large centralized plants can be replaced with distributed networks of flexible, "reprogrammable" manufacturing sites since the only things that move from place to place are digitally codified. Large buildings, physical pipelines, and trucks and ships to aggregate, move, and process raw materials all lose importance.

Smaller and less sophisticated infrastructure reduces the need for allocating financial resources upfront and shortens the time needed to build large sites. Ventures can reach the market faster without burning limited cash reserves before generating revenue.

The redefinition of economics, however, does not end at the infrastructure level. For synthetic biology, living, engineered organisms represent the real value-creating infrastructure in the process, while "traditional infrastructure" (capex) producing the end-product becomes a commodity. For advanced materials, algorithms and IP to obtain the desired properties become the important capital dimension, also relieving traditional infrastructure from its former central role.

Organisms as capital expenditure

In nature co-design, organisms take on the role that used to be that of "traditional" capex, which decreases in value, while the importance of feedstock and material costs, opex, increases.

The choice and the procurement of feedstock becomes strategic, requiring thorough examination as it impacts cost along multiple dimensions, not only as input but also as output. Production location becomes an important variable as it can directly impact feedstock cost, especially if it is waste from other processes, meaning a premium could be paid, rendering feedstock purchasing costs negative.

On the opex front, power cost can play a very important economic role, representing in certain instances up to 15% of the opex cost. Decreasing power cost from between six cents and eight cents per KWh to two cents per KWh using renewables can represent a 10% cost difference in the final product.

If we merge nature co-design with the ongoing trend toward a descaled and distributed energy infrastructure where we begin moving toward near-zero marginal cost power generated by renewables, the picture becomes even clearer: the production infrastructure not only becomes smaller, localized, and distributed, it also becomes more flexible and hence more resilient.[9]

Business leaders embracing nature co-design need to understand these distinctly different economic structures and adopt a different mindset and framework. When looking at nature co-design, businesses need to incorporate these economics in their planning. For instance, markets that previously appeared unattractive because of high capex required compared to their small size may suddenly become attractive, and vice versa.

Still, this is not enough, since the different economic structure of nature co-design is not limited to size, flexibility, impact of opex, and feedstock. Nature co-design includes additional intrinsic characteristics that require a different economic approach, including some that are specific to synthetic biology such as the importance of scaling down.

The scaling up challenge

Because biology is nonlinear, insights at the lab level do not translate into commercial execution. Things that work in the lab at the microliter scale will not necessarily work the same way at the liter or thousand-liter scale. This requires a different approach than rapid prototyping or the creation of a minimum viable product (MVP) starting from lab scale as favored by the lean start-up methodology.

Instead, it is essential to start keeping the end in mind and scale down processes from the final production volume to obtain a MVP. The MVP in this case is the beginning of the "kilogram-to-commodity" part of the S-curve, not the zero-to-milligram part. Companies need to consider their final production size and design a process to reach that output since, in many cases, organisms that produce at the microliter or liter scale will not work the same in hundred- or thousand-liter tanks. Achieving scale practically could be accomplished by renting experimental time in fully scaled, cloud-based biofermenter plants to test how the organism operates at different scales. (Exhibit 14)

Inorganic materials produced utilizing nanotechnology also have similar issues in scaling up production and moving from the lab to commercial execution. Building at the atomic level and scaling remains nontrivial.

9. "World Energy Investment 2020," IEA, October 2020.

Design-to-cost matters

The consequence of needing to scale from top down instead of from bottom up is that design-to-cost is intrinsically embedded in the economics.

Of all nature co-design companies, Zymergen is probably the one with the most sophisticated design-to-cost approach. Zymergen's Hyaline, a film for electronics applications, emerged from a series of earlier projects and invited challenges that were aimed at developing capabilities for biomanufacturing molecules and materials with unique performance characteristics that could not be produced using conventional means.

From the onset, Zymergen looked at the cost range they would need to achieve to support the value offered by the product. They did so by looking at the properties of the material and the number of design-build-test-learn cycles needed to reach their final product. Zymergen also examined the overall process (including fermentation and biofabrication) needed to deliver at the targeted cost.

Design-to-cost is not new, but specifically with synthetic biology two intertwined layers of economics impact the cost. On one side is traditional cost development with capex, opex, and materials, and on the other side are the economics of the organisms, which can be designed to produce higher concentrations of the desired biosynthetic product. A higher concentration allows for more efficient downstream processing—the isolation and purification of the product—which is an important cost factor. Consequently, increasing the organism's production allows reducing cost. Microbes can also be designed to increase yield and reduce the required feedstock. Or they can be designed to grow faster, thus reducing capex and opex. This is exactly what Zymergen did in selecting the best strain to achieve their target goals for Hyaline and other products.[10]

Precision fermentation is showing the way

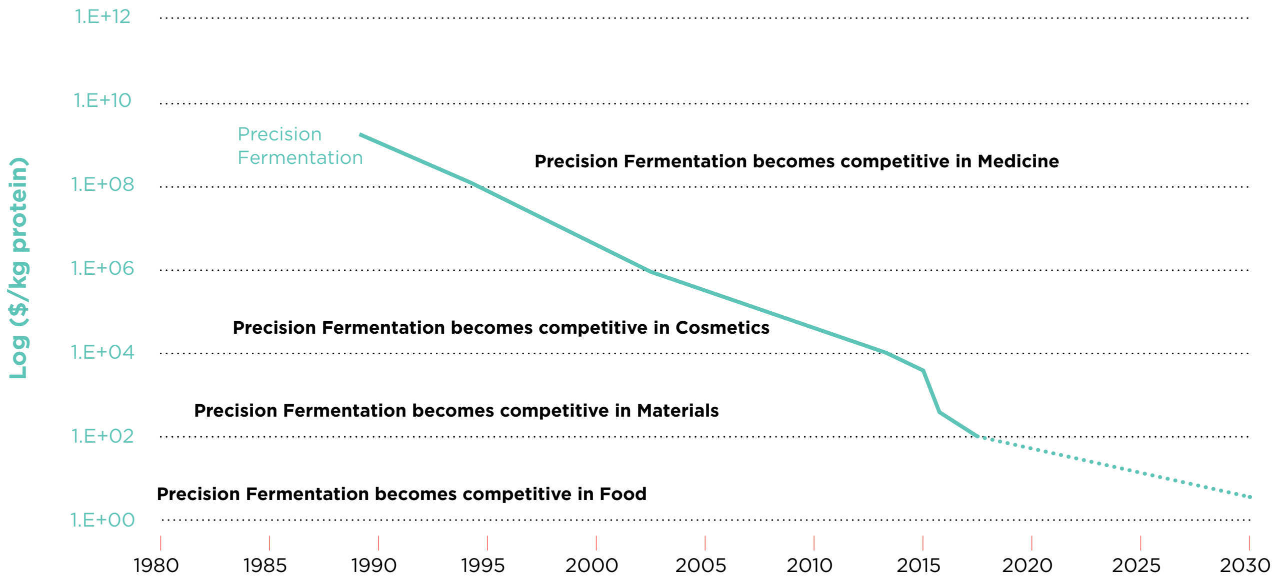
The evolution of precision fermentation cost shows the importance of understanding the economics and provides a glimpse into possible future developments in terms of cost. Precision fermentation, a nature co-design manufacturing technology, enables to program microorganisms to produce complex molecules such as proteins at a fraction of their cost.

According to the think tank RethinkX, precision fermentation cost has decreased exponentially over

10. Culture, "Best Practices in Fermentation Bioprocess Development," The Biomanufacturing Blog, June 2020.

the past years by leveraging technological developments and increased cumulated production, making new markets viable. The current boom of plant-based meat and dairy alternatives is likely accelerating the trend. (Exhibit 15)

Exhibit 15: Precision Fermentation is rapidly going down the experience curve



Source: RethinkX

Experience curve and the right value strategy

Absolute scale plays a smaller role in nature co-design, but the cost advantage generated through experience curves continues to be crucial. One way to achieve such advantage is by modularizing infrastructure, creating standards, and sharing data (both positive and negative), allowing equipment producers and the whole industry to profit from aggregated volumes and increased intelligence.

While the industry is still nascent, this aspect will be of paramount importance very soon since it will be key to limit scale disadvantage. Another possibility to drive down costs is to design products that can use existing infrastructure, leveraging its experience curve and potentially its scale.

Finally, the experience curves of photovoltaic[11] and lithium-ion batteries[12] have shown that the velocity with which the cumulative capacity is built can significantly reduce costs, faster than initially estimated and anticipated (Exhibit 16). Nature co-design has the potential to follow such a development.

The choice of the right value strategy becomes crucial in **leveraging the experience curve**.

The choice of the right value strategy becomes crucial in leveraging the experience curve.

Sila Nanotechnologies followed Tesla's example with a decision to focus first on consumer electronics where the premium for a better battery hardly drives total costs up. This enables Sila to drive up volumes and reduce unit costs while progressing along the experience curve and before moving to electric vehicles where batteries make up a substantial part of the total cost.

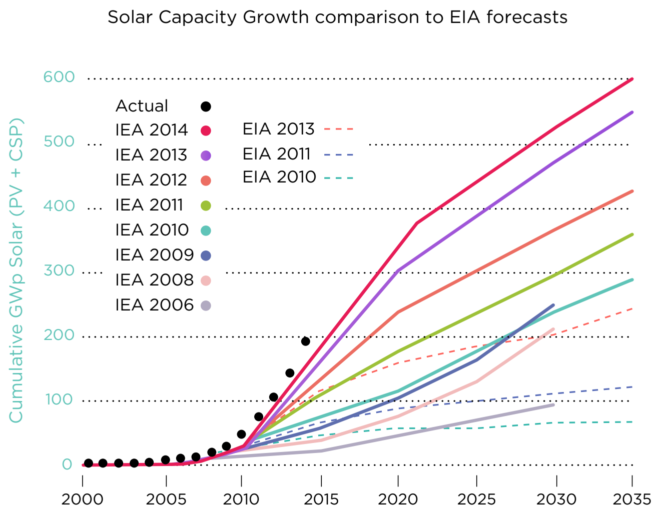
Another option to drive cost down is to leverage the experience of the ecosystem either through partnerships (Spiber-ADM), joint ventures (Ginkgo Bioworks-Bayer), or by licensing technologies to incumbents (Genomatica-Novamont).

Nature co-design requires redefined economics, as exemplified by the flexible, smaller, modular infrastructure, the feedstock and energy role, and the different relevance of scale. Additionally, the need to scale from the top down instead of the bottom up, design-to-cost, and understand the "organisms' economics" alongside the imperative to deliver value further emphasizes the difference in economics. Corporations must recognize the unique economics of nature co-design to create value and generate competitive advantages.

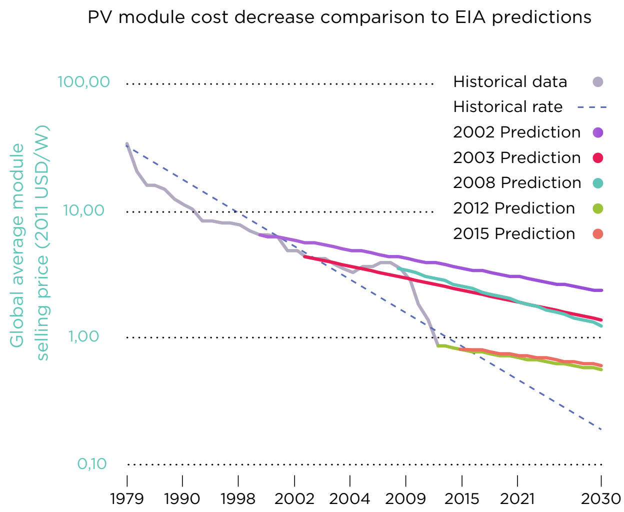
11. "Solar Photovoltaic Summary Charts," IRENA.
12. Gene Berdichevsky and Gleb Yushin, "The Future of Energy Storage: Towards A Perfect Battery with Global Scale," Sila Nanotechnologies, September 2020.

Exhibit 16: The velocity with which cumulative capacity is built cansignificantly reduce costs, faster than initially estimated and anticipated

Predictions for solar capacity growth have fallen short year after year



Underestimating the velocity with which capacity build was going to reduce costs over time



Source: MIT; EIA; IRENA; BCG and Hello Tomorrow Analysis

Increased Importance of Scientific Knowledge

The progress made in synthetic biology and nanotechnology in the last five to ten years is impressive, but we should remember that nature co-design is at the very beginning of its journey. It is as if we are back in 1992 and a few leading-edge actors have started to “play” with this new thing called the Internet. We are definitely not in 2020, with two decades of digital transformation behind us.

According to the BioGenome Project 2018, 80% to 90% of the world’s species are still unknown to science. 10 million to 15 million eukaryotic species exist worldwide, with only 3,500 completely sequenced and only 100 sequenced at the “reference level.” A great deal of foundational knowledge emerged from those sequences, facilitating advances in agriculture, medicine, and biology. We are only a few years into the revolution offered by the gene-editing tool CRISPR, with the first “CRISPRed” calf born in 2020. New life science technologies like CRISPR prove how new technologies can work efficiently and see rapid adoption, but still raise fundamental scientific and ethical challenges.

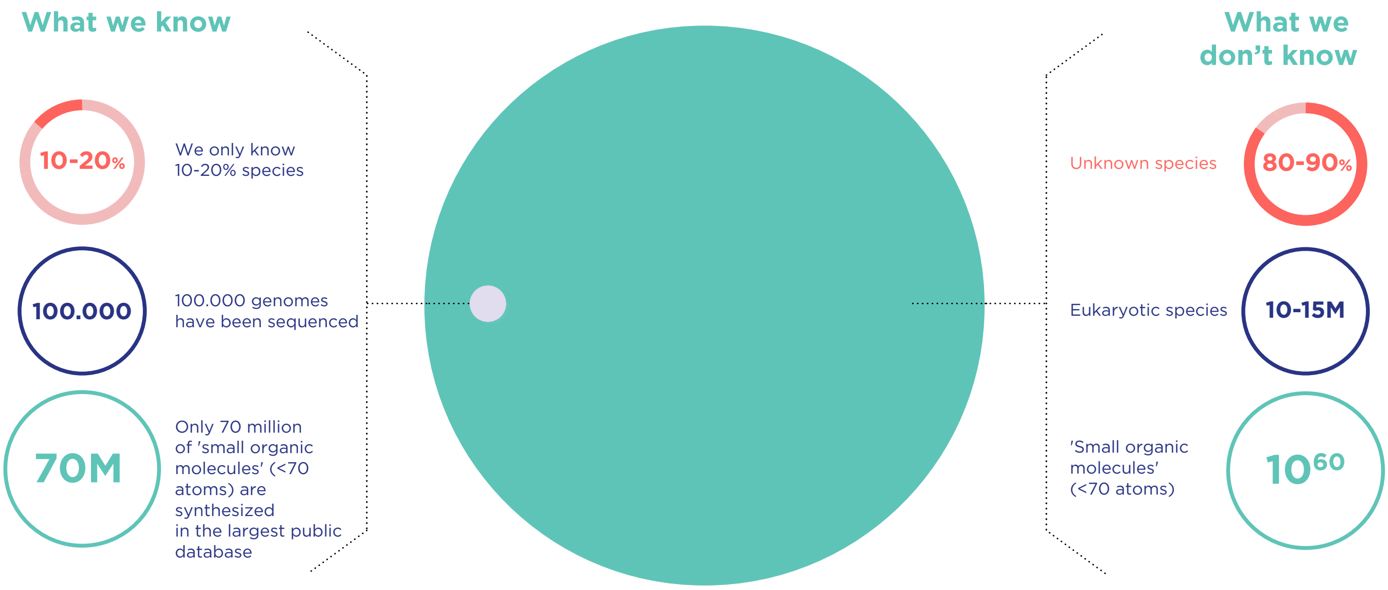
The chemical space is as vast as the universe, yet we only know a fraction of it. Looking only at small organic molecules with fewer than 70 atoms, it is estimated that there are about 10^60 molecules. A minuscule fraction of these chemicals have been manufactured today since the largest public database contains around 70 million molecules synthesized to date[13] (Exhibit 17).

The chemical space offers infinite degrees of freedom for output design and creation, generating increased complexity in the scientific innovation process. While the rules of biology limit the option space, the number of possible molecules to be designed using chemistry is huge. The number of atomic combinations—types and number of atoms in a molecule, location within the molecule, geometry and binding properties—is almost infinite. Huge computing capacity is therefore required to help design and test new molecules in silico.

Moreover, the impact of chemistry and material science comes from the properties of these atoms and molecules. The property space is also largely unknown, with nanotechnology obtaining properties that were impossible to obtain by traditional larger-scale structures. The reason is that nanomaterial property changes derive from quantum forces intrinsic to the nanoscale. Again, science must continue to advance to pave the way for the invention of materials with properties not existing in nature.

13. Ball P. Navigating Chemical Space, 2015

Exhibit 17: There's a lot that we don't know and that needs scientific knowledge to progress



Sources: BioGenome Project, 2018; Ball P. Navigating Chemical Space, 2015; BCG and Hello Tomorrow analysis

The power of quantum computing

Quantum computing could be a powerful catalyst for nature co-design, boosting new molecule discovery and accelerating organism design. Quantum computers can process large amounts of data in parallel. In some cases, quantum computers can execute algorithms exponentially, faster than standard computers. By using quantum physics to operate, quantum computers are the perfect platform to simulate quantum phenomena such as molecule interaction and energy states, as nature itself operates according to quantum mechanics. Because of this, molecular structures, properties of complex materials, and aqueous solutions containing complex dissolved species could be simulated faster and more accurately than with most advanced current methods.

Today, using classical computing hardware requires hours or days to get the result of a molecular simulation, if even possible. With quantum computing, we should be able to start running commercially relevant problems (or use cases) on quantum hardware and obtain meaningful results that outperform what classical hardware is capable of, from a few thousand simulations per week to tens/hundreds or hundreds of thousands per day.

While the full deployment of quantum computing is years, if not decades away, there are already examples of contributions to nature co-design.

Rahko, a start-up, has built a robust quantum chemistry platform that provides best-in-class toolboxes for running quantum and quantum-inspired methods. The company can simulate materials more accurately for discovery and the development of new molecules at greatly reduced cost.

OTI Lumionics, another start-up, uses quantum computing to solve molecule design challenges in material sciences and chemistry. The company is aiming to accelerate material simulations and to deliver more accurate property predictions, excited states mapping, chemical reaction modeling, molecular geometry, and strong electron correlation. OTI's promising results show that we might be using quantum technology for commercial simulations in the near future, possibly earlier than we think.

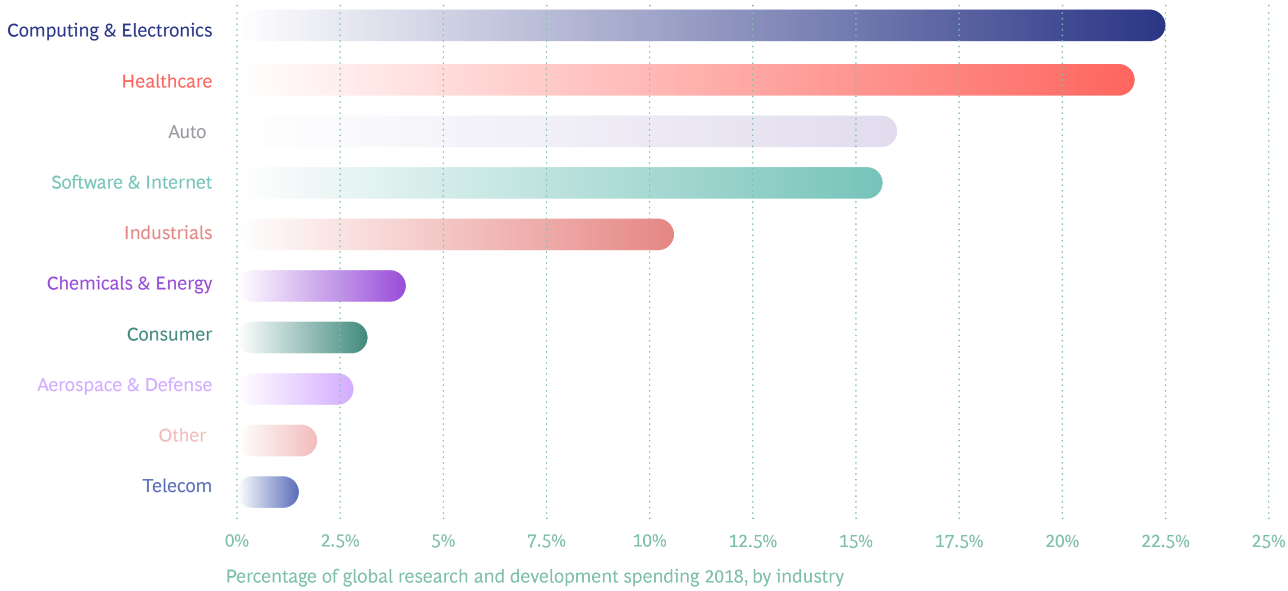
Quantum computing is just one of the areas where corporations need to increase their game. The bar for corporations and business leaders is set extremely high. Not only do they need to develop a basic understanding of nature co-design and the science behind it, they also need to understand its trajectory. The task is not simple.

Corporate strategies for leading-edge innovation

Returning to the 1992 analogy, while corporations might not have needed to understand the ins and outs of the TCP/IP protocol, they did need to realize that computers would be connected worldwide, revolutionizing business. Possibly, they should have anticipated the mobile revolution.

Today, business leaders need to understand that the complexity of nature is far from fully understood, there are new seminal platform technologies like CRISPR waiting to be discovered or improved, and nature co-design will be a computation and data

Exhibit 18: Scientific knowledge will pose serious challenge for industries that have under-allocated funds to R&D



Source: Bloomberg, Capital IQ, Thomson Reuters, Statista

play. This data play points to an urgent need to continue monitoring developments, developing capabilities, and understanding implications.

Historically, such a task has not been easy, even in industries with a traditionally high R&D spend like ICT and biopharma. As such, it will pose a serious challenge for industries that have under-allocated funds to R&D (Exhibit 18).

The alternative is to externalize innovation leveraging M&A, as biopharma and ICT have done over recent years. However, without the proper infrastructure and R&D budget to metabolize and leverage acquisitions, M&A might become a difficult or even counterproductive path.

The first signals from the market show that partnerships may be a better option, given the required level of scientific sophistication. Good examples of partnerships include those between Ginkgo Bioworks and Bayer for Joyn Bio and between Zymergen and FMC in crop protection products. Both Ginkgo and Zymergen are among the nature co-design companies with the best scientific understanding and, more importantly, the best data sets and data capabilities. We do not expect any traditional incumbents to be able to reach such level of sophisticated biological knowledge anytime soon.

Enabled by Problem Orientation, Powered by Imagination

Value creation by broadening the option space, shifting from waste to resource, and strengthening the role of scientific knowledge does not happen by itself. Business leaders play a key role in making nature co-design possible and driving it forward. For business leaders, as described in the deep tech approach (Exhibit 3), a clear problem orientation is at the core.

In true deep tech fashion, all business leaders involved in the examples above started their venture from a clear problem, not a solution. Finding the best use case for a technology is not enough. Instead, your technology must be the best solution among all possible solutions for the problem you want to solve.

Joyn Bio and Pivot Bio did not start from the Haber-Bosch “solution” but went back instead to the original problem—how to increase plant growth by providing exogenous ammonia. This problem orientation also holds true for Zymergen, Geltor, C16 Biosciences, Niron Magnetics, and Sila Nanotechnologies.

Beginning with the solution and not with the problem, thus limiting the option space, is very easy in a corporate (and start-up) environment. The old Silicon Valley mantra, “fall in love with the problem, not with the solution”, is essential for nature co-design.

Problem orientation is contrary to the traditional approach of new technologies (new solutions) looking for new use cases. In many cases, that approach has led to extremely long lead times for new technologies to find economically viable levels of deployment, if they were found at all.

For instance, in the second half of the 20th century, the applications that would make a specific plastic famous came on average almost nine years after the plastic's first commercialization. Of all the "new" plastic created, only 6% of the expected applications for a particular plastic were the first application commercialized. Plastic materials were invented with a "solution-first" orientation, where the material was first invented and different applications were tested before finding the application that made the material successful. In other words, plastic was successful once the problem it was uniquely positioned to solve was discovered.[14]

In nature co-design, both problem orientation and value focus are paramount because, with the precision of nature co-design, we can develop solutions instead of brute forcing our way to them.

Focus on value

If you want to revolutionize a value chain, you must focus on adding value and solving a problem, not on competing on cost. Nature co-design makes delivering added value possible, even in markets where incumbents and dynamics seem firmly established.

To be successful, the key is to know where value is currently created in a market, where potential value pools exist, and what particular innovations enable you to access those value pools, given that you are leveraging nature's design principles. Being successful with nature co-design requires radical questioning and reimagining the existing frameworks, ranging from current manufacturing practices to the organizational setup of your company. This reimagination could lead to a radical shift in which R&D and procurement departments closely connect and leverage nature co-design principles together to access the most promising value pools.

In the above examples, we have seen that nature co-design turns century-old paradigms on their head, while also radically changing supply options, making that link between procurement and research & development units not only sensible but necessary.

Powered by imagination

Ultimately, managers are solely responsible for broadening the option space, the most critical step in creating value; and **imagination is the crucial factor in seizing and creating nature co-design opportunities and finding new paths to growth. Imagination**, *the capacity to create, evolve, and exploit mental models of things or situations that don't yet exist*, **is essential to create value with nature co-design.**

Nature co-design offers unique properties and capabilities that do not fit with many elements of the status quo. Broadening the option space will seem impossible or even illogical at first. Assumptions that seem like natural laws within an industry are hard to see for what they are: illusions. To leap first requires seeing these illusions as such.

Rather than living in a world of tradition or "what is," managers need to be able to explore the realm of "what could be." Only then will they be able to create new opportunities and shape the "what is."[15]

To be able to fully leverage the potential of nature co-design, business leaders need to apply the deep tech approach and look at all available technologies, combining them where appropriate to generate maximum value within the considered value chain.

Finally, changes in value chains do not happen overnight. Reimagining business, products, processes, and operating models is required to thrive in the nature co-design space, and it takes time. In particular, the increasing speed of innovation cycles, together with the broadened option space to shape the value chain, contrast with the time needed to adopt innovations and with the variable economics of adoption, which need to be sorted out. The managers' role consists in understanding this asymmetry and prioritizing the biggest value pools.

Business leaders need to apply the key nature co-design principles of rethinking products and processes, shifting value pools by using imagination, creating appropriate value nets, deeply understanding the economics, and building a deep enough scientific understanding. They need to continue monitoring investor behaviors to spot where the next disruption waves will occur. Business leaders will also need to develop the capability to understand what is possible and how.

Partnerships and strategic investments seem to be the best path forward in terms of building capabilities. Some have gone as far as recommending the creation of a Chief Biology Officer to institutionalize this. This might sound far-fetched in today's context, but who would have thought in the 1960s that one day companies would have a Chief Information Officer?

14. Christopher Musso, "Beating the system: accelerating commercialization of new materials," Massachusetts Institute of Technology, February 2005.

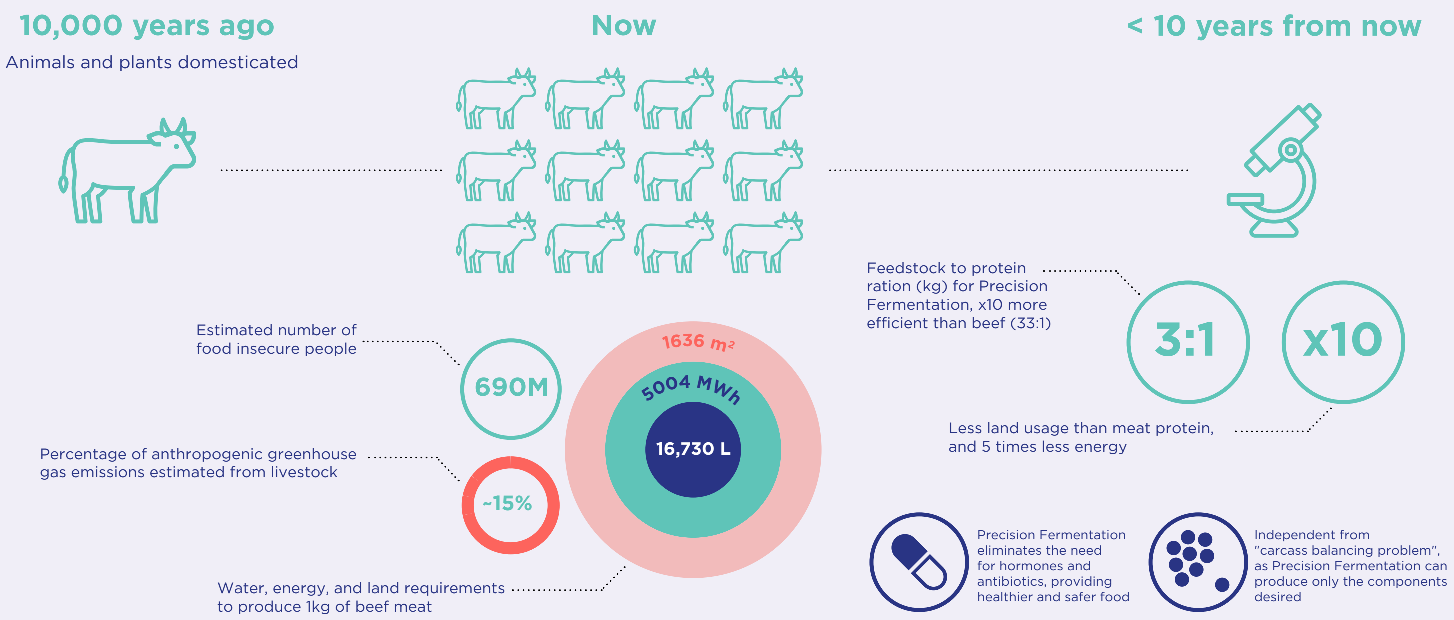
15. Martin Reeves and Jack Fuller, "We Need Imagination Now More Than Ever," Harvard Business Review, April 2020.

Nature Co-Design in Action: Value Chains Being Disrupted

Nature co-design has the potential to disrupt entire value chains or impact significant portions of them. Two industries fundamentally disrupted by nature co-design are animal farming and textile/fashion.

The farming industry (and the food industry alongside it) will be fundamentally reshaped by nature co-design through precision fermentation, which enables a new wave of products ranging from cultivated meat to synthetic milk to lab-grown leather to synthetic collagen.

Exhibit 19: The farming industry will be fundamentally reshaped by Nature co-design

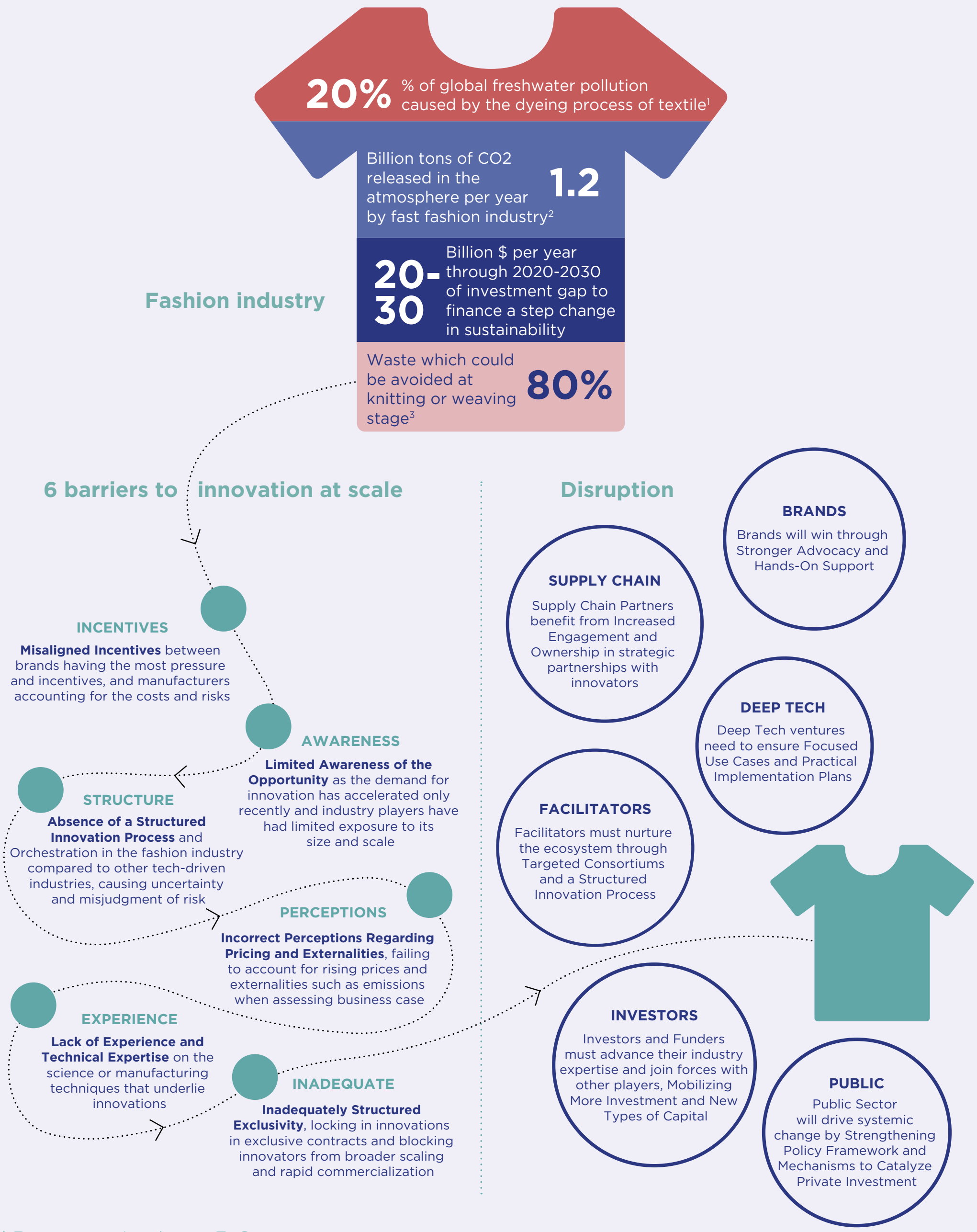


Source: Food and Agriculture Organization (FAO); RethinkX; Good Food Institute; Liz Specht (2019) Alt-Meat Trounces Animal Meat's Massive Inefficiencies; BCG and Hello Tomorrow analysis

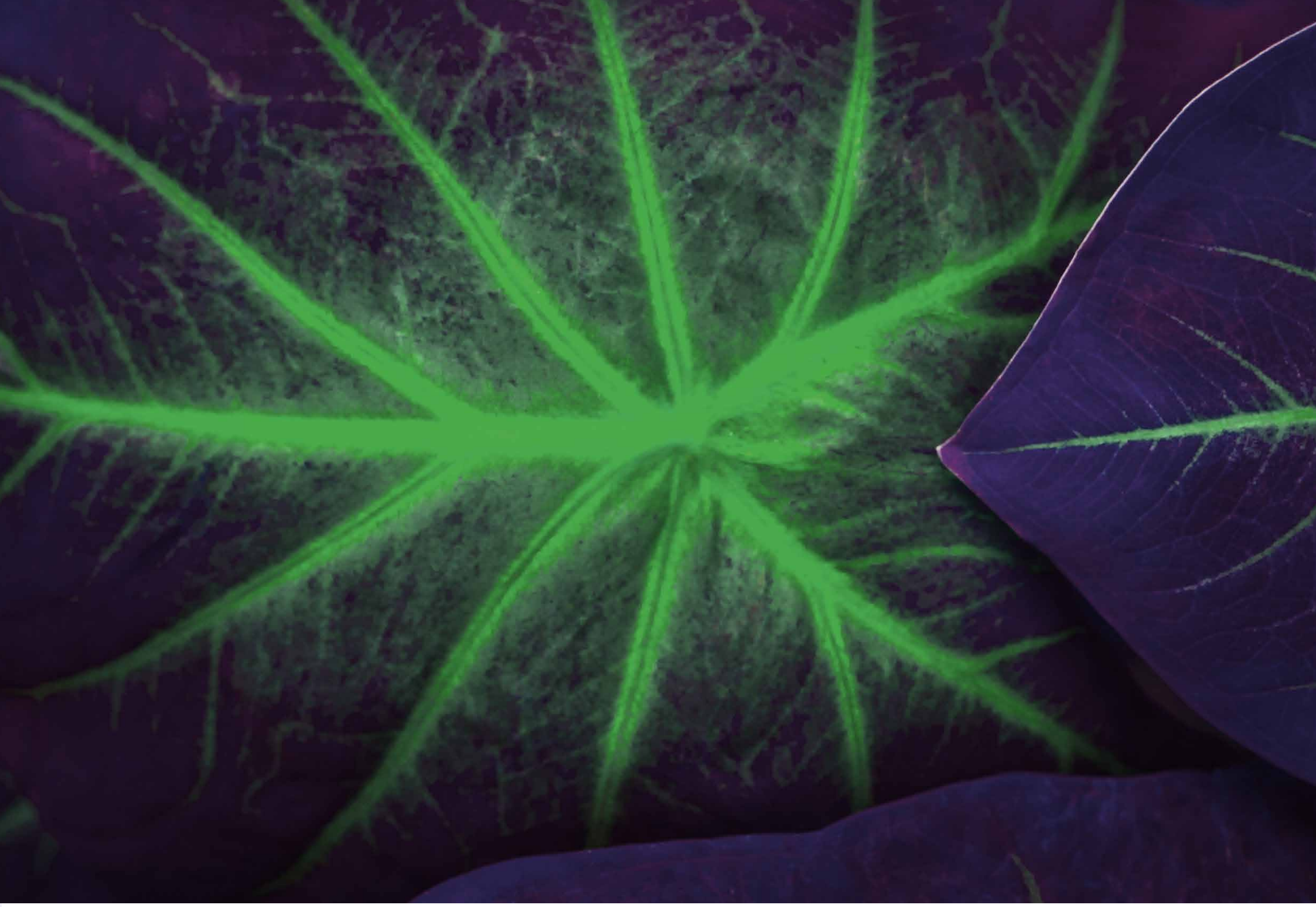
Leveraging nature co-design, the textile and fashion industries could address current productivity, environmental impact, supply chain resilience, and personalization challenges. Nature co-design has the potential to reshape the textile/fashion value chains, replacing millennia-old materials and decades-old chemical fibers with new ones co-designed by nature. At the same time, textile and fashion are a good example of how difficult reshaping whole value chains can be, and how important it is to approach such a transformation from an ecosystem point of view (Exhibit 20). While the potential of nature co-design is huge, the path to fully realize this potential will not always be easy. Business leaders must recognize this.

These are only two examples out of many, since the impact of nature co-design extends to those industries one would not even expect to be impacted by it. Among these industries are aerospace and defense, energy, building materials, and technology.

Exhibit 20: Nature co-design has the potential to disrupt the fashion industry



1. Algalife; 2. World Resources Institute; 3. Smartex
Source: Financing the Transformation in Fashion - Unlocking Investment to Scale Innovation, janvier 2020 BCG / Fashion for Good report, BCG et analyse Hello Tomorrow



Non-Reductionist Approach and Strong Ethical Framework Required

Two final considerations need to be included in any discussion around nature co-design: first, a non-reductionist approach to nature requires businesses and society to think differently; and second, a strong ethical framework is required to navigate the ambiguity of the future and manage risks.

Let's examine each consideration in detail.

Non-Reductionist Approach

Due to the intrinsic complexity of nature co-design, a non-reductionist approach is required. Biology is nonlinear, the whole being far more complex than the sum of its parts. As a result, nature co-design businesses will need more "biological" thinking and management, particularly when it comes to dealing with inherent complexity and lack of predictability in biology. This approach is even more important as we are building on top of the digital revolution, which is intrinsically reductionist and enabled by breaking down problems into parts (for example, applications or software tools) and aggregating them in a linear fashion.

Because they leverage forces that are intrinsic to the nanoscale, advanced materials also require a non-reductionist approach. Understanding material behavior at different scales becomes increasingly complex, and crucial to determine the properties of a material, which may be properties that are not found in nature. Nature co-design is not only nonlinear, but an unintended release of altered biology in nature, with all its consequences, can hardly be reversed. This also applies to advanced materials, where working at the nanoscale also means working at the scale of DNA and understanding the implications of that work is critical to avoid environmental, health, and safety risks. As a result, second- and third-order implications must be considered from the start.

The need to think biologically was already in place as businesses were becoming increasingly complex adaptive systems.[16] The rise of nature co-design accelerates this trend and brings it to a different level of urgency.

Ethical Considerations

Nature co-design teams will also face issues not previously considered from an ethics point of view, since for the first time, we are leveraging nature as an engineering and manufacturing platform. Teams will need to identify and mitigate risks related to new discoveries from the beginning of every project, considering the second- and third-order implications of their work on the environment and society.

Nature co-design covers a broad scope, but the area that will require the most ethical scrutiny is life sciences. The areas of concern that will need to be addressed include (but are not limited to) potential error(s), (un)intended misuse, unethical use(s) that could be passed onto future generations, and unintended consequences. These broader discussions are beyond the scope of this paper.[17] Institutions should drive the regulatory environment and lead the ethical discussion that will help navigate the ambiguity of the future and manage the risks related to nature co-design.

But institutions are not the only ones needing to play an active role in promoting the responsible use of the life sciences. Business leaders and corporations will also need to play an active role, regardless of industry, and proactively participate in the ethical and societal discussion. In some cases, business should even drive the debate. For example, a group of international scientists and thinkers have proposed to build a community to promote responsible research and address societal and ethical challenges.[18] These challenges will grow in importance.

Most importantly, corporations and business leaders will need to address the gap between the speed of scientific and technological progress and ethical and societal adoptions, since the former progresses exponentially while the latter evolve at a much slower pace. This is where businesses must play a leading role that cannot be delegated to institutions, as they will never be structurally able to address the issue.

Nature co-design requires an ethical compass at both corporate and team level, supported by a set of procedures that embed the right questions at the beginning of each project. These questions should explore the second- and third-order consequences of the project, not only the direct ones.

While business needs to play an active role on the ethical front, it is on the societal one that corporations and business leaders need to take an undisputed lead. They must imperatively assume this role from the very beginning, as past experiences have shown how difficult it can be to introduce scientific and technological changes that have a societal component.

Starting from the assumption that companies that embrace nature co-design adopt a genuinely generative mindset and not an exploitative one, corporations and business leaders will need to develop an authentic, transparent, and fact-based narrative to engage with society at large. The potential value to be created with nature co-design is immense, with positive benefits for the planet and beyond. At the same time, nature co-design comes with the responsibility of building a positive narrative and an open dialogue around benefits and advantages, dangers and downsides.

Nature co-design addresses areas like food, agriculture, health, fashion, environment – all of which have intimate impact on human lives. It is therefore important to address emotional as well as rational issues. Trying to convince the public with facts alone is not going to work, particularly when those facts will be beyond most people's scientific

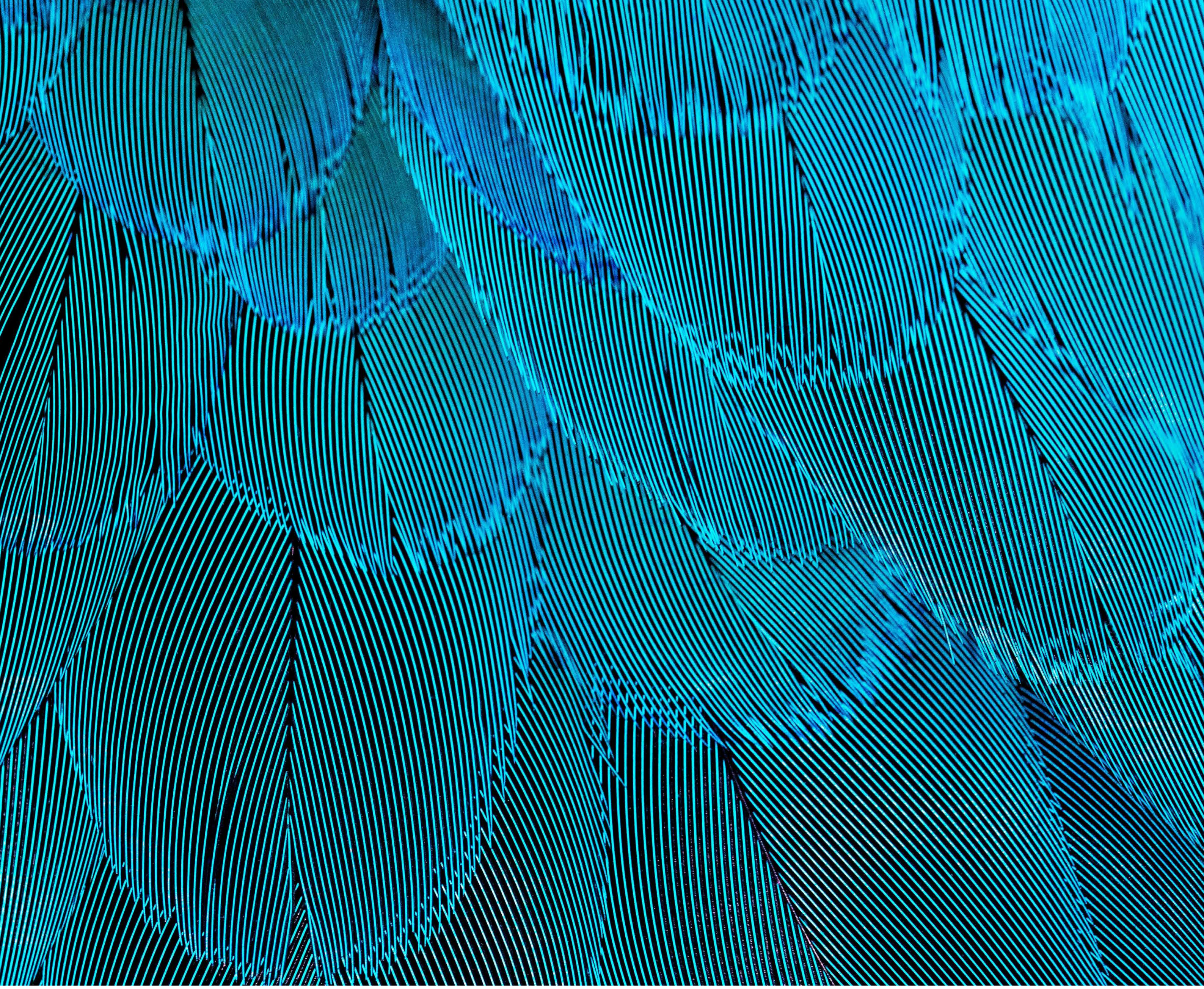
16. "Think Biologically: Messy Management for a Complex World," BCG article, July 2017.
17. Françoise Baylis, "Altered Inheritance: CRISPR and the Ethics of Human Genome Editing," Harvard University Press, September 2019.
18. "Multi-cellular engineered living systems: building a community around responsible research on emergence," International Society for Biofabrication, July 2019.

understanding. To be clear, we are not advocating for an artificial and "marketing-driven" narrative. We are advocating for a genuine dialogue and for the emergence of a new narrative. A good place to start is by expanding the conversation transparently, engaging with biodesigners, bioartists, chefs, and entertainers, leveraging their roles to push back boundaries while playing a key part in helping society absorb and react to novel ideas and technologies. Including more of society in these conversations is essential to avoid an unintended anti-science backlash.

An example of how this could look is the Mice Against Ticks project in Massachusetts, where scientists, thinkers, and the community have come together to eliminate Lyme disease through genome editing. The project has included numerous forums designed to educate the community and encourage participation, since the goal of the project would modify future generations of mice. The project aims to develop the smallest field trials with the least impact to minimize unintended consequences. This effort serves as one model, and businesses would do well to pay attention.

We have seen how societal opposition has slowed down the market introduction of first-generation biotechnology in food systems. Bridging the support for climate action, general willingness to allow innovation when it comes to health with the concerns deriving from all relevant world views is crucial. We also need a regulatory framework that equally keeps up with the pace of change propelling nature co-design and is generally welcoming or at least open-minded about new possibilities.

In this context, traditional life science companies might be advantaged by their capability to manage complex regulatory processes across wide geographies. Innovators and start-ups may attract enough capital to advance their ideas but need the regulatory bandwidth and production capability that larger partners can sometimes bring to accelerate market implementation. The BioNTech and Pfizer partnership to develop mRNA vaccines is a great example. Indeed, the ubiquity of the coronavirus pandemic offers a valuable opportunity of demonstrating the value of advanced technologies to society at large.



Conclusion

Nature co-design offers the opportunity to completely reinvent value chains and create value nets. To be successful, companies not only need to find ways to leverage the expanded option space but also create value nets by understanding the differences in economics and the need to start with a problem orientation and plan with imagination, as well as strengthening the role of scientific knowledge.

Forward-looking companies are already leveraging nature co-design to reinvent product design, manufacturing, and logistics.

As with deep tech, corporations cannot master nature co-design on their own. They need to create a whole ecosystem to succeed. Often, that ecosystem will include players outside a company's industry. More often, it will need them, however, to accelerate market implementation.

Forward-looking investors have already started shifting their portfolios to include nature co-design. This indicates a mentality shift, since investors need to commit significant amounts to succeed while staying patient with long investment horizons. Investors with biopharma experience may have an easier time investing in nature co-design even if they need to adapt to a different set of requirements: the risk profile will be different (than investing in therapeutics), the economics are different, and downstream activities are even more important. That said, some biotech investors will be hampered by the idea that biotechnology is a subset of the pharmaceutical industry. It is actually the other way around.

Governments are well-placed to support nature co-design innovation and should consider it as a core strategic pillar. They can play a crucial role in de-risking the initial stages of deep tech start-ups, embedding nature co-design in society, supporting the upscaling to the whole bioeconomy, and serving as connectors for the business ecosystem.

Nature co-design requires that governments and institutions continue to support and push pure research while helping build the infrastructure and defining standards that could lead to the creation of a distributed industrial base, inherently more resilient. Building this infrastructure will help early entrants avoid the chasm of death that comes with investing in that first production facility. Governments have a central role to play in boosting scientific education to ensure there is a pipeline of talent capable of harnessing these advanced technologies. In addition, governments and institutions play a crucial role in defining regulations and ethical norms.

In conclusion, corporations, investors, and governments represent the three major stakeholders that can drive and benefit from nature co-design and who have already begun preparing for the revolution. We have entered the era of nature co-design, and the future is bright. While much work remains, opportunities abound for those willing to lead.

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Acknowledgments

The Authors are grateful to Mickey McManus, Jérôme Moreau, Nicolas Eid, Laura Bogaert, Silvia Gelonch, Thibaut Willeman, Anne-Douce Coulin Kuhlmey, Yannick Vesters, Jean-Francois Bobier for the development of the content and the analyses. They thank Usman Chaudhry and Wendi Backler and the BCG Center for Innovation Analytics for the help in developing and analyzing the data. A special thank goes to Karl Schmieder (MessaginLab) for his support in structuring the content and writing. They are grateful to Liz Bolshaw (Kite Insights) for the writing support, and Martin Saive (Cartoonbase) for design and production support. And are thankful to Matthias Berninger (Bayer), John Cumbers (SynBioBeta), John Paschkewitz (DARPA), Alex Lorestani and Erin Kim (Geltor), Shara Ticku (C16 Biosciences), Jennifer Holmgren (LanzaTech), Andrew Hessel (Genome Project Write), Megan Palmer (Standford), David Michael (Anzu Partners), Andy Cooper (Liverpool University), Alvise Perosa and Carlo Bagnoli (Ca' Foscari – Venice University), Davide De Lucrezia (Doulix), Stephen Van Helden, Erica Carlisle and Michael Dulin (Zymergen), Christina Agapakis and Emilie Fitch (Ginkgo Bioworks), Gene Berdichevsky (Sila Nanotechnologies), Emmanuelle Martiano Rolland (Aqemia), Christoph Kreisbeck and Scott Healey (Kebotix), Aaike van Vugt (VSPARTICLE), Thomas Wolf (Plasmion), Amaël Cohades (CompPair) for their input and insights.

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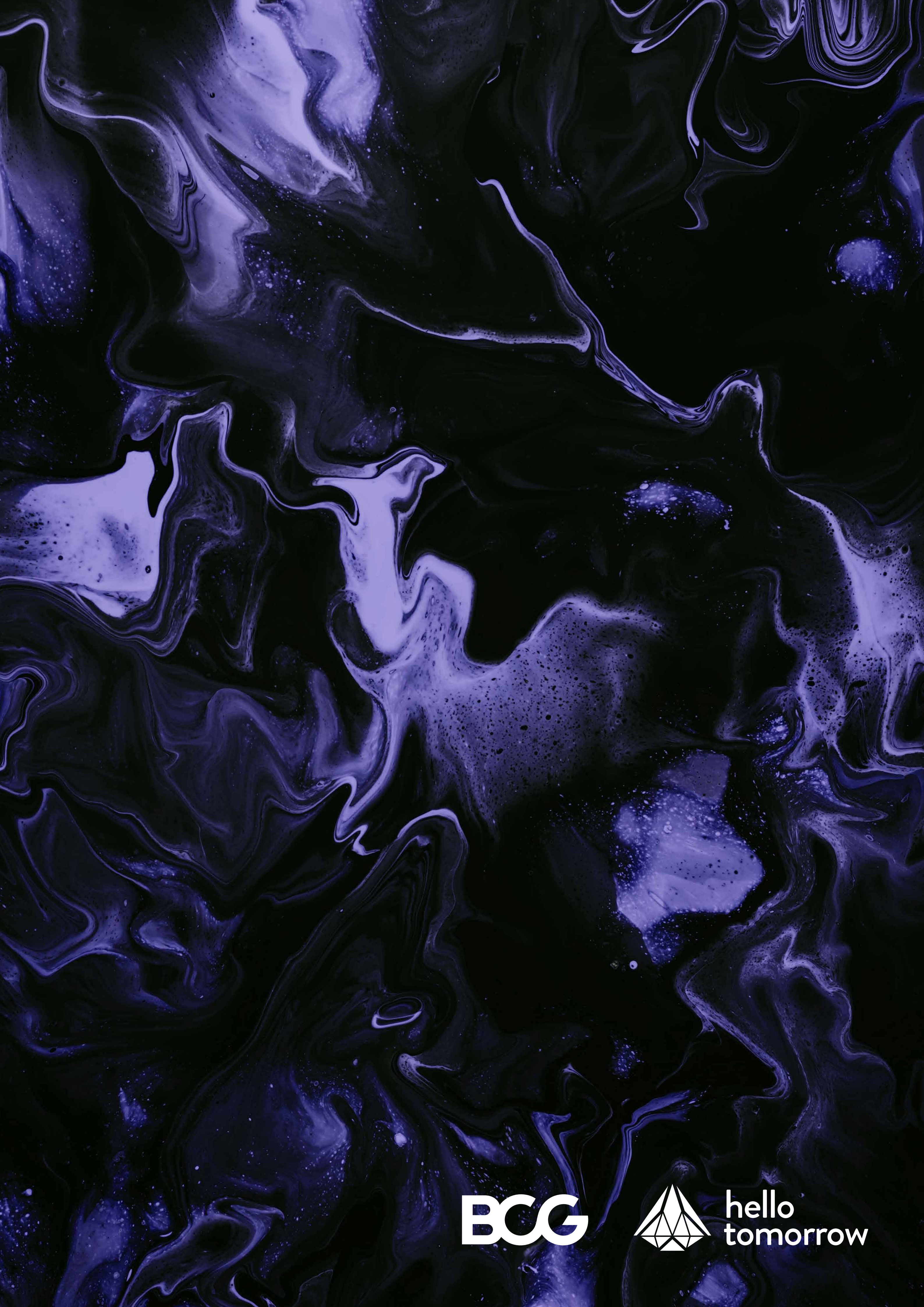

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