Investment Recipes

by AtonRā Partners

9 SEPTEMBER 2020

9 SEPTEMBER 2020

AtonRâ Partners

AtonRâ Partners SA
www.atonra.ch

research@atonra.ch
+41 22 906 16 16

7, rue de la Croix d'Or
1204 Geneva | Switzerland

On the Menu

SYNTHETIC BIOLOGY: A NEW ERA OF DESIGN AND CREATION

Synthetic Biology: A Revolutionary Tool For Biotechnology

Cells are becoming programmable

Synthetic Biology is a genetic engineering approach that manipulates the organisms' genomes using chemically synthetized DNA, for medical and industrial purposes. Synthetic Biology is a tool to unlock the unlimited opportunities of Biotechnology.

- Synthetic Biology has a wide-range of potential applications, including life science, chemicals, energy, and agriculture.
- Scientists are no longer limited to manipulate a single gene at a time; they now have the power to design entire genomes.

Synthetic Biology is accelerating at a fast pace

DNA synthesis methods originated 70 years ago. Since then, the number of Synthetic Biology companies and funding have grown at a remarkable rate. The huge potential of this market has attracted high government and private equity funding.

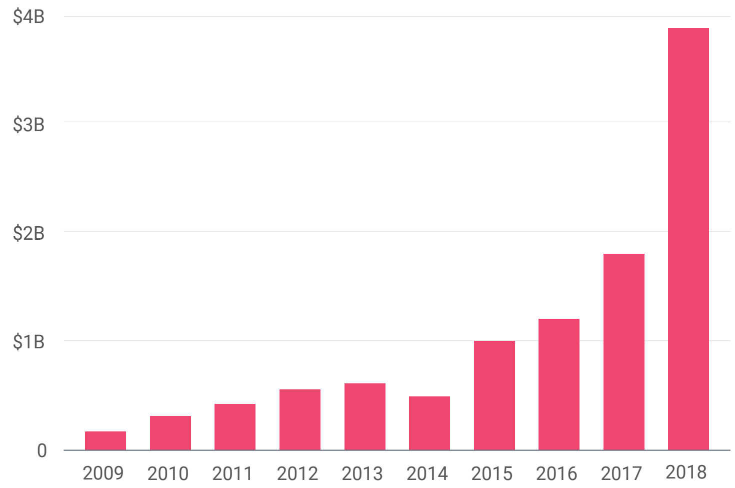
- In the past ten years, the synthetic biology industry rised over $12bn.
- China invested over $200mn from 2011 to 2015, and $500mn have been budgeted over 2018-2022.

From R&D to real products

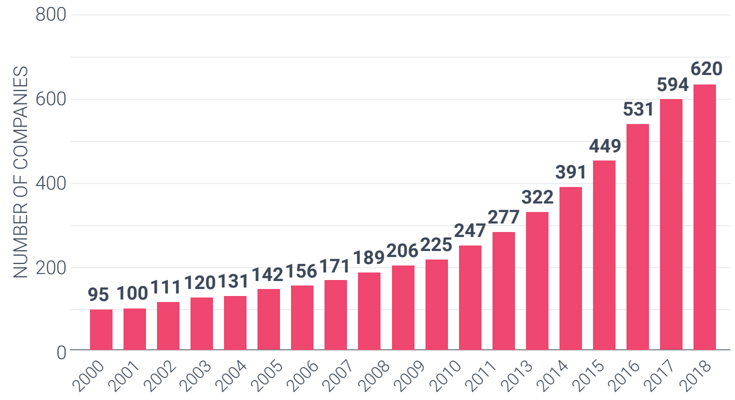
Synthetic Biology is now expanding from proof of concept projects to real-world applications. The approach has endless applications in several industries and may soon start to live up to its promises.

- According to IndustryARC, the global Synthetic Biology market size is estimated at ~$13bn in 2018 and is expected to grow at a CAGR of around 38% over 2019–2025.

FUNDING FOR SYNTHETIC BIOLOGY COMPANIES, 2009-2018



NEW SYNTHETIC BIOLOGY COMPANIES FORMED



SOURCE:
Synthetic Biology Has Raised $12.4 Billion. Here Are Five Sectors It Will Soon Disrupt.
Meet Eight Tech Titans Investing In Synthetic Biology

Biology Fundamentals: DNA To mRNA To Protein

DNA is the code that powers life

We all are made up of different types of cells. Each cell contains, in its DNA (deoxyribonucleic acid), the instructions that determine how it looks like and what it does. Cells of the same type join to generate a specific type of tissue, which in turns, organizes itself in a 3D structure with specific functions, called organ.

- The alphabet of the DNA's code is composed of only 4 elements (nucleotide bases): Adenine (A), Thymine (T), Guanine (G) and Cytosine (C).

From bases to DNA

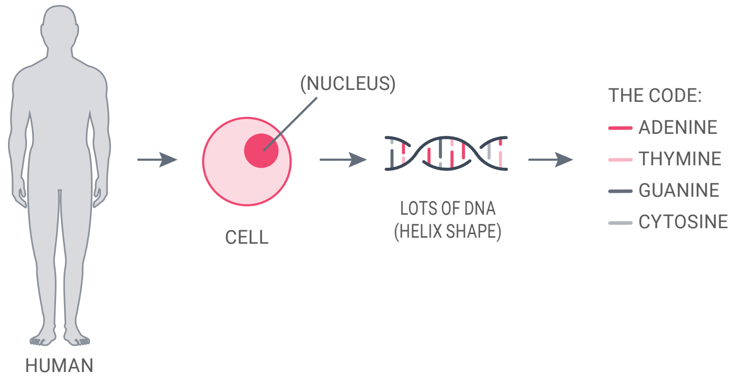
Each base is part of a so-called nucleotide (generated by the link of a sugar-phosphate and a base). Nucleotides connect to each other by the sugar-phosphate bone to form a single helix of DNA. Complementary bases (base-pairs or bp) link together, through hydrogen bonds, forming the double helix that we all are familiar with.

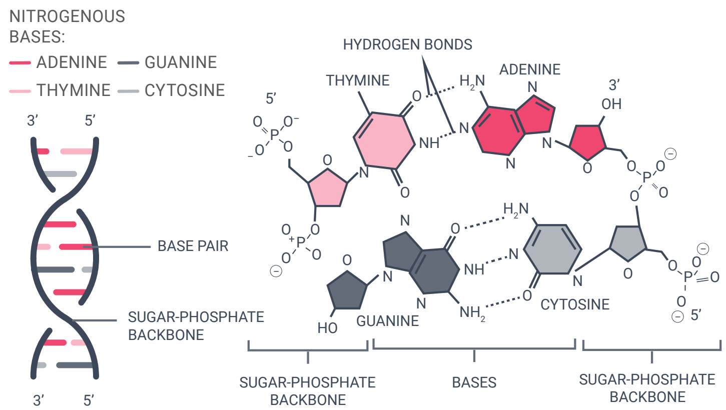
- Bases are complementary by pairs: A forms hydrogen bonds only with T while G will form hydrogen bonds only with C.

From genes to proteins

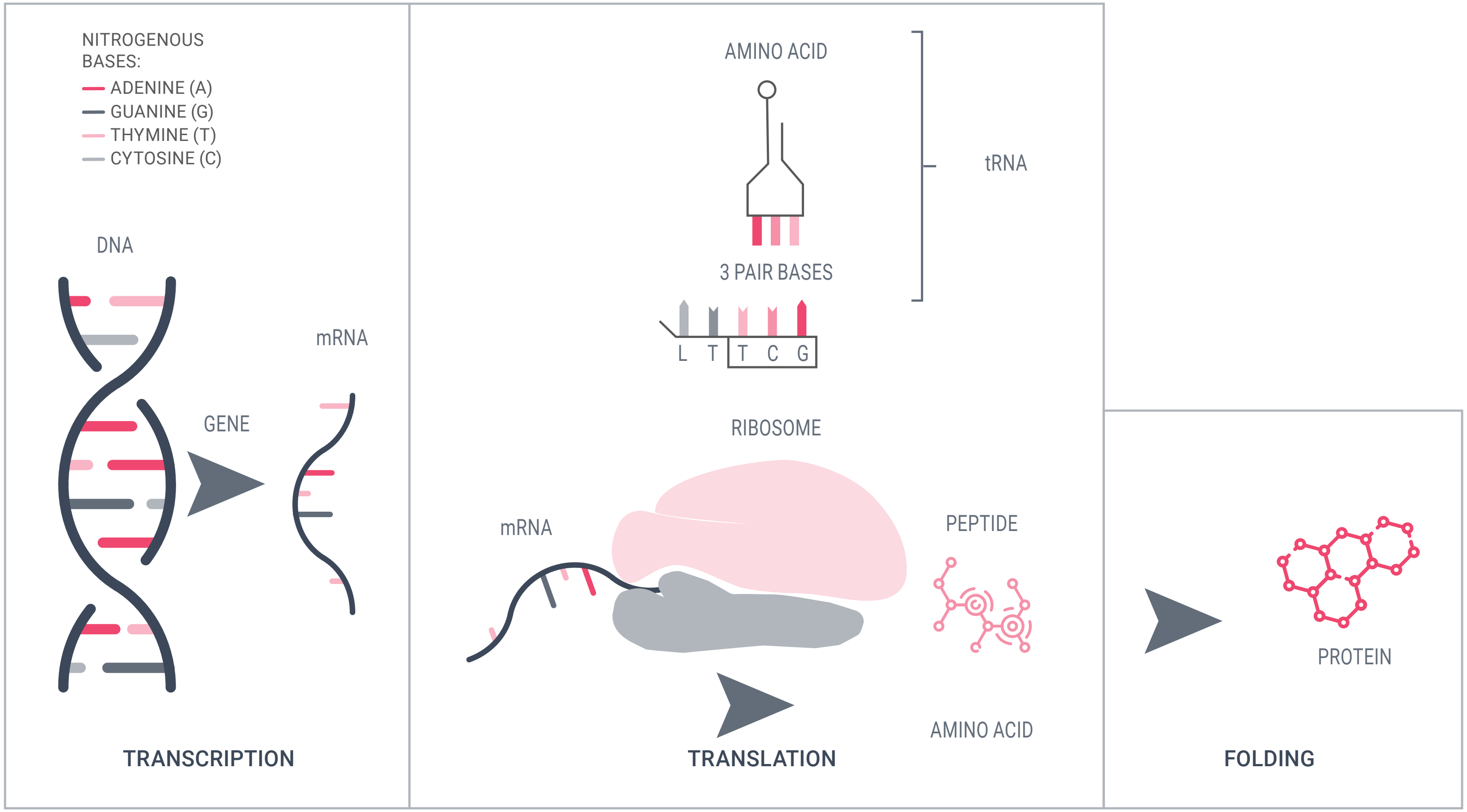
A sequence of nucleotide bases in a segment of DNA which encodes a specific functional protein is called gene. The mRNA will copy the information contained in the gene and carry it to ribosome for protein synthesis.

- The ribosome, together with the tRNA, will translate the information of the mRNA into a sequence of amminoacids, called peptide. Finally, the peptide will fold (assume a specific 3D structure) and become a protein.





Biology Fundamentals: DNA To mRNA To Protein



Biology Fundamentals: Gene Expression Explained

What makes us so different from a cat?

All the cells of our body have the same DNA; the same genes in the same order. Even the DNA of two humans or two distinct animal species is not so different. It is gene expression that makes a cell of our skin so different from that of our liver. And that makes us so different from a monkey, a cat or our neighbor.

- 99% of our genome is similar to that of another human being, 96% to that of a chimpanzee, 90% to that of a cat.

Gene expression

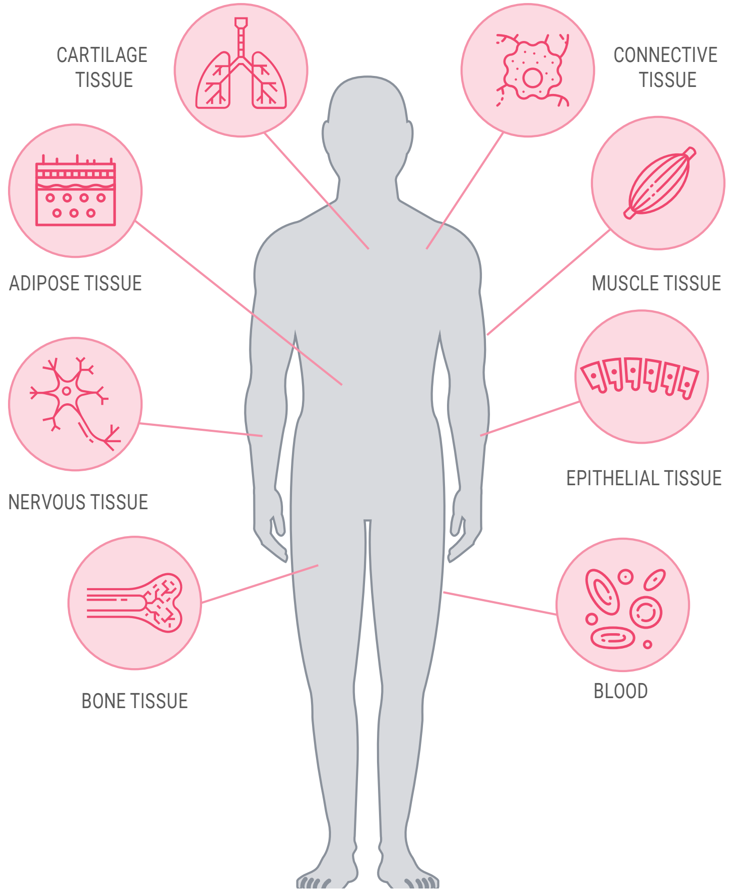
Gene expression is the process by which genes are activated or turned off. When a gene is activated it produces a protein. Gene expression causes the cell to differentiate, therefore, to become a specialized cell (with specific functions).

- Cells of different tissues (or different species) are different because they produce different proteins.

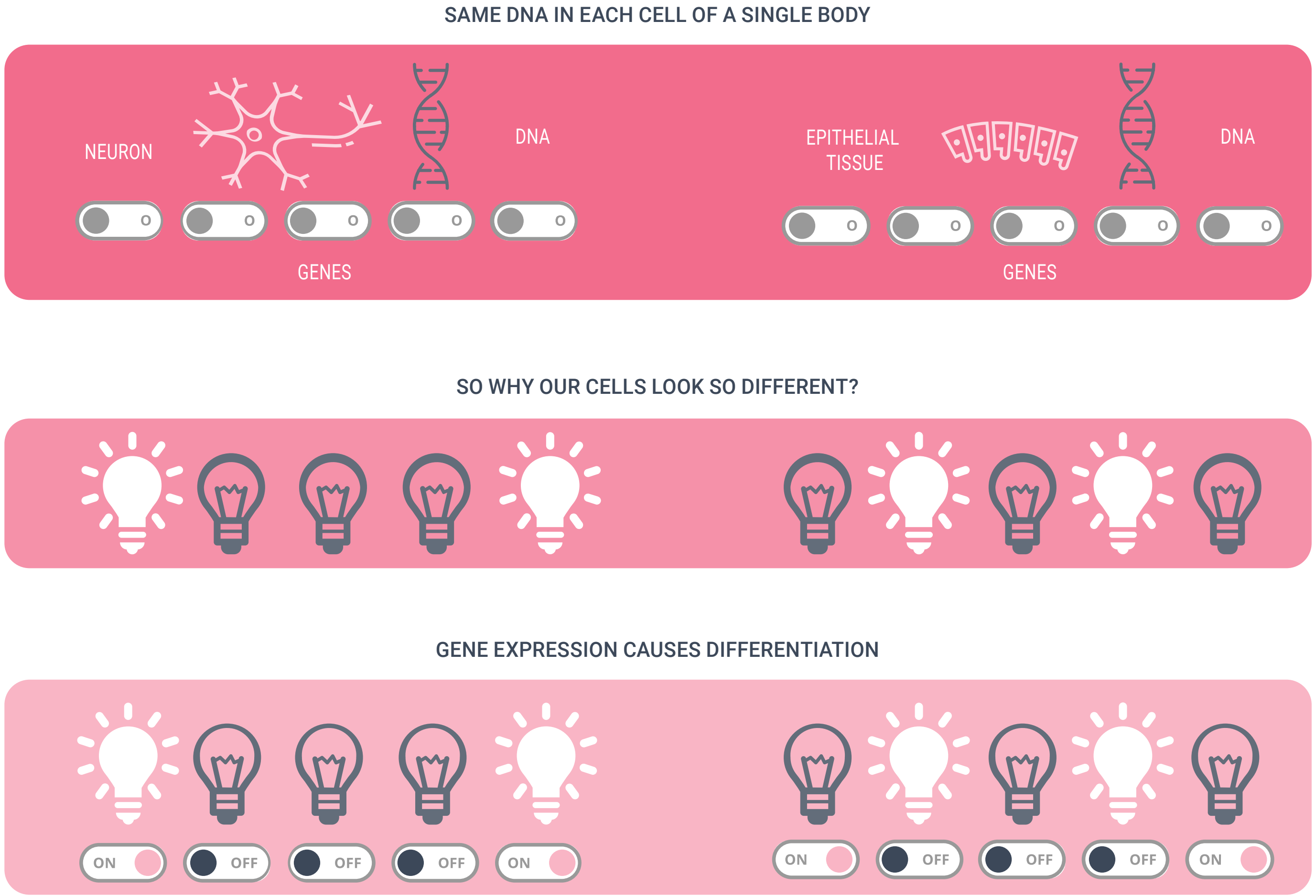
From Genetic Engineering to Synthetic Biology

Genetic Engineering involves the manipulation of a cell's genome, by either removing or introducing DNA, to control its output. Synthetic Biology uses artificially synthetized DNA.

- New DNA may also be obtained by isolating the genetic material from a living organism and copying it into another (recombinant DNA methods).
- Humans have directly and indirectly beed using biology to their own purposes for more than 10,000 years.



Biology Fundamentals: Gene Expression Explained



Synthetic Biology: Value Chain (1/2)

Enabling technologies: bioinformatics, microfluidics, sequencing, & semiconductors

Synthetic Biology profits from advancements in DNA sequencing, bioinformatics, semiconductors and microfluidics These fields have enabled the DNA synthesis to become more efficient and less expensive.

- Today's faster way to synthetize genes relies on a silicon-based platform that allows to reduce the use of chemical reactors while increasing throughput.
- Cheaper, faster sequencing allows the expansion of synthetic biology applications.

Core technologies: DNA synthesis & biofoundries

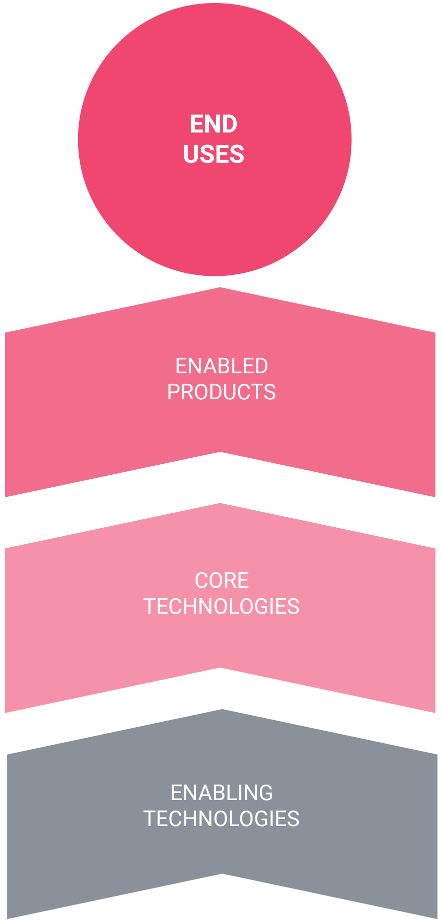
DNA synthesis and biofoundries (cell factories) are the two core technologies of Synthetic Biology where specific cells are used to produce the required output, by instructing them with appropriate, user-defined DNA.

- A close analogy is for synthetic DNA to be seen as a software, and cells are the computers that can run on the DNA software.

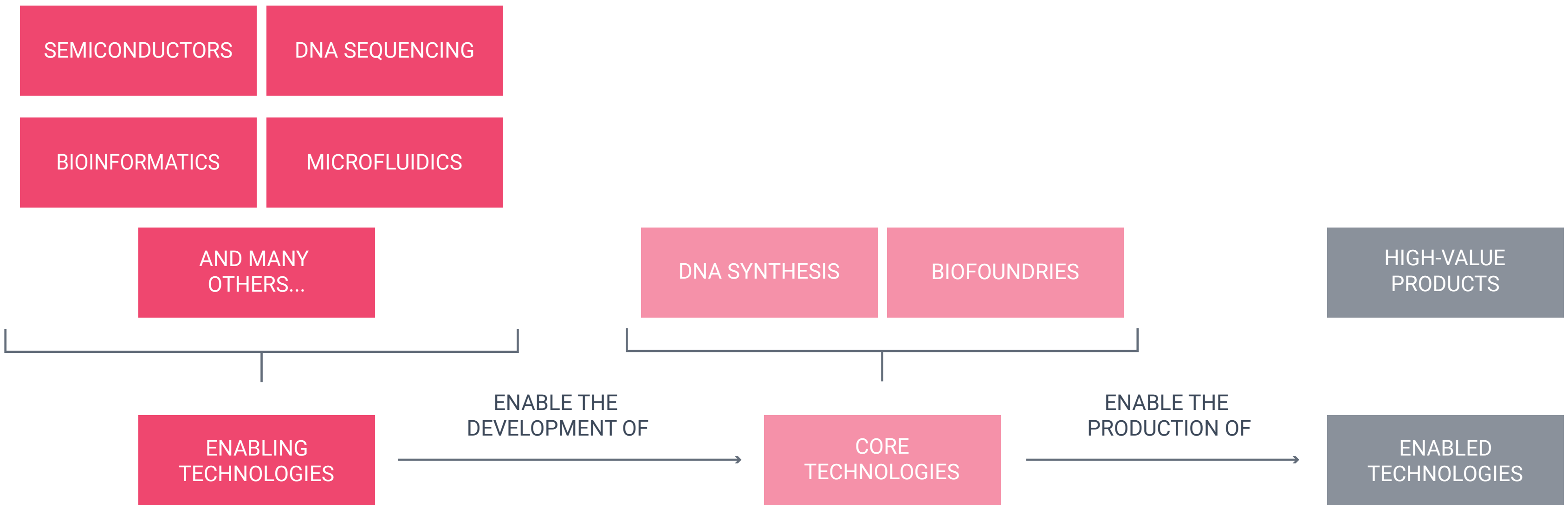
Enabled technologies: High-value products

Synthetic Biology may allow the creation of more efficient organisms through the introduction of synthetic genes; fish can be designed to breed twice as quickly as usual and apples can be engineered to not turn brown when bruised.

- Synthetic Biology finds applications in four main areas: healthcare, industrial, environment and agriculture.
- Synthetic Biology also provides an alternative to existing DNA data storage technologies.



Synthetic Biology: Value Chain (2/2)



Enabling Technologies Play A Key Role In Synthetic Biology Performance

Bioinformatics: a powerful tool to design new biological functions

Sequencing produces a huge amount of data that needs to be analyzed and stored. Bioinformatics allows to understand and organize information, design genes as well as synthtize biological systems.

- In 2016 Twist Bioscience, the leading gene synthesis manufacturer, acquired Desktop Genetics, a software company using AI to create CRISPR tools, and Genome Compiler, a software used to design DNA.

Microfluidics: bringing down costs

Microfluidics is the science of manipulating very small samples of liquids in very small channels (below the micron scale). Microfluidics reduces the use of reagents, decreasing the cost to sequence and synthetize DNA. Players in these fields are expanding through acquisitions and partnerships.

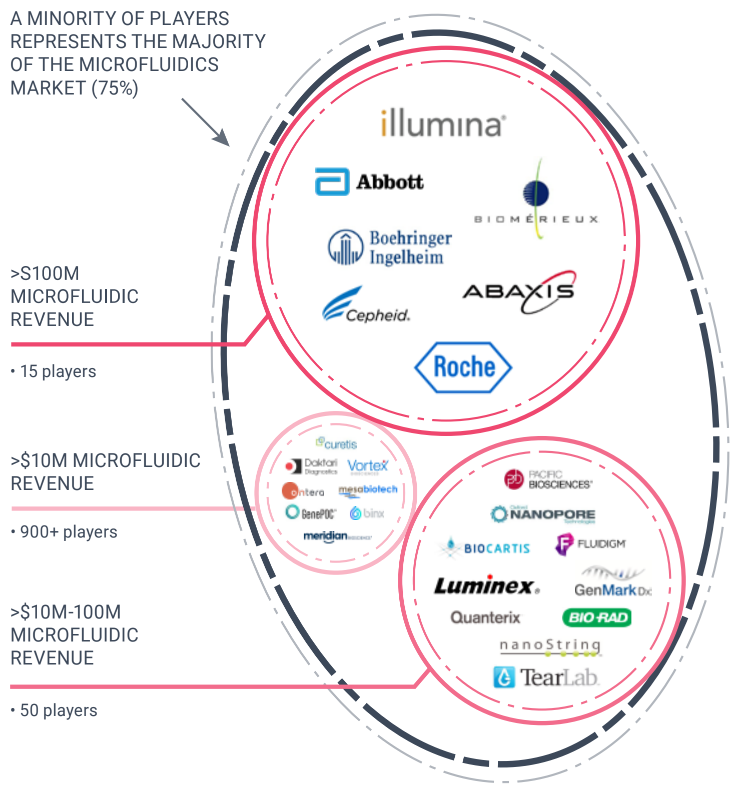
- 15 players represented 75% of the microfluidics market in 2019.
- Twist Bioscience has recently started collaborations with digital microfluidics developer Miroculus.

Semiconductors: scaling up synthetic biology

Synthetic Biology companies leverage on semiconductors to increase the capacity and performance of their gene synthesis platforms.

- Evonetix has partnered with Imec, a nanoelectronics research and innovation hub, to scale-up the DNA synthesis of its silicon-based platform.
- Twist Bioscience's Board of Directors includes semiconductors expert Nelson C. Chan.

MICROFLUIDIC PLAYERS* LANDSCAPE PER REVENUE



SOURCE:
Yole Developpement

A Dynamically Evolving Competitive Landscape

STRATEGIC MOVES WITHIN THE MICROFLUID SUPPLY CHAIN BETWEEN 2015 AND MAY 2017

LEGEND
- SUPPLY CHAIN:
  - BIG DIAGNOSTICS COMPANIES
  - DIAGNOSTICS COMPANIES
  - FABS
  - DESIGN, FLOW CONTROL

MOVE TYPES
- ACQUISITION (A ACQUIRED B)
- COLLABORATION
- SUPPLY AGREEMENT

SOURCE:
Yole Developpement

DNA Sequencing & Synthesis Go Hand In Hand

DNA sequencing empowers DNA synthesis

Sequencing technologies allow to read the precise order of each base within the DNA. Researchers exploit this to study the function of each gene, thus expanding the knowledge-base of biology.

- Sequencing is required to determine the best way to divide the whole gene into fragments that may be synthesized and assembled, as well as, to verify the accuracy of the generated sequence.

DNA synthesis empowers DNA sequencing

Short DNA sequences, called target enrichment probes, have been synthetized to accelerate the sequencing of specific spots in the DNA. Taget enrichment probes are particularly useful for diagnostic applications (genetic tests or liquid biopsy), where faster sequencing allows to provide results to patients more quickly.

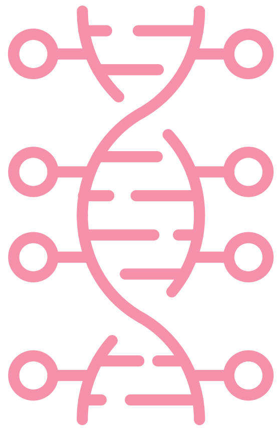
- Twist Bioscience has entered this market in 2018, leveraging its gene synthesis platform for the manufacturing of these probes.
- Target enrichment probes has an estimated market size of $500mn per year.

A one-stop solution

DNA sequencing and synthesis are complementary technologies enabling each other's applications. And as customers may find advantageous to have a single provider, many companies are providing a one-stop shop for such solutions.

- Genscript Biotech, Thermo Fisher and Eurofins offer DNA sequencing and synthesis services.

DNA SEQUENCING
"READ the precise order of nucleotides within a DNA"



DNA SYNTHESIS
"WRITE a DNA linking together the nucleotides"

SOURCE:
synthesis, Time for New DNA Synthesis and Sequencing Cost Curves

After The Ability To Read Came The Ability To Write

The next step is writing DNA

The Human Genome Project (HGP) finalized decoding the entire human DNA in 2003. Now, the Human Genome Project-Write (HGP-Write), launched in 2016, aims at synthetizing an entire human genome within 10 years.

- HGP-Write is expected to attract over $1bn in funding.
- The project has the potential to dramatically advance DNA synthesis technologies.

DNA sequencing has exceeded Moore's law

Similar to the drastic decline in the cost of sequencing, driven down by technological advancement and a large number of companies supplying this technology.

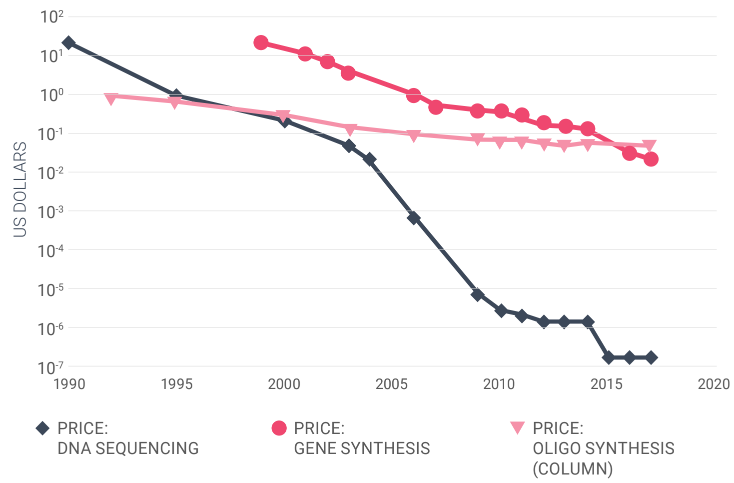
- Advanced DNA sequencing technology reduced the cost of sequencing a complete human genome from $3bn to less than $1,000 in just over a decade.

DNA synthesis cost still lags behind

Gene synthesis cost per base pair has dropped dramatically, but there is still a long way to go. To reach the same level of cost of sequencing (i.e. $1,000 per genome), synthesis cost should still fall by around 5 orders of magnitude.

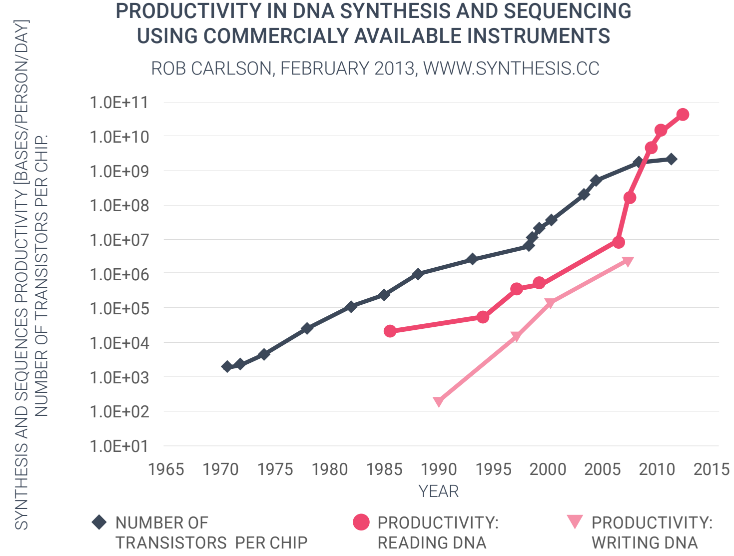
- Writing a whole human genome would cost between $300mn and 1.8bn, at the current rate of $0.1-$0.60 per base pair.

PRICE PER BASE OF DNA SEQUENCING AND SYNTHESIS (CIRCA 2017)



PRODUCTIVITY IN DNA SYNTHESIS AND SEQUENCING USING COMMERCIALY AVAILABLE INSTRUMENTS

ROB CARLSON, FEBRUARY 2013, WWW.SYNTHESIS.CC



SOURCE:
synthesis, Time for New DNA Synthesis and Sequencing Cost Curves

DNA Synthesis

DNA synthesis: a long history

The term "Synthetic Biology" was coined in 1974 when the possibility of making DNA in laboratory was first explored. Originally, DNA was manufactured by hand, now companies are using computers and robots making the process faster and cheaper.

- DNA synthesis begun in academic labs in the 1950s, machines capable of synthesising it letter by letter started to appear in the late 1980s, progressing into high-throughput methods in the 1990s.
- Most sequences up to 1k base pairs can be assembled in a standard molecular biology lab, while commercial gene synthesis providers routinely synthesize sequences over of 10k base pairs.

Two main approaches

DNA synthesis is the process by which nucleotides are linked together to create DNA strands. Synthetic Biology uses genes chemically synthesized from scratch that may or may not exist in nature.

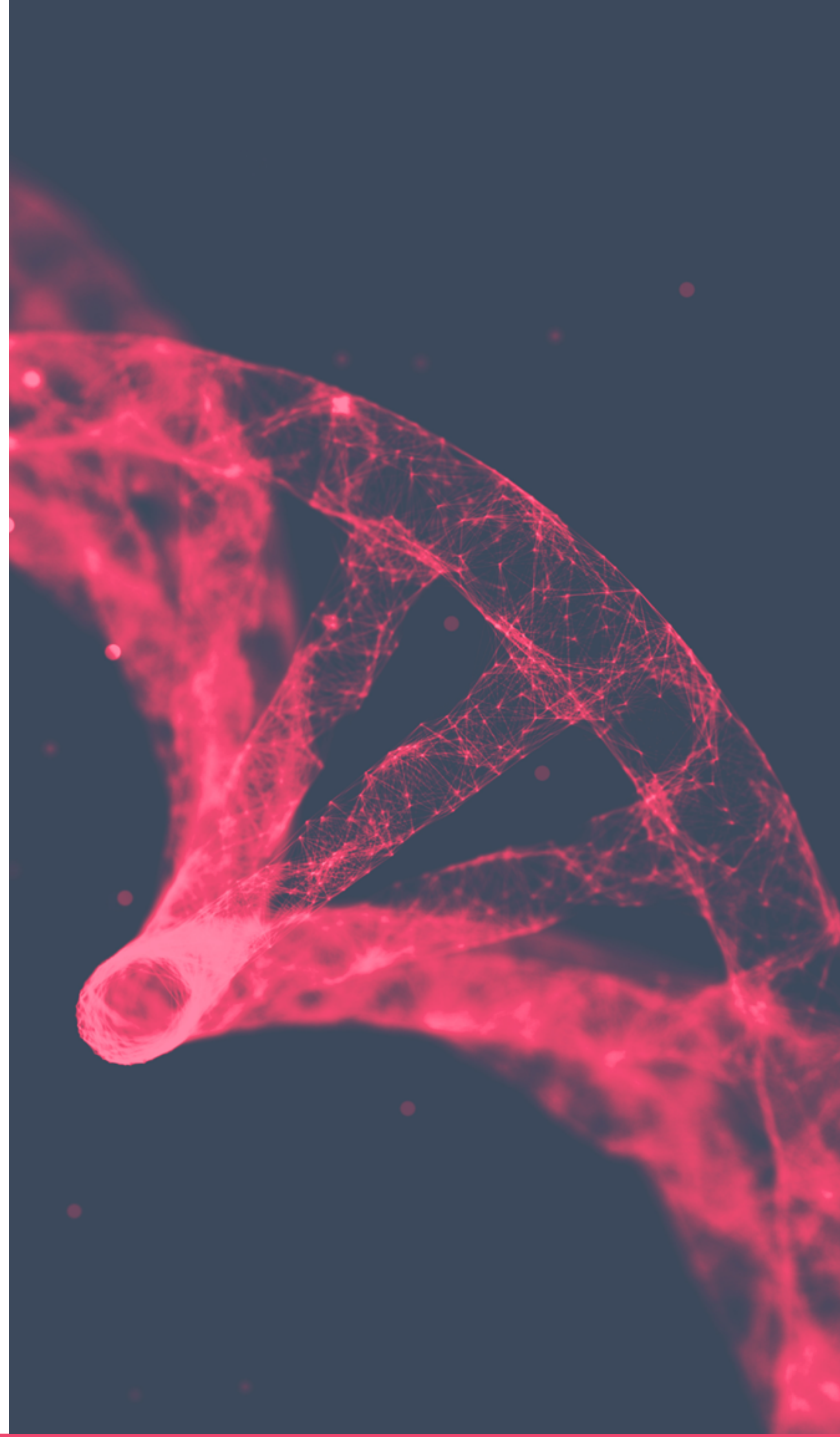
- Top-down approach aims to synthetize genes that already exist in nature to build functions in cells.
- Bottom-up approach aims to build genes and biological systems from scratch.

Order your DNA online!

Synthetic genes are becoming widely and easily available. Today it is possible to type the DNA sequence of interest into a computer (or copy it from a database) and order it over the internet.

- Twist Bioscience has launched an eCommerce platform, where customers can design and order genes online.

SOURCE:
[The Countries With The Highest Density Of Doctors]



Gene Synthesis Timeline

1950
DNA polymerase isolated from E. coli. Arthur Kornberg wins 1957 Nobel Prize.

1955
First DNA molecule synthesized when two thymidine nucleo-sides are joined by a phoshate link. Sir Alexander Todd wins 1957 Nobel Prize.

1967
DNA ligase is isolated and characterized by five independent laboratories.

1970
First synthesis of an enre gene, a 77 bp yeast tRNA, by Gobind Khorana's group.

1983
Polymerase chain reacon (PCR) is invented. Kary Mullis wins 1993 Nobel Prize.

1983
Caruthers and Maeucci invent phosphoramidit-eDNA synthesis.

1989
First automated oligonucleode synthesizer machines become commercially available.

1990
Improved assembly methods allow synthesis of increasingly long genes.

2003
First synthesis of an enre viral genome, that of phiX174 bacteriophage.

2004
Microchip- and microfuidics-based methods for high-throughput gene synthesis are first published.

2008
First complete synthesis of a bacterial genome.

2011
Sc2.0 project launched to build the first syntheeukaryoc genome.

Gene Synthesis Methods

Traditional methods have limits

Traditional molecular cloning require to cut and put an existing DNA sequence into a microorganism that duplicates spontaneously (cloning method) or into a Polymerase Chain Reaction (PCR) machine.

- DNA cloning (or cell cloning) obtains copies of the DNA fragment of interest using a virus and a bacterium.
- PCR creates DNA copies from just one original strand using polymerase enzymes, primers (small DNA sequences, complementary to the beginning or the end of the sequence to amplify) and multiple thermal cycles.

Replacing PCR and cloning with synthetic genes

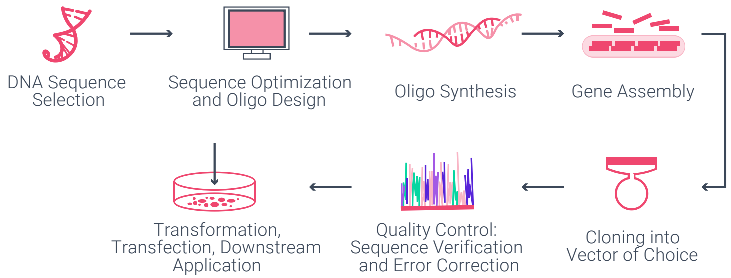
Gene synthesis involves the addition of nucleotides to create a single-stranded molecule, which then serves as the building block for the creation of a complementary strand.

- The single-stranded sequence is typically produced by synthesizing oligos made of 40-500 base pairs and then assembling them in the proper order.

Advantages over existing alternatives

Unlike DNA replication that occurs in cells or by PCR, the chemical synthesis of DNA does not require a pre-existing template. Therefore, gene synthesis allows to synthetize sequences that do not exist in nature.

- DNA synthesis is more straightforward, faster, and cheaper than using alternative methods.
- It is possible to make a completely synthetic double-stranded DNA molecule with no apparent size limits.



COMPARING GENE SYNTHESIS AND MOLECULAR CLONING

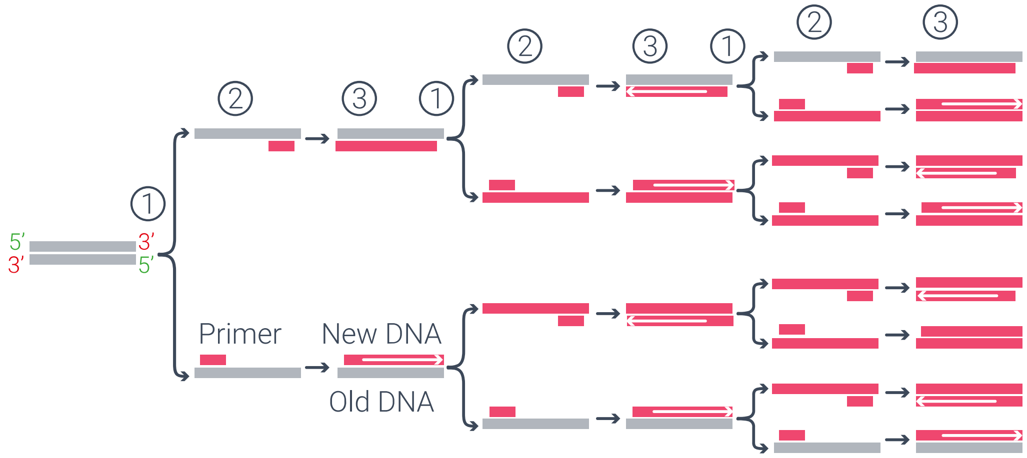
Technique	Features
Traditional Molecular Cloning	• limited to sequences that appear in nature • codon optimization is not feasible • time- and resource-intensive for end-user
Gene Synthesis of Bare DNA Fragments	• cystomizable sequence–no template required • error-prone; yields mixed pools of variants • lower cost for "quick and dirty" high-content, high-throughput screens
Gene Synthesis with Subcloning into a Plasmid Vector	• customizable sequence–no template required • uniformly accurate sequences from a clone • easy to verify complete sequence using primers that flank gene insert • fast and cost-effective

SOURCE:
Gene SynthesisHandbook

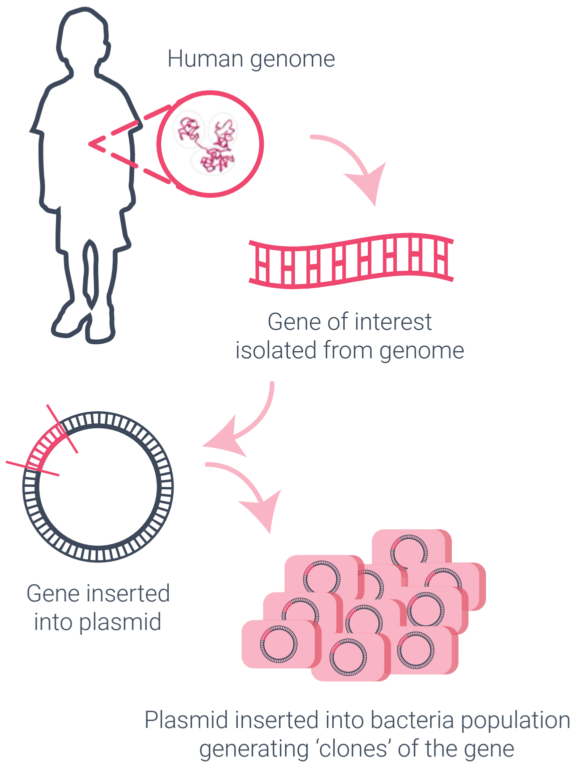
Alternatives To Gene Synthesis

PCR MACHINE EXPLAINED

1. DNA is heared to 90°–100°C; to seperate the two strands.
2. The is quickly cooled to 30°–65°C; to allow short single-strand primers to anneal to their complementary sequences.
3. The solution is heated to 60°–70°C; DNA polymerasa synthesizes new DNA strands, creating two new, double-stranded DNA molecules.
4. The entire cycle is repeated. Each time the cycle is repeated, the amount of target DNA doubles.



MOLECULAR CLONING EXPLAINED



SOURCE:
The Biotechnology Revolution: PCR and the Use of Reverse Transcriptase to Clone Expressed Genes

Core Technologies (1/2)

Two main technologies

There are basically two methods for oligonucleotides synthesis: phosphoramidite column-based synthesis and microarray synthesis.

- The first involves synthesizing individual oligonucleotides in small columns.
- In the latter, different kinds of oligonucleotides are synthesized in different specific parts of the chips, called assembly pools, which are then amplified and finally assembled into the finished product.

Phosphorilamidite column-based synthesis

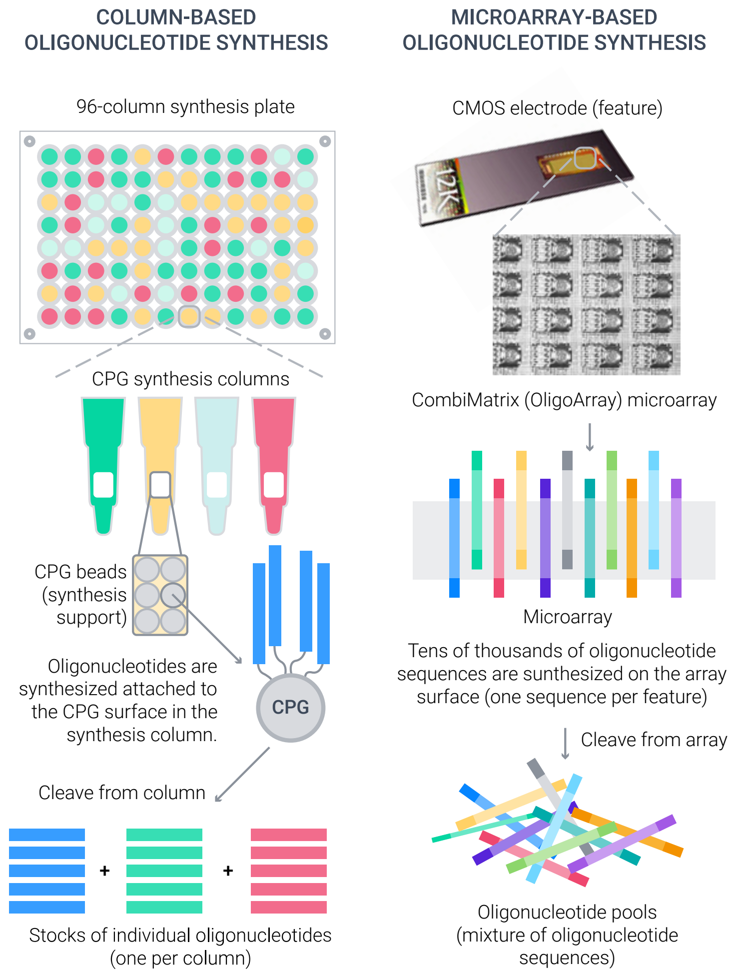
A small volume of solution is processed in a column full of chemicals. The oligos are synthesized through a four steps process, repeated over a 96-wells plate. The 96 oligos are then removed from the plate, amplified, and then assembled into one gene using enzymes. The gene is then inserted into bacteria (cloned) to produce billions of copies and make it available for further use.

- The four steps are: de-blocking, coupling, capping, and oxidation.
- This synthesis procedure evolved to the 96-well plate method already in 1995.

Column-based synthesis's limits

The primary advantage of this method is the high accuracy, but it comes at a high cost and low output.

- Cloning is an extended, expensive and time-consuming process (generally takings ~10 business days to complete).
- The technique requires the use of acetonitrile, the most expensive bulk reagent.



SOURCE:
Gene SynthesisHandbook

Core Technologies (2/2)

Microarrays

Since their inception in 1990, microarrays (also called chip-based DNA synthesis) have dramatically revolutionized genomics through massive parallelism and automation. In this method, researchers take a flat surface made of either plastic or glass and directly synthesize DNA on it in discrete locations.

- Column-based method allows to obtain 1 gene from 96 oligonucleotides. With microarrays it is possible to obtain almost 96 genes from 10,000 oligonucleotides.

Microarray synthesis vs column-based synthesis

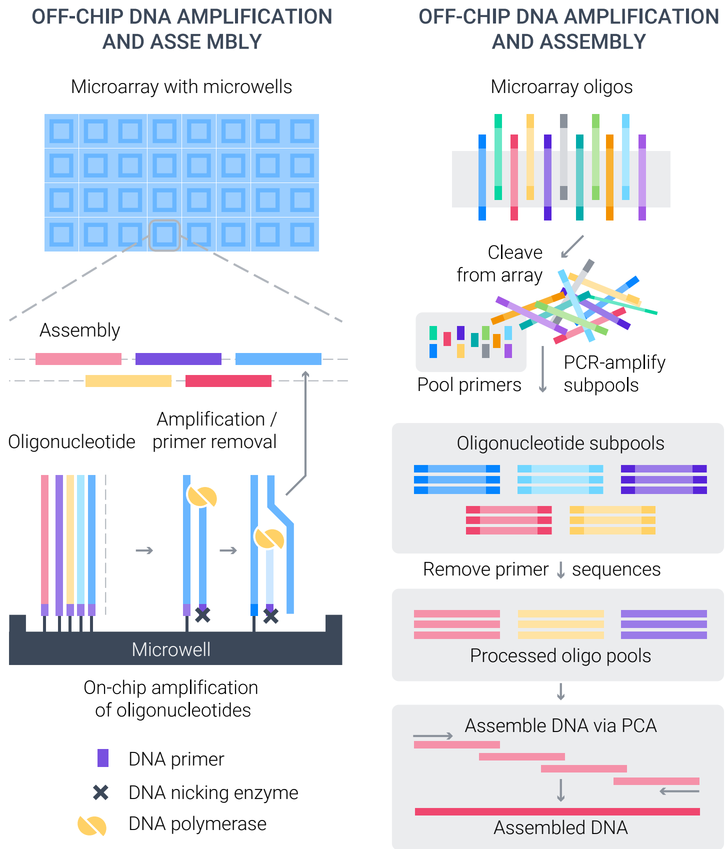
Microarray is cheaper than column-based synthesis because the smaller diameter of capillaries reduces significantly reagent volumes. In addition, it can yield a larger amount of the target gene in a shorter turnaround time, although this comes at a cost in terms of accuracy.

- Microarray costs on average $0.09 per pb ($0.001 for large volumes) while column-based ranges $0.15-$2.00 per pb.
- Error rates are 1 in ~300 pb for column-based; 1 in ~200 pb for microarray

Sylicon-based synthesis platforms

Using a silicon chip, it is possible to miniaturize the platfrom, requiring even lower volumes of reagents, which coupled with high automation, has the potential to dramatically reduce costs and increase production per base pair of DNA.

- Twist Bioscience's microarrays allow to obtain 9,600 genes from 1mn oligos with turnaround times of 7 to 9 days and an error rate of about 1 in ~600 pb
- Cost of $0,07 per bp for genes up to 1800 pb compared to $0.15—$2.00 per bp for the main competitors.



SYNTHESIS AND ASSEMBLY COMPARISION

	96-well Plate	Microarray	TWIST
Amount of DNA	Too much (waste) Nano-mol	Too little (amplification) <Femto-mol	Right amount (no amplification, no waste) Pico-mol
DNA processing	Pooling required	De-pooling required	No pooling No de-pooling
Genes per 96-well	1	96	9,600

SOURCE:
Synthetic DNA Synthesis and Assembly: Putting the Synthetic in Synthetic Biology

Biofoundries (1/2)

Turning cells into factories

Companies are reprogramming microbes using synthetic genes. Synthetic DNA, encoding enzymes and precursors, are introduced into the organisms' genome. The microorganisms consume the feedstock and build the product's precursors (e.g., fatty acids, polyamines, and proteins), and finally, the enzymes convert the precursor into the desired product.

- Yeasts and bacteria are commonly used to mass produce multiple industrial products, while mammalian cells are used for therapeutics.

Biology is the most advanced manufacturing platform

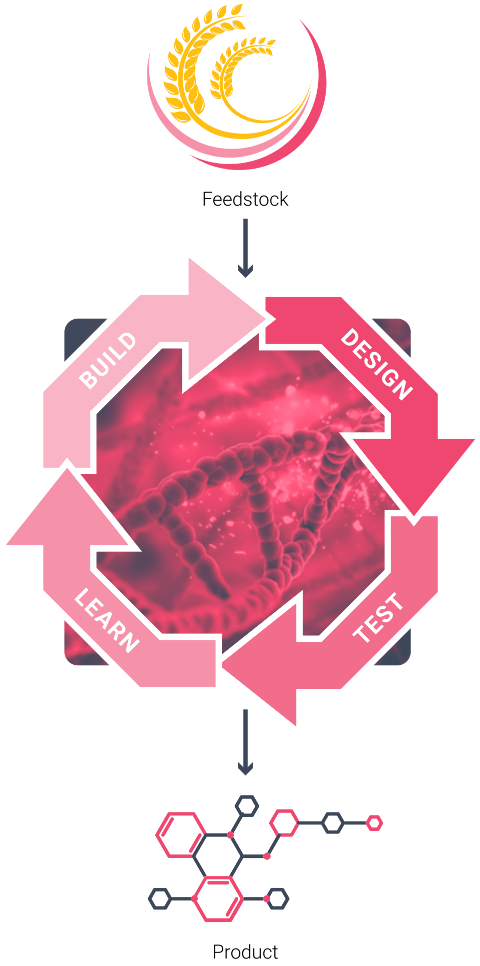
Cellular reprogramming depends heavily on the ability to efficiently synthetize and sequence the DNA. Unlocking the metabolic pathways of the microbial hosts will open the doors to wide range of novel applications such as the production of medicines, bioplastics, biofuels and others.

- DNA sequencing technologies are being used to generate libraries of genes, as well as to verify the appropriate construction of engineered organisms.

CRISPR/Cas tools accelerate the creation of cell factories

CRISPR/Cas is a novel one-step, precise, easier and faster genome editing technique that relies on RNA-guided cleavage of the target DNA by CRISPR-associated endonuclease (Cas).

- A major advantage of CRISPR-Cas tools is the simultaneous introduction of multiple genetic variants.
- CRISPR/Cas has been successfully applied in various groups of organism such as bacteria, E. coli, S. cerevisiae, fungus, Caenorhabditis elegans etc.



SOURCE:
The renaissance of yeasts as microbial factories in the modern age of biomanufacturing

Selected List Of Biomolecules Produced In CRISPR-Cas Modified Cell Factories

SUMMARY OF CRISPR/CAS-MEDIATED PRODUCTION OF BIOMOLECULES IN MICROBES

Host	Strategy	Biomolecules
Escherichia coli	Modification in the 50 UTR region of gltA using CRISPR/Cas9	n-Butanol
Escherichia coli	CRISPRi mediated balancing of mevalonate pathway	Terpenoid
Escherichia coli	One-step large integration of metabolic pathway using CRISPR/Cas9	Isobutanol
Escherichia coli	Increasing metabolic flux using a combination of CRISPR and CRISPRi tool	1,4-Butanediol
Escherichia coli	CRISPR enabled trackable genome engineering (CREATE) for generating ribosome-binding sites library for enhancing translational rates	Isopropanol
Schizosaccharomyces pombe	CRISPR/Cas9 led disruption of pyruvate decarboxylases, L-LDH, a minor alcohol dehydrogenase, and insertion of acetaldehyde dehydrogenase enzymes (MhpF and EutE)	D-Lactic acid
Saccharomyces cerevisiae	Combinatorial engineering based on CRISPR led transcriptional activation, transcriptional, interference, and gene deletion (CRISPR-AID)	b-Carotene
Aspergillus fumigatus	Single nucleotide insertion in the polyketide synthase gene of nonproducing strain using CRISPR/Cas9	Trypacidin
Clostridium ljungdahlii	Precise deletions of pta, adhE1, ctf, and pyre genes using CRISPR/Cas9 for conversion of single carbon gas (CO and CO2)	Ethanol
Corynebacterium glutamicum	CRISPRi mediated repression of pgi and pck genes	L-Lysine and L-glutamate

SOURCE:
Chapter 6 - A CRISPR Technology and Biomolecule Production by Synthetic Biology Approach

Biofoundries (2/2)

Biofoundries require a three-step process

Many companies are now genetically-engineering microbes to manufacture a massive range of goods more efficiently and sustainably. The production of those goods requires a three-step process: the identification of the product to create; the design of the microbe that will manufacture the product; and the production at scale.

- Production still relies on the well-known, age-old fermentation process (the same used to make beer or cheese).

Two unicorns in the landscape with different approaches

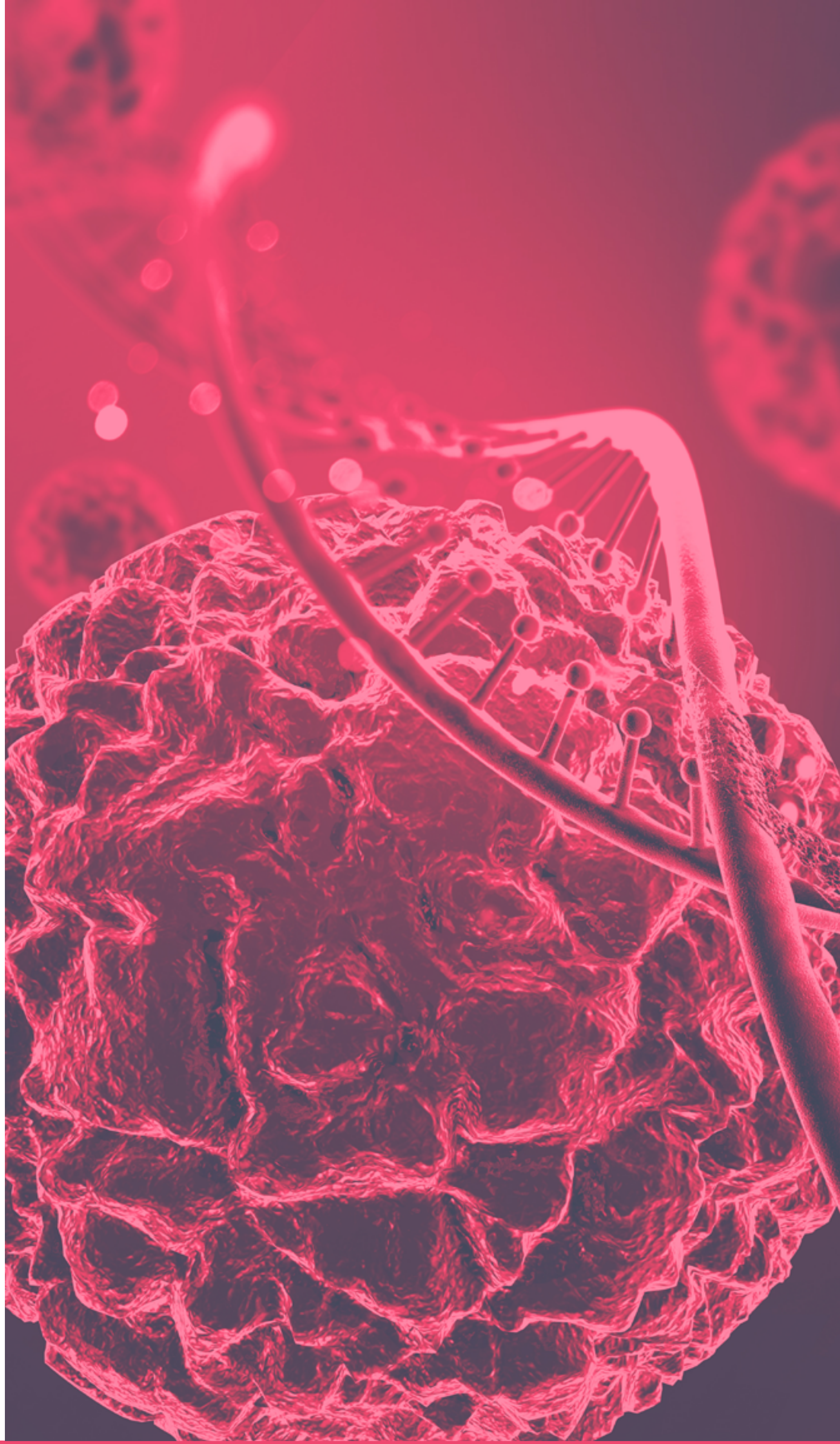
Two main players, Ginkgo Bioworks and Zymergen, aim to scale the process of organism engineering by using machine-learning algorithms that help design potential microbes for customers across multiple markets. Despite their shared mission, they follow different approaches.

- Zymergen has built a database for the discovery of totally novel substances and has a network of partners to produce the end-product "in-house".
- Ginkgo has concentrated its focus on finding better means to manufacture already existing substances.

Vertical integration: bringing DNA synthesis capacity in-house

DNA synthesis companies represent an interesting target for these players. Economies of scale are still crucial, so buying in bulk or having the technology in-house helps reduce costs and accelerates production times.

- In 2017 Ginkgo Bioworks acquired the DNA synthesis company Gen9 and continues to buy large quantities of DNA from Twist Bioscience.
- Zymergen and peers may follow Ginkgo's move and bring synthesis capabilities in-house.



Synthetic Biology Applications (1/2)

Healthcare industry

Synthetic Biology has the potential to improve health by enabling the synthesis of viral genomes producing safer, more effective vaccines, engineering novel enzymes that fight cancer, and replacing defective genes with healthy ones.

- Engineered yeast with synthetic genes has been used to produce artemisinin, an anti-malarial compound, faster and at a lower price.
- CytoSeek aims to improve CAR T-cell therapies, where a patient's own T cells are engineered to fight cancer.

Consumer goods, chemicals and materials

More sustainable consumer goods may be produced by using Synthetic Biology, as classical petro-chemicals are replaced with bio-synthetic materials.

- Bolt Threads will use synthetically produced spider silk as a key ingredient of a skin care cream.
- Ecovative has partnered with IKEA and Dell to deliver bio-synthetic derived packaging material.
- Ginkgo even reproduced the perfume of an extinct mountain hibiscus flower.

Environmental industry

Synthetic Biology has the potential to clean up the environment by producing enzymes that break down pollutants in the soil, air and water.

- Clothes can be washed with enzymes that breakdown organic materials in cold water, decreasing the use of electricity and producing fewer greenhouse gases.
- Joule has engineered bacteria to convert CO2 into fuels in a single-step, continuous process.

Synthetic Biology Applications (2/2)

Agriculture & Food

Synthetic Biology has the potential to improve crop yield, reduce vulnerability to common pests and plant diseases, improve food nutritional values, and help limit the use of chemicals and fertilizers.

- Pivot Bio allows to fertilize crops without the use of polluting chemicals.
- Finless Foods and Memphis Meats grow animals' cells without the animals.
- Codexis develops zero-calorie sweeteners and enzymes for food and beverage.

DNA storage: more bytes than starts in the sky

In 2025 we will have more bytes than the stars in the observable universe. As synthetic DNA has become more affordable and accessible, academic institutions and technology firms are looking at ways of using DNA to store digital data.

- 90% of all the data in the world was created in the last two years, amounting to nearly 2.5 quintillions (2.5*1018) bytes generated each day.
- In 2025 we expect to have 163 zettabytes* (163*10^21) of data per year, enough to fill the memory of 1.2 trillion iPhones.

DNA storage

DNA-based storage systems requires a huge amount of synthetic DNA to work. DNA synthesis must become more affordable, robust, and scalable to really enable large scale application, but prototypes are already in the making.

- Twist Bioscience's second-biggest customer, after Ginkgo Bioworks, is Microsoft, with whom they have partnered to develop the first DNA computer.

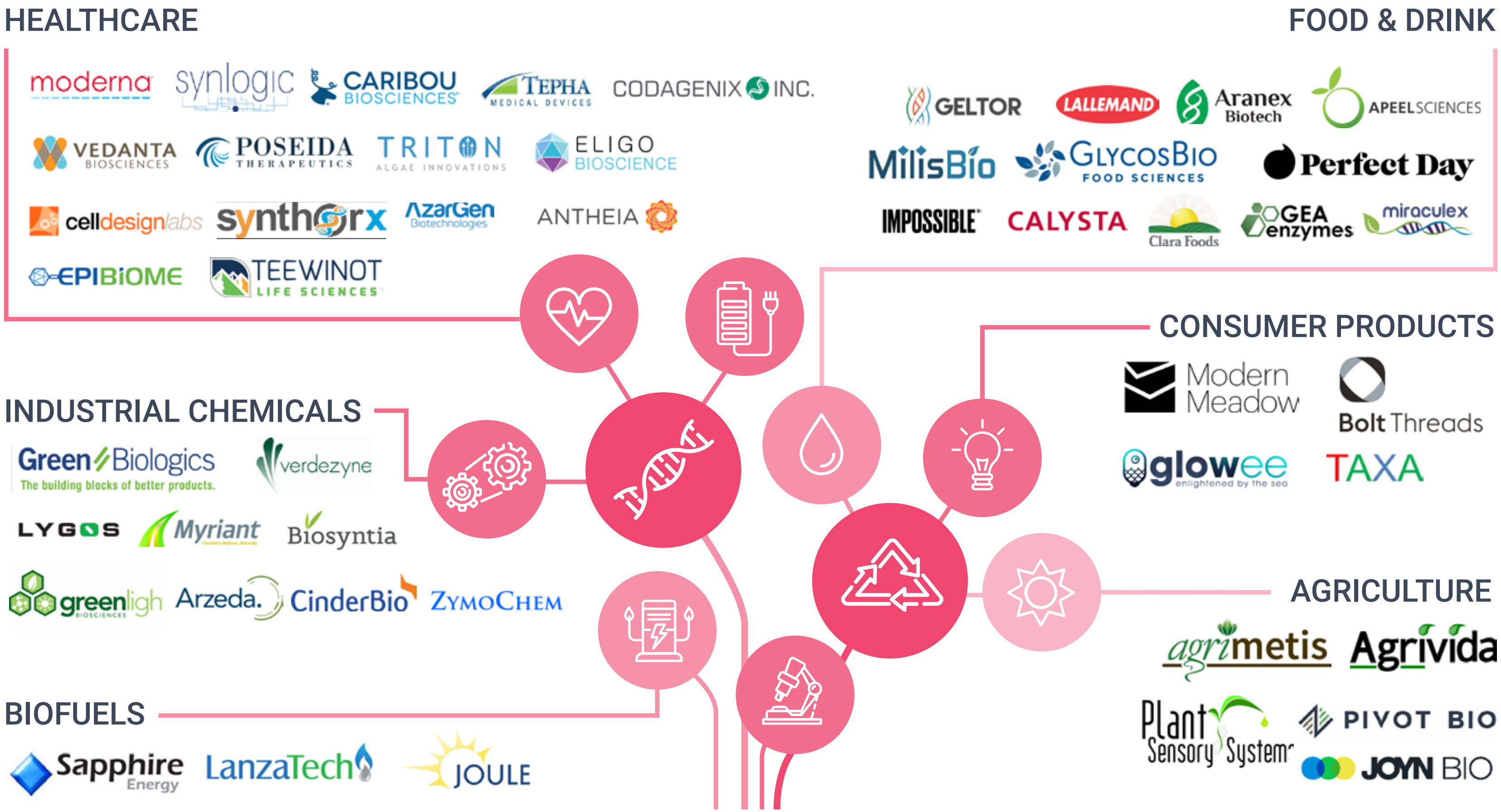
COMPARISON OF DATA STORAGE TECHNOLOGIES

	Capacity	Access Time	Retainability
SSD Flash	0.5 ~ 1 Terabyte	µsec	Months~Year
HDD	1 ~ 10 Terabytes	10 msec	5~10 Years
Magnetics	100x Terabytes	Minutes	9,10~50 Years
DNA	Peta ~ Exabytes	Hours~Days	Centuries~Millenia

Synthetic Biology – Players' Overview By Segment

Microfluidics	Bioinformatics	DNA sequencing	DNA synthesis	Biofoundries	High-value products
Luminex (LMNX US)	Google (GOOGL US)	Illumina (ILMN US)	Twist Bioscience (TWST US)	Ginkgo Bioworks (not listed)	Geen Biotechnology (not listed)
10x Genomics (TXG US)	Microsoft (MSFT US)	Thermo Fisher (TMO US)	Genscript Biotech (1548 KH)	Zymergen (not listed)	Moderna (MRNA US)
Thermo Fisher (TMO US)	IBM (IBM US)	Roche (ROG SW)	NanoString Technologies (NSTG US)	Genomatica (not listed)	Synlogic (SYBX US)
Illumina (ILMN US)	Illumina (ILMN US)	BGI Genomics (300676 CH)	Brooks Automation (BRKS US)	Conagen (not listed)	Caribou Bioscience (not listed)
Roche Holdings AG (ROG SW)	Golden Helix (not listed)	Qiagen (QGEN US)	Danaher (DHR US)	Arzeda (not listed)	Geltor (not listed)
Abbott Laboratories (ABT US)	Sophia Genetics (not listed)	Agilent Technologies (A US)	Eurofins Scientific (ERF FP)	MetaMixis (not listed)	Calysta (not listed)
Fluidigm Corporation (FLDM US)	Nebula Genomics (not listed)	10x Genomics (TXG US)	Thermo Fisher (TMO US)	Synthetic Genomics (not listed)	Amyris (AMRS US)
Danaher (DHR US)	Benchling (not listed)	Genewiz (not listed)	Sigma-Aldrich Corp (SIAL US)	Muse Bio (not listed)	Cronos Group (CRON US)
Bio-Rad Laboratories (BIO US)		Pacific Bioscience (not listed)	Evonetix (not listed)	Synbiota (not listed)	Motif Foodworks (not listed)
Zoetis (ZTS US)		Oxford Nanopore Technologies (not listed)	Molecular Assemblies (not listed)	Amyris (AMRS US)	Pivot Bio (not listed)
1CellBio (not listed)			Synthego (not listed)	Biopetrolia (not listed)	Bolt Threads (not listed)
			AskBio (not listed)	iMicrobes	Codexis (CDXS US)
					Ecovative (not listed)
					Spiber (not listed)
					Novozymes (NZYM DC)
					Joule (not listed)
					Modern Meadow (not listed)

Players In Synthetic Biology Applications By Sector



Catalysts

- **Declining costs of DNA synthesis.** DNA synthesis is becoming less expensive and widely available. Further reductions in the cost of synthesis technology will allow to further scale the production for end-market products.
- **Declining cost of DNA sequencing.** Advancements in sequencing technology will allow to expand the knowledge of what to do with cheaper and cheaper synthetic genes that will translate into new applications.
- **M&A opportunities.** We expect to see a vertical integration across the entire value chain, especially between players in DNA synthesis, DNA sequencing, and biofoundries.

Risks

- **Lack of standardization.** There is a huge unmet need for standardization (mostly in the manufacture) and regulation to allow scientists to assess and manage the risks associated with their work.
- **Scalability and demand.** If demand for synthetic DNA grows at a slower rate than the fall in price per base, the total value of the market could remain stagnant or even decrease.
- **Ethical, social and legal limitations.** The possible dangerous effects of modified organisms on the environment, the specter of bioterrorism (creating dangerous pathogens), and eugenics (approaches to improve the human genome), have raised concerns all around the world.

Bottom Line

- Synthetic Biology opens up a completely new prospective on biological based technologies. The long-term impact of this industry is difficult to predict but we believe it will be massive. As technologies prove themselves at increasing scales, new exciting opportunities will arise to fuel innovation in many industries.
- Our Bionics certificate is already exposed to the thematic, especially to the DNA synthesis and sequencing technology, and we are committed to increase our expose as new opportunities unlock.

Companies mentioned in this article:

Twist Bioscience (TWST US), Zymergen (not listed), Ginkgo Bioworks (not listed), Illumina (ILMN US), Thermo Fisher (TMO US), Sanofi (SAN FP), Evonetix (not listed), Miroculus (not listed), Eurofins Scientifics (ERF FP), Imec (not listed), CytoSeek (not listed), Ecovative (not listed), Bolt Threads (not listed), Joule (not listed), Pivot Bio (not listed), Finless Foods (not listed), Memphis Meat (not listed), Codexis (CDXS US), Microsoft (MSFT US)

CHARTS FOR THOUGHTS

Are Cryptos Becoming Currencies?

Bitcoin showed peculiar behavior

The FED chairman Powell's speech at Jackson Hole was being followed by the whole financial world, and it had an impact on a number of assets, including Gold and Bitcoin.

- The notable intraday spike was related to the dovish comments made by Powell.
- Remarkably, Bitcoin behaved almost exactly as Gold.

Gold plays more than one role

Gold is considered as a peculiar asset class – a store of "real value" and an alternative currency.

- The limited quantity of Gold available reduces any inflation – value of gold in terms of purchasing power have remained fairly stable across long periods of time.
- Gold used to be the standard currency, at least until the Bretton Woods agreement, and remains for many as the main non-fiat alternative currency.

Is a newfound correlation there? What would be the implications?

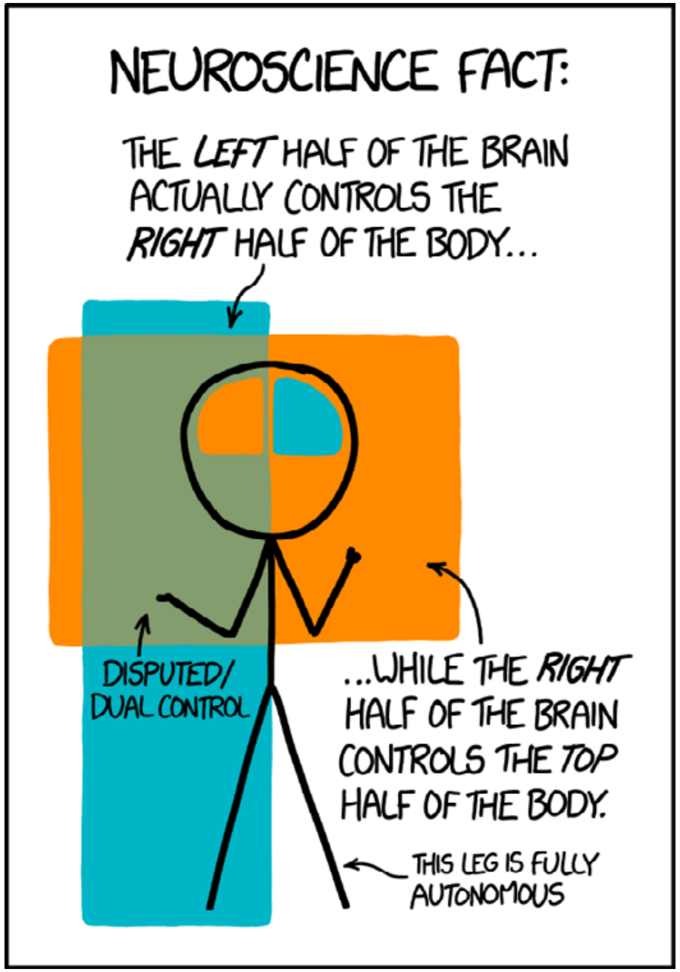
Looking beyond intraday charts, it seems that Bitcoin and Gold have been correlating over the last few months, notably since the post-COVID monetary stimulus announcement.

- Is Bitcoin simply starting to behave as a currency and responding to USD ebbs and flows?
- Or is it taking the role of what some already dub as "digital Gold"?

INTRADAY CHART – "JACKSON HOLE SPEECH"

APRIL–AUGUST '20

CASUAL FRIDAY



SOURCE:
https://xkcd.com/2120/

Invest Beyond The Ordinary

Explore our investment themes:

www.atonra.ch/investment-themes/

HEALTHCARE M&A	SUSTAINABLE FUTURE	BIOTECHNOLOGY	AI AND ROBOTICS	FINTECH	SECURITY AND SPACE	MOBILE PAYMENTS	BIONICS

About AtonRâ Partners

AtonRâ Partners is an asset management company, founded in 2004 with head office in Geneva, incorporated under Swiss law, duly approved by the Swiss Financial Market Supervisory Authority (FINMA) under the Swiss Collective Investment Schemes Act.

AtonRâ Partners is a conviction-driven asset manager combining industrial and scientific research with financial analysis. AtonRâ Partners focuses on long-term trends powerful enough to be turned into thematic equity portfolios.

Disclaimer

This report has been produced by the organizational unit responsible for investment research (Research unit) of AtonRâ Partners and sent to you by the company sales representatives.

As an internationally active company, AtonRâ Partners SA may be subject to a number of provisions in drawing up and distributing its investment research documents. These regulations include the Directives on the Independence of Financial Research issued by the Swiss Bankers Association.

Although AtonRâ Partners SA believes that the information provided in this document is based on reliable sources, it cannot assume responsibility for the quality, correctness, timeliness or completeness of the information contained in this report.

The information contained in these publications is exclusively intended for a client base consisting of professionals or qualified investors. It is sent to you by way of information and cannot be divulged to a third party without the prior consent of AtonRâ Partners. While all reasonable effort has been made to ensure that the information contained is not untrue or misleading at the time of publication, no representation is made as to its accuracy or completeness and it should not be relied upon as such.

Past performance is not indicative or a guarantee of future results. Investment losses may occur, and investors could lose some or all of their investment. Any indices cited herein are provided only as examples of general market performance and no index is directly comparable to the past or future performance of the Certificate.

It should not be assumed that the Certificate will invest in any specific securities that comprise any index, nor should it be understood to mean that there is a correlation between the Certificate's returns and any index returns.

Any material provided to you is intended only for discussion purposes and is not intended as an offer or solicitation with respect to the purchase or sale of any security and should not be relied upon by you in evaluating the merits of investing in any securities.