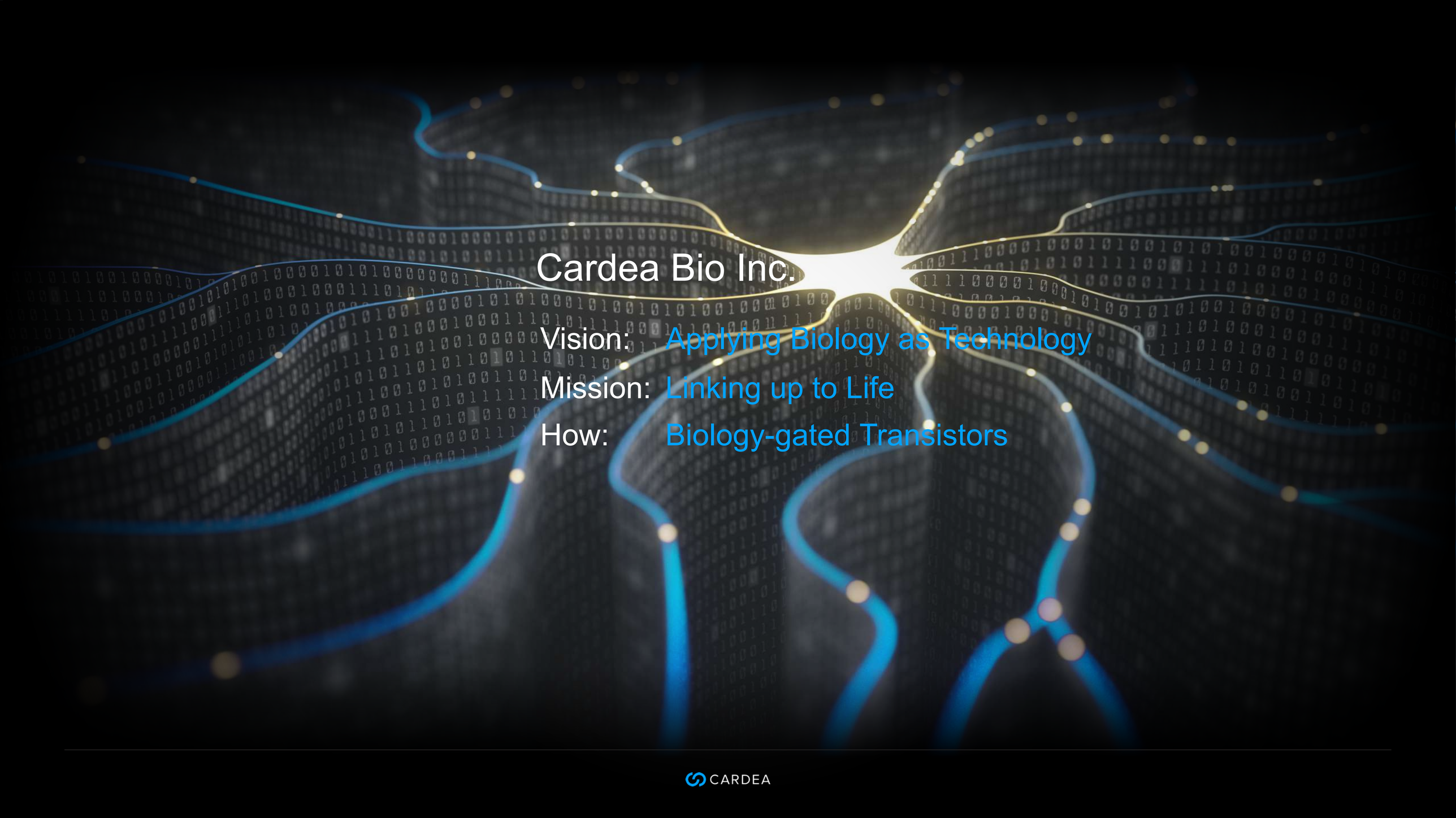
Cardea Bio / **A Tech+Bio Paradigm-shift** / 2020

Michael Heltzen – **CEO & Co-founder**



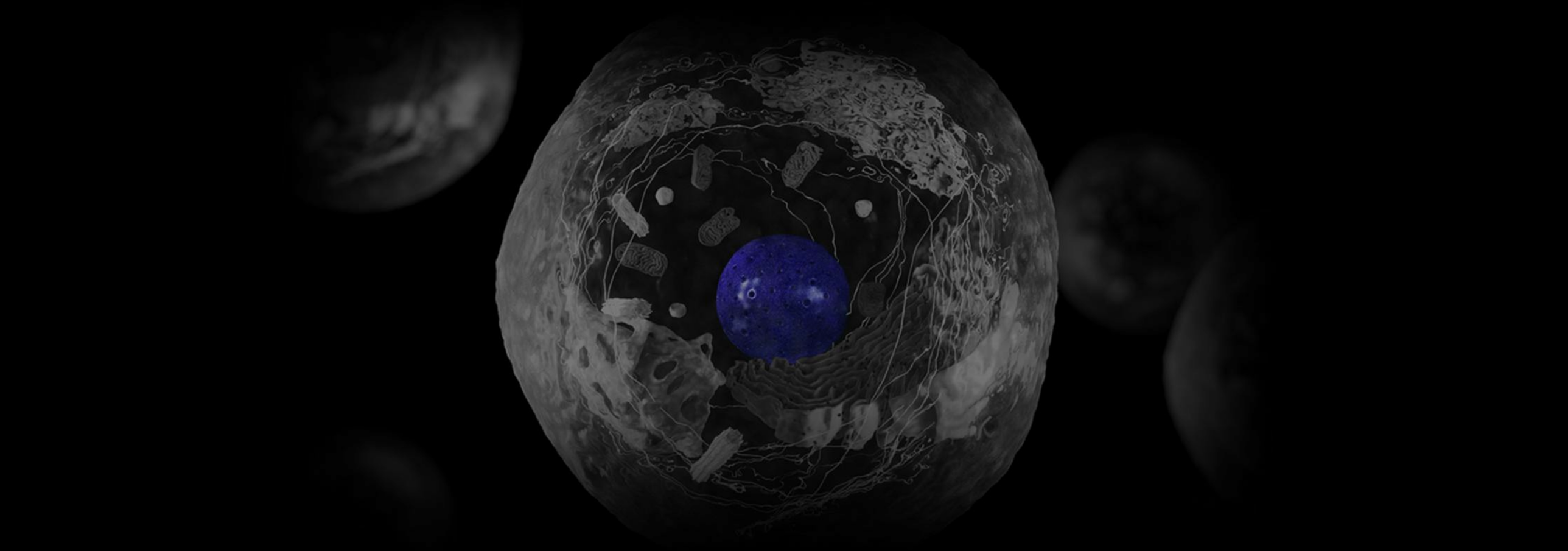
Cardea Bio Inc.

Vision: Applying Biology as Technology

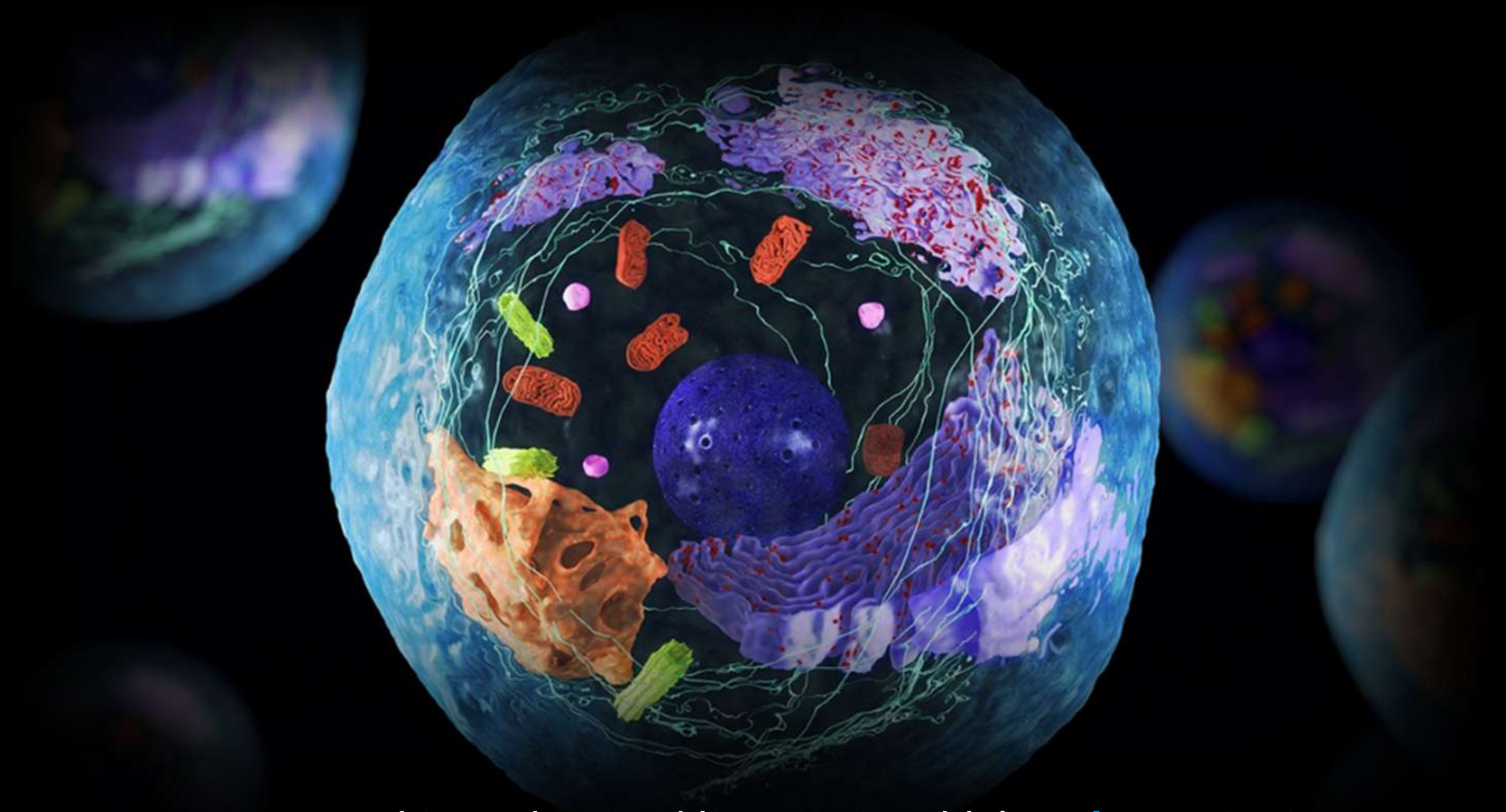
Mission: Linking up to Life

How: Biology-gated Transistors

To truly understand **biology…**

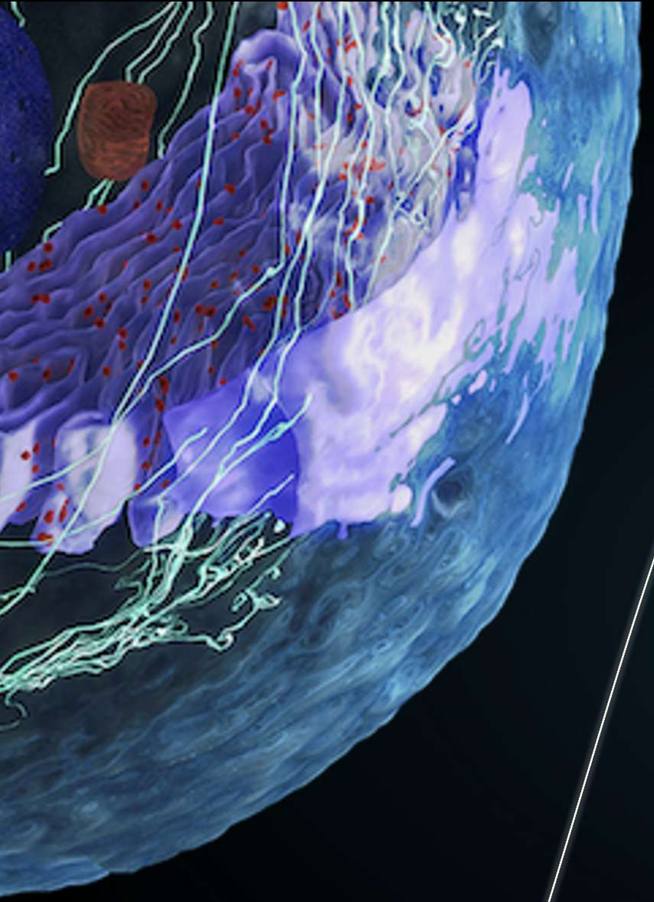


To truly understand **biology…**

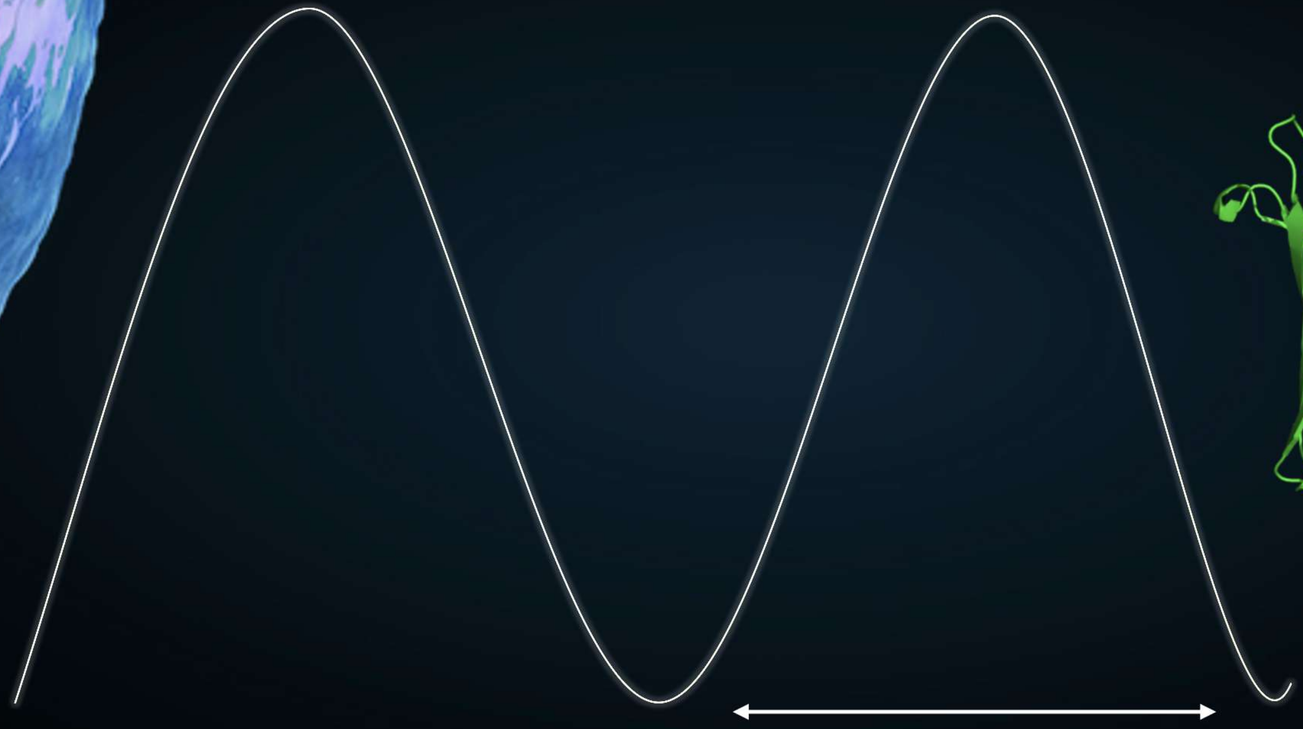


…we need to understand it as system biology **in context.**
As multi-omics data-streams not just single-omics data-sets.

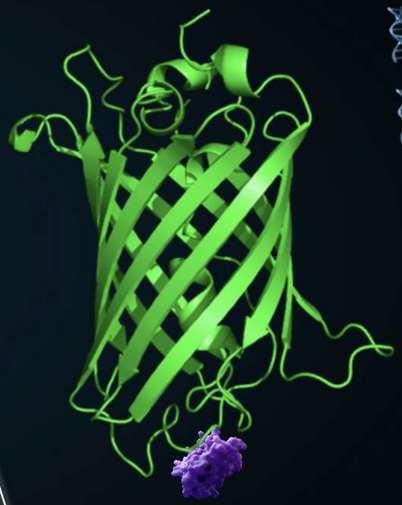
Why current life science is stuck with “omics” tunnel vision:



Cell
10,000nm



Lightwave
500nm



Protein
10 nm

OR

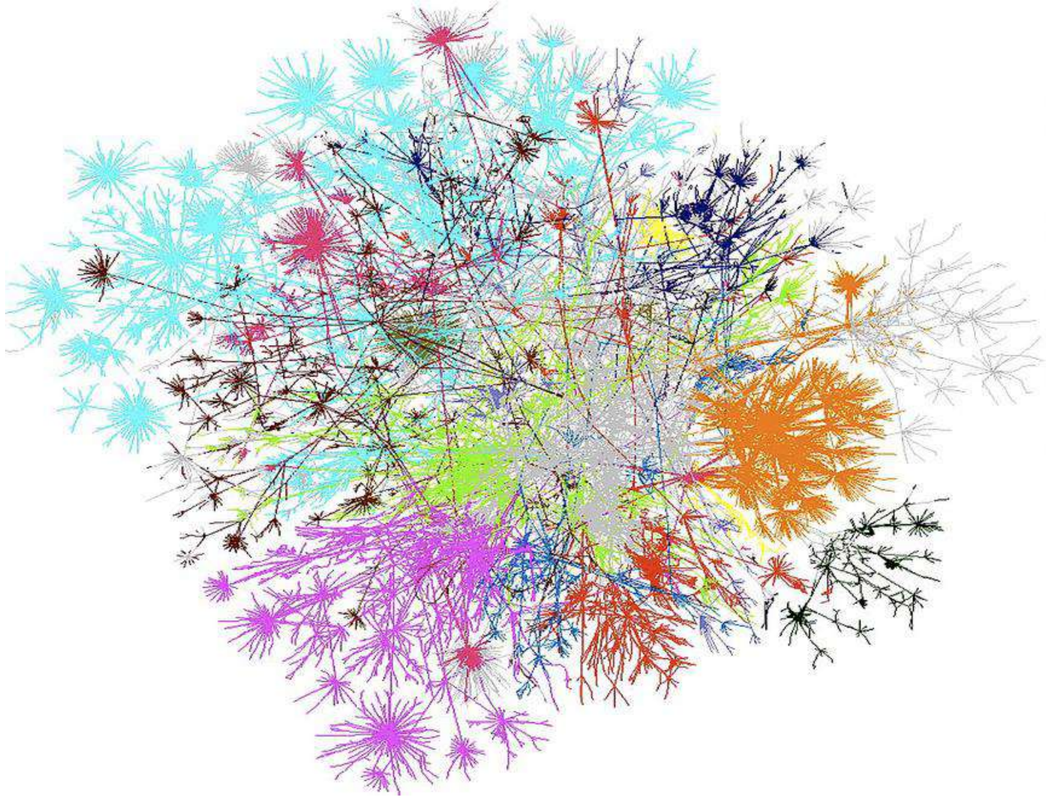
DNA
2.5 nm

Digital Networks

Large digital networks are driven by electronic data exchange and described by exponential network diagrams.

Digital Networks are:

- Global + Local
- Human-engineered
- Easy interface
- Scale Invariant
- Near instant
- Complex



Biological Networks

Biological networks are found in e.g. cells, organisms, and ecosystems. These systems of system networks exchange information through electrical, chemical, and biochemical signaling.

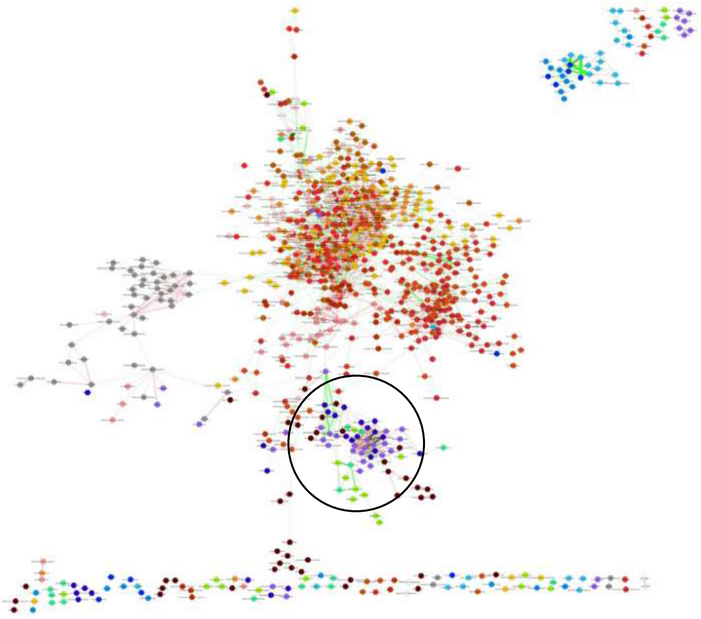
Biological Networks are:

- Hyper local
- Self-Replicating
- Self-Organized
- Scale Invariant
- Near instant
- Complex

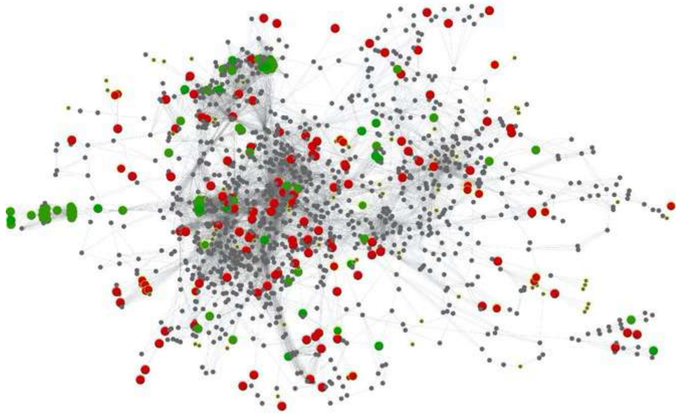
Differs

Aligns

… compared to Digital Networks.



Rough Map of human microbiome



Example of Gut microbiome system-of-systems

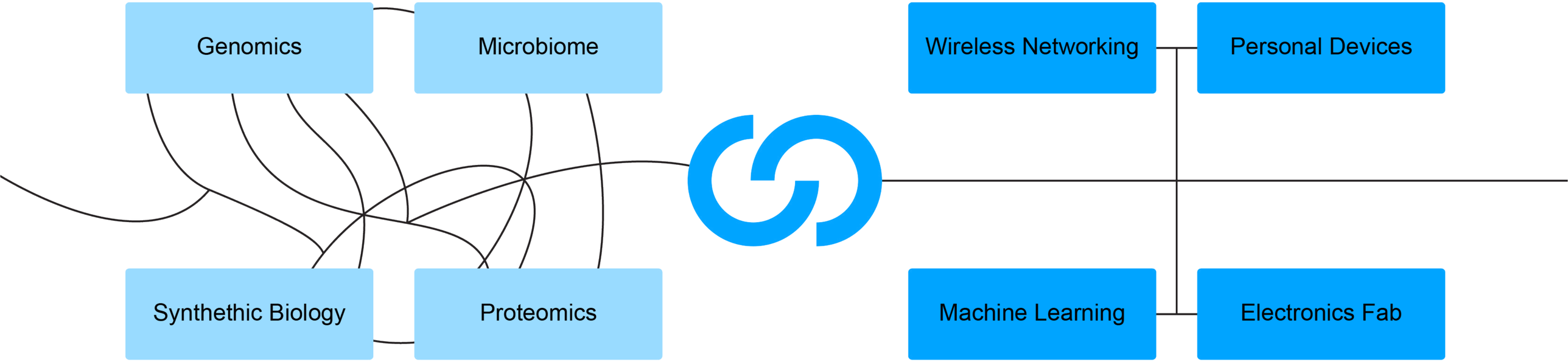
The Back-of-a-napkin Perspective:

With Cardean Biology-gated Transistors it Becomes Possible to Connect:

Biological Networks & Digital Networks

E.g.:

- Personalized Medicine
- Stem Cells
- Environmental Monitoring
- Live Health and Wellness
- Global Communication
- Local Applications
- Instant and Personal Access
- Market Access and Scale



- Engineered Biosystems
- Cross-species App's
- Cell Signaling
- Research & Development
- Fueled by Complexity
- Pattern Recognition
- Worldwide Infrastructure
- Low-Cost Manufacturing

Cardea Bio - in One Sentence

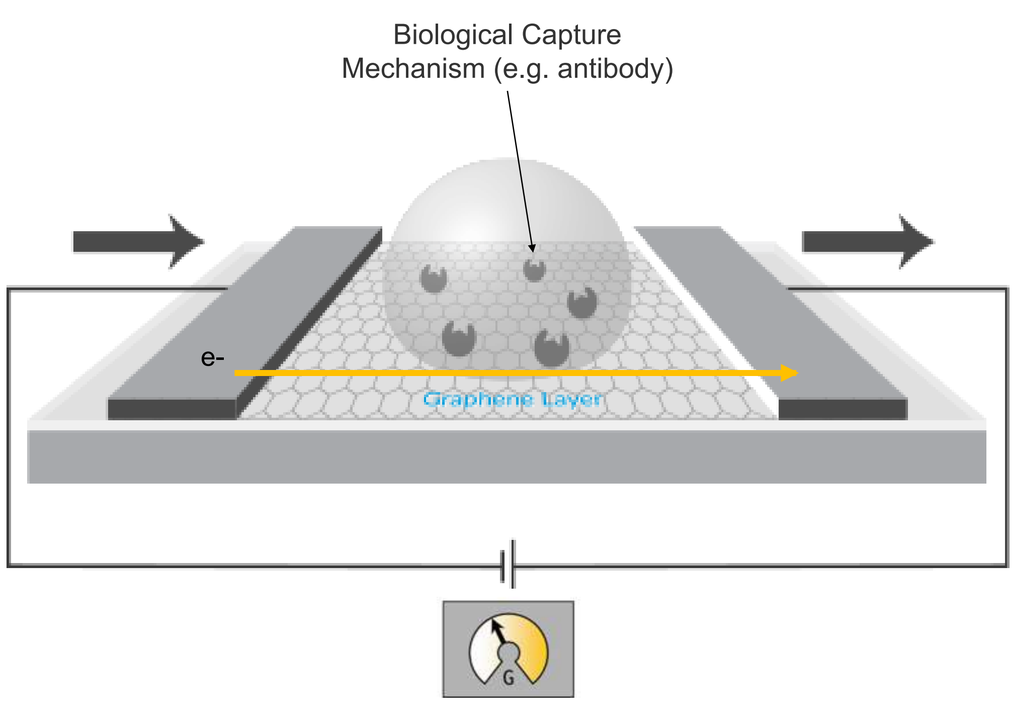
”

*A Tech+Bio infrastructure company using **Biology-gated Transistors** to live stream biological information to computers allowing for a new generation of apps **Linking up to Life** and using **Biology as Technology**.*

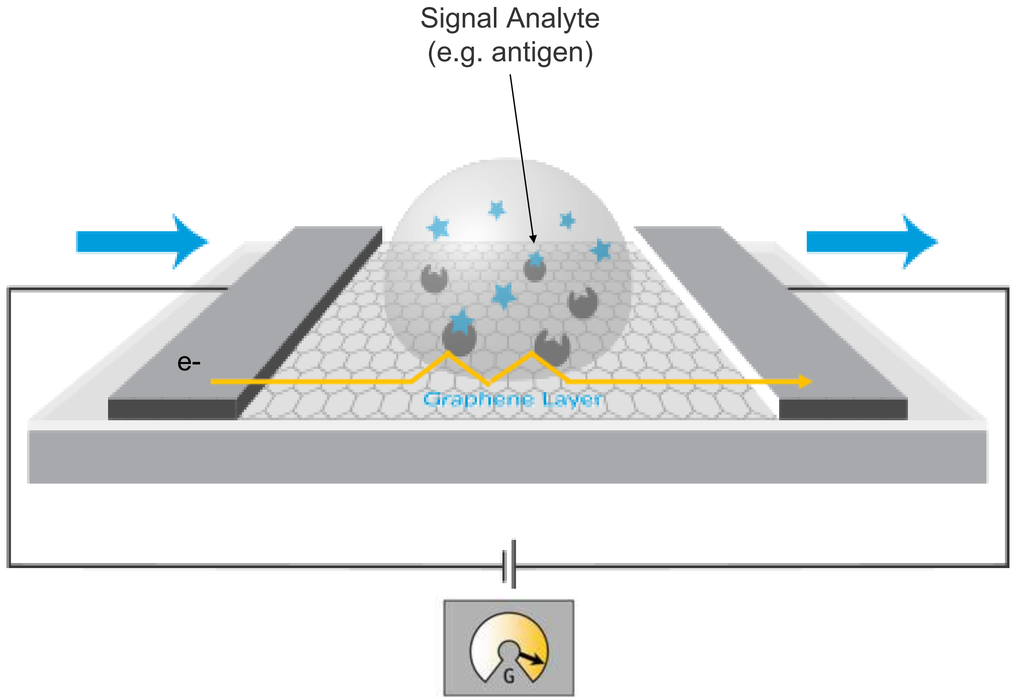
#Biology-gatedTransistors + #LinkingUpToLife

= #BiologyAsTechnology

The Cardean Biology-gated Transistor Principle



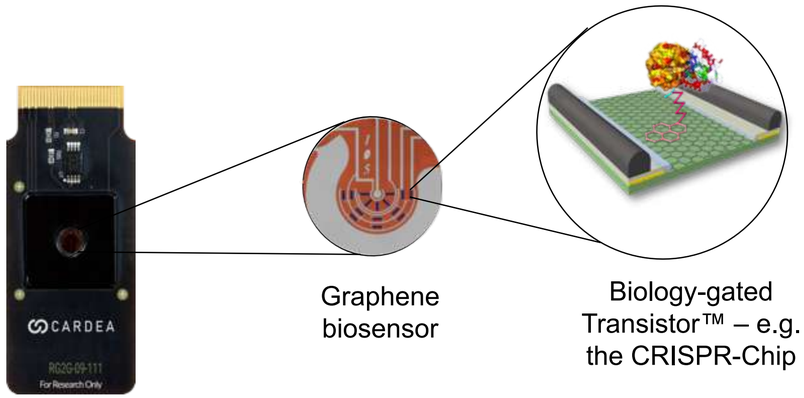
Base signal from the functionalized transistor



Real-time change in “Base signal” upon the target analyte is attracted to the biology-gated transistor

Cardean Chips, Biosensors, and Transistor Designs

Commercially available via the Cardea Innovation Partnership Program



A Cardea (consumable) Chip

Graphene biosensor

Biology-gated Transistor™ – e.g. the CRISPR-Chip

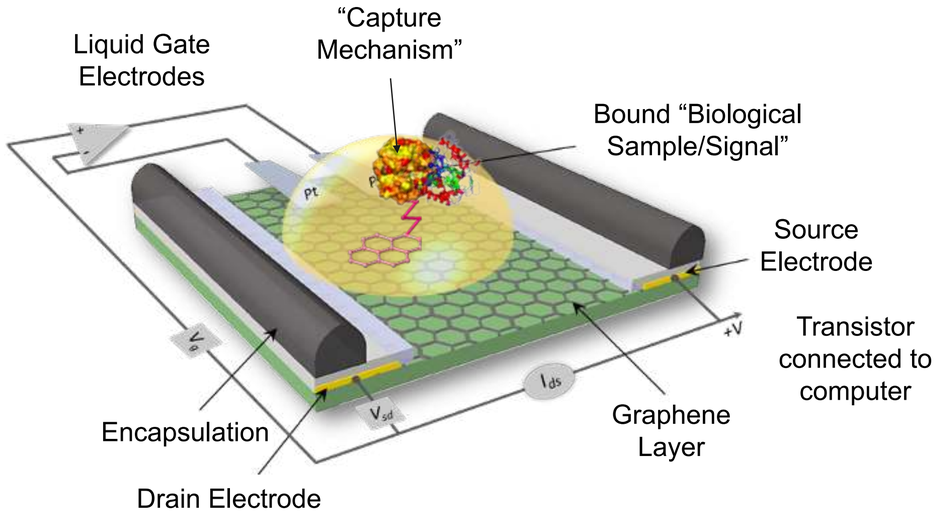
Click here to see a short video of how the Cardean Transistors™ work

CARDEA

Cardea's Modular Biology-gated Transistors™ Infrastructure*

New tech modules are continually being built and available to Innovation Partners via the Cardea Tech Catalog.

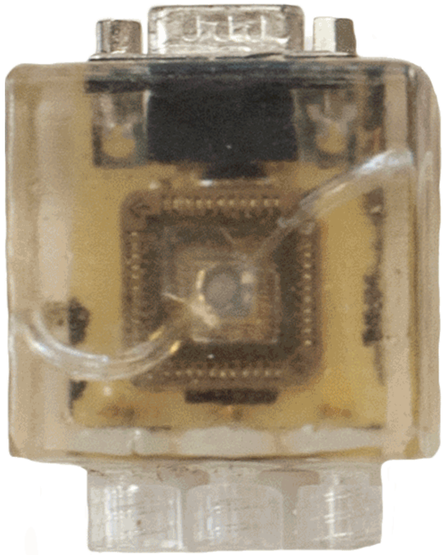
Our Innovation Partners have access to all existing core modules – saving significant development time and cost. If a new feature/module is needed, that is not in the catalog, we can rapidly develop the needed module at cost via an investment from the Innovation Partner – enabling new products to quickly seize market opportunities. Partners can also wait for modules to be developed without additional investment, but they may miss the launch window needed to win their market.



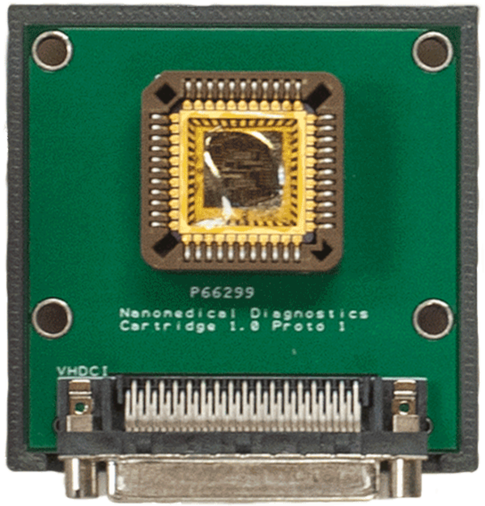
* Proprietary technology protected with a large portfolio of issued and pending patents and multiple layers of trade secrets. Core technology proven and published in Nature Biomedical Engineering & Nature Scientific Reports in 2019. First commercial product development partnerships started in Q1 2020.

Rapid Economies of Scale – **Outpacing Moore's Law**

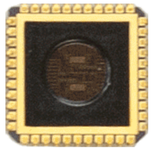
2013 → 2020



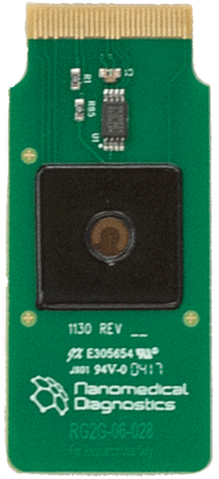
Alpha



Prototype 1



Beta Chip



Commercial Alpha Chip

Commercial Beta Chip

First Cardea Chip

	Pre-commercial Chips	Commercial Chips
Overview	Custom, large, and expensive Very low yield	Low Space & Power Requirements Low Material Requirements
Design	1 gFET transistors, 40 circuits, 1 analyte per chip	15 gFET transistors, 3 circuits, 1-3 analyte per chip (soon many more)
Production time	6-7 months/chip	Time to manufacture measured in weeks, thousands of chips per batch
Cost	**$x00,000/chip**	**$x0/chip**

Strong Patent Portfolio & IP Position

20 issued Patents, 20+ patent pending, and numerous trade secrets effectively letting Cardea own the “white space” opportunity of linking modern electronics up to biology.

Patent/Appt. No.	Title	Link to patents:
US20170307562A1	Chemically Differentiated Sensor Array	https://patents.google.com/patent/US20170307562A1/en?oq=US20170307562A1
US20160054312A1	Chemically Differentiated Sensor Array	https://patents.google.com/patent/US20160054312A1/en?oq=US20160054312A1 US10429342
US10429342	Chemically Sensitive Field Effect Transistor	https://patents.google.com/patent/US10429342B2/en?oq=14%2f963%2c253
US16/586,964	Chemically Sensitive Field Effect Transistors	publication pending
US9857328	Chemically Sensitive Field Effect Transistors	https://patents.google.com/patent/US9857328B2/en?oq=US9857328
US10429381	Chemically Sensitive Field Effect Transistors	https://patents.google.com/patent/US10429381B2/en?oq=16%2f014%2c838
US10006910	Chemically Sensitive Field Effect Transistors	https://patents.google.com/patent/US10006910B2/en?oq=15%2f256%2c493
EP3491370A1	Chemically Sensitive Field Effect Transistors	https://patents.google.com/patent/EP3491370A1/en?oq=EP3491370
EP3344980A1	Chemically Sensitive Field Effect Transistors	https://patents.google.com/patent/EP3344980A1/en?oq=EP3344980
US62/883887	Devices and Methods for Label-free Detection of Analytes	publication pending
US9859394	Graphene FET Devices, Systems, and Methods of Using the Same for Sequencing Nucleic Acids	https://patents.google.com/patent/US9859394B2/en?oq=15%2f182%2c533
US9618474	Graphene FET Devices, Systems, and Methods of Using the Same for Sequencing Nucleic Acids	https://patents.google.com/patent/US9618474B2/en?oq=15%2f065%2c744
US20190181273A1	Graphene FET Devices, Systems, and Methods of Using the Same for Sequencing Nucleic Acids	https://patents.google.com/patent/US20190181273A1/en?oq=US20190181273A1
US20180315750A1	Graphene FET Devices, Systems, and Methods of Using the Same for Sequencing Nucleic Acids	https://patents.google.com/patent/US20180315750A1/en?oq=US20180315750A1
US20170218442A1	Graphene FET Devices, Systems, and Methods of Using the Same for Sequencing Nucleic Acids	https://patents.google.com/patent/US20170218442A1/en?oq=15%2f483%2c983
US16/656,470	Graphene FET Devices, Systems, and Methods of Using the Same for Sequencing Nucleic Acids	publication pending
US10020300	Graphene FET Devices, Systems, and Methods of Using the Same for Sequencing Nucleic Acids	https://patents.google.com/patent/US10020300B2/en?oq=15%2f225%2c764
EP3459115A1	Graphene FET Devices, Systems, and Methods of Using the Same for Sequencing Nucleic Acids	https://patents.google.com/patent/EP3459115A1/en?oq=+EP3459115
EP3308153A1	Graphene FET Devices, Systems, and Methods of Using the Same for Sequencing Nucleic Acids	https://patents.google.com/patent/EP3308153A1/en?oq=EP3308153
US20190112643A1*	Immobilized RNPs for Sequence-Specific Nucleic Acid Capture and Digital Detection	https://patents.google.com/patent/US20190112643A1/en?oq=US20190112643A1
US20160025675A1	Method for Electronic Biological Sample Analysis	https://patents.google.com/patent/US20160025675A1/en?oq=US20160025675A1
US20180037952A1	System and Method for DNA Sequencing and Blood Chemistry Analysis	https://patents.google.com/patent/US20180037952A1/en?oq=US20180037952A1
US20150307936A1	System and Method for DNA Sequencing and Blood Chemistry Analysis	https://patents.google.com/patent/US20150307936A1/en?oq=US20150307936A1
EP3280822A1	System and Method for DNA Sequencing and Blood Chemistry Analysis	https://patents.google.com/patent/EP3280822A1/en?oq=EP+3280822+A1
US9618476	System and Method for Electronic Biological Sample Analysis	https://patents.google.com/patent/US9618476B2/en?oq=14%2f263%2c954
JP2017514141A	System and Method for Electronic Biological Sample Analysis	https://patents.google.com/patent/JP2017514141A/en?oq=JP2017514141A
EP3149464A4	System and Method for Electronic Biological Sample Analysis	https://patents.google.com/patent/EP3149464A4/en?oq=EP3149464A4
CN110385151A	System and Method for Electronic Biological Sample Analysis	https://patents.google.com/patent/CN110385151A/en?oq=CN110385151A
CN106461586B	System and Method for Electronic Biological Sample Analysis	https://patents.google.com/patent/CN106461586B/en?oq=CN+106461586+B
US62/801555	Systems and Methods for Chip-assisted CRISPR	Publication pending
US62/866312	System and Method for Electronic Detection of Cleavage and Collateral Activity of CRISPR-associated Endonucleases	Publication pending
US16/459298	Systems and Methods for Exosome Capture and Detection	Publication pending

Key Publications

Some Early Partners Publications:

- Lab on a Chip
- Bioorganic & Medicinal Chemistry
- Nature
- Angewande Chemie
- JACS

Our Publications:

- Nature Biomedical Engineering
- Nature Scientific Reports
- Biosensors and Bioelectronics
- Sensors and Actuators

CARDEA

Many Product Form Factors, Applications and Use Cases

– All Built with the Same Modules

Examples of instruments

High-throughput screening compatible with robots

A Cardean Transistor Called: CRISPR-Chip™

- First-ever Amplification-free DNA testing
- Nature BME June 2019 cover story, and most read article + many international news articles.
- Without the need for amplification, DNA testing will no longer be trapped inside of complicated DNA labs. CRISPR-Chip™ enables easy-to-use rapid DNA testing for Point-of-Care & Point-of-Need environments.

> *CRISPR on graphene can search through **whole genomes in minutes,** with no cost of expensive lab reagents and no amplification errors.*

Dr. Kiana Aran – **CSO & Co-founder**

Click here to download the paper

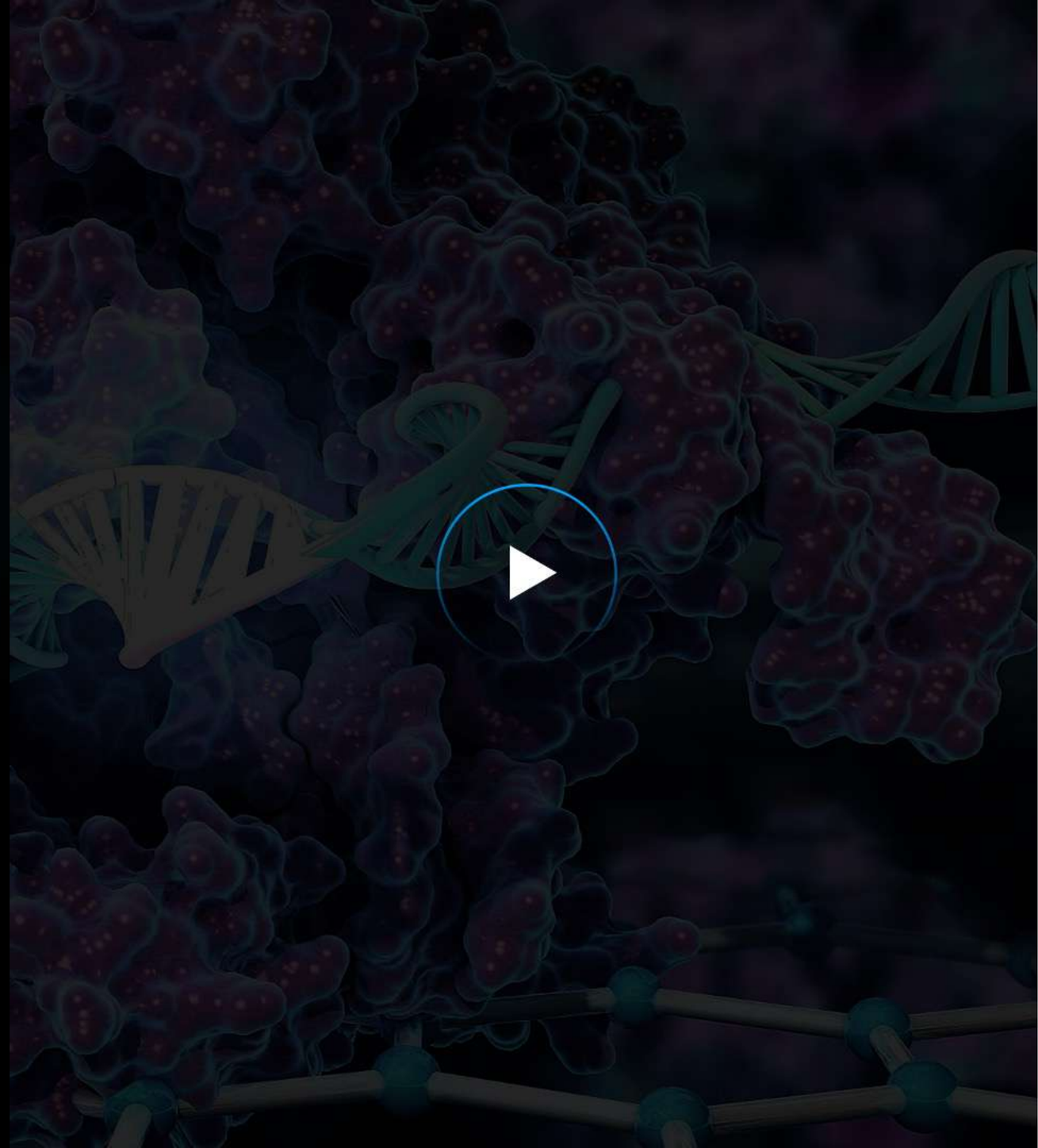
CARDEA

CRISPR-Chip in Action

This Video was produced by University of California, Berkeley, as Cardea Co-founder and CSO, Dr. Kiana Aran, is a Berkeley visiting professor.

For more news about CRISPR-Chip

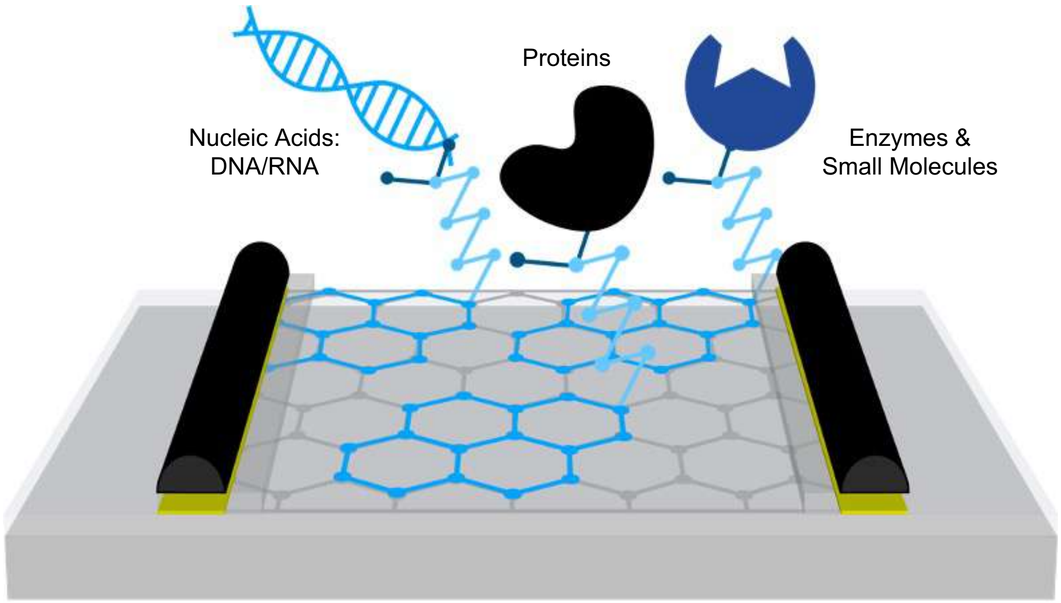
- Visit **Cardeabio.com/CRISPR-Chip**



True Multiplexing

The Cardean Transistor Infrastructure integrates any type of biological signal into actionable information

- Cardea powered products will perform "true multi-omics" analysis and applications. End-product biosensor chips can have multiple unique capture mechanisms and transistor types for application-relevant combinations.
- For example: Any combination of DNA, RNA, proteins, enzymes, small molecules ***and/or*** other capture mechanisms can be built into relevant combinations – uniquely allowing for near-real time data streams and analysis at both the systems and individual analyte level.
- These multi-analyte data streams will lead to a paradigm shift in the analysis and true insight to “live” system biology.



The Cardea Team's Way of Thinking

We have a cross-disciplinary and very innovative winner culture, and we do not believe in the limitations of the last generation of life science detection methods.

We hold a strong believe in that there is a huge white space in between electronics and biology.

*We, Cardea, have set out to change how people think about biology. They will all come to understand that **Biology is Technology**, and that there is almost unlimited information available in biology if we can train our computers to listen to biology's signals.*

*With a new way of conducting biology via our new biological electronics infrastructure, we will empower our **Innovation Partners** with new competitive advantages and product types for their ever-changing markets. Our impact will be felt everywhere.*

*If you believe an impossible problem lies in front of you, you will be trapped in stasis. We believe **there are no impossible problems**. We aim to invent the possible, by killing all old assumptions on day one.*

Strategy & Business Model

- “Powered by Cardea” is similar to “Intel Inside” and Qualcomm’s tech design business model. We keep our focus on chip set design and manufacturing while earning revenue from licensing royalties, chip sales.
- Leveraging our unique expertise in commercial, large scale, graphene transistors, and biosensor manufacturing to enable partners access to first-of-a-kind technology not available elsewhere.
- Companies admitted to the Innovation Partnership Program are selected based on their intended market-ready applications and the competitive advantages our technology will provide them.
- Our module-by-module tech+bio infrastructure approach (inspired by LEGO) avoids “design by request” bottlenecks and focuses on partner-ready catalog options allowing the same modules to be used in different markets.

Universe of Addressable Market Opportunities (>>$Bn)

Innovation Partners use the same scalable infrastructure modules regardless of market. All market-specific and custom efforts are handled by the different partners.

	Agriculture				Human Health		Operations	Government	Environmental
Product Development	Plant	Feed Animal	Companion Animal	Consumer Foods	Life Sciences	Drug Discovery		Public Health	Environmental Monitoring
Detection & Diagnostic Tools	Genotyping		Animal diagnostics	Pest Identification	Diagnostics	Drug Monitoring		(Bio)Chemical Warfare	Soil, Water, Waste
Security & Safety	Quality Check	Spoilage	Drug Safety	Contamination	Drug Safety	Drug Efficacy	Biosensor & Manufacturing Improvements	Public Safety	Ecological Safety

The Innovation Partnership Program is Firing on all Cylinders (Currently +150 partners in the pipeline)

Partner Size by Valuation: >$1Bn $50MM - $500MM <$50MM

	Agriculture				Human Health		Operations	Government	Environmental
Product Development	Plant	Feed Animal	Companion Animal	Consumer Foods	Life Sciences	Drug Discovery		Public Health	Environmental Monitoring
Detection & Diagnostic Tools	Genotyping		Animal diagnostics	Pest Identification	Diagnostics	Drug Monitoring		(Bio)Chemical Warfare	Soil, Water, Waste
Security & Safety	Quality Check	Spoilage	Drug Safety	Contamination	Drug Safety	Drug Efficacy	Biosensor & Manufacturing Improvements	Public Safety	Ecological Safety

Case example 1 of 100s: New Precision QC Tools for the Genome Editing Industry

Together with COBO Technologies, Cardea is building new types of (QC) tools for biotech and agritech companies in the genome editing and engineering space.

Cardean Transistors are being configured to build:

- A liquid handling robot to perform CRISPR experiment measurements.
- Quality Control upstream of genome editing.
- By observing “CRISPR at work” editing errors and inefficiencies can be avoided and make genome editing safer and at the same time more effective and efficient.
- Product development started late Q1 2020 and the first generation will be commercially launched in Q3/Q4 2020.

CARDEA

September 2020: The CRISPR QC tool launched in a first version

Read the press release about the Cardea – COBO partnership

Case example 2 of 100s: DNA Tricorder for Farmers to Identify Trans-genes and Variants in Crops

End-product will enable users to quality check seed lots via timely identification of effectively edited crops. It's "Precision Medicine" for agriculture.

Cardean Transistors will be configured to build:

- A handheld device giving farmers digital insight to identify edited crops and asses their health via multiplex analysis
  - The end-product and setup is estimated to take 3-4 years with a market potential of $10B
  - Our Innovation Partner will own commercial rights and distribution of the seeds and fungicides
  - Future generations will integrate pathogen identification and environmental monitoring tools

Partnership budget and terms are approved and agreed to on both sides – final signature and start expected July 2020

Prototype. Not final product design

*

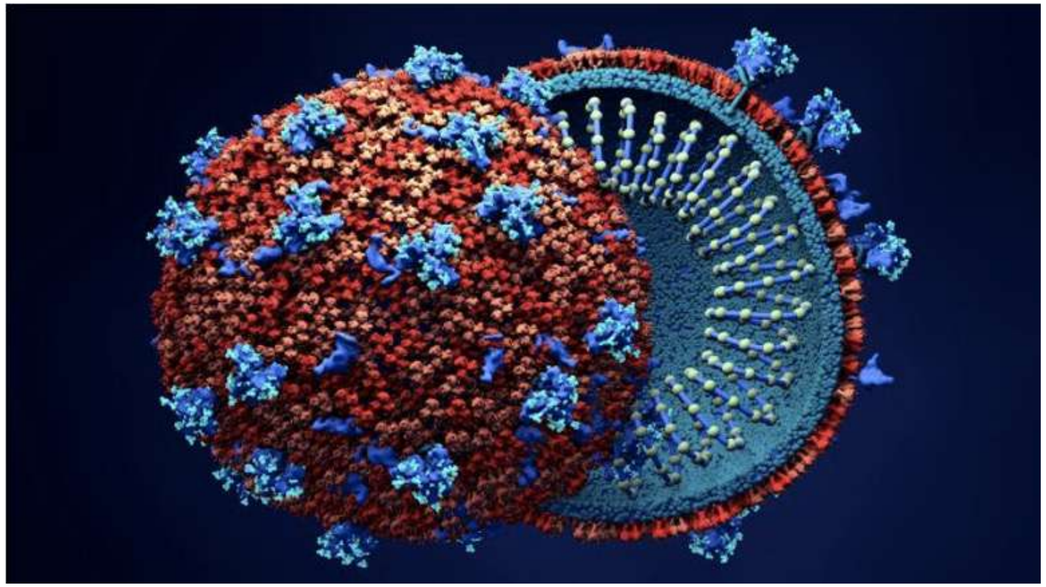
Case example 3 of 100s: A New Generation of Coronavirus Testing

Current Coronavirus testing is done with PCR (invented in 1985) that requires DNA/RNA amplification and a lab.

Cardean Transistors will be configured to build:

- A handheld device that works outside the lab (no amplification or other lab processes necessary).
- A one-of-a-kind multiplex DX that tests for viral RNA, surface proteins, and host immunity; enabling a fast, precise, and personalized approach for pandemic management.
- The capability to test for multiple infectious diseases (e.g. the Flu), bacterial infections, and immunity (serology test) – all at the same time from a single sample.

Product development design and terms have not been finalized yet, but multiple partners are very interested.

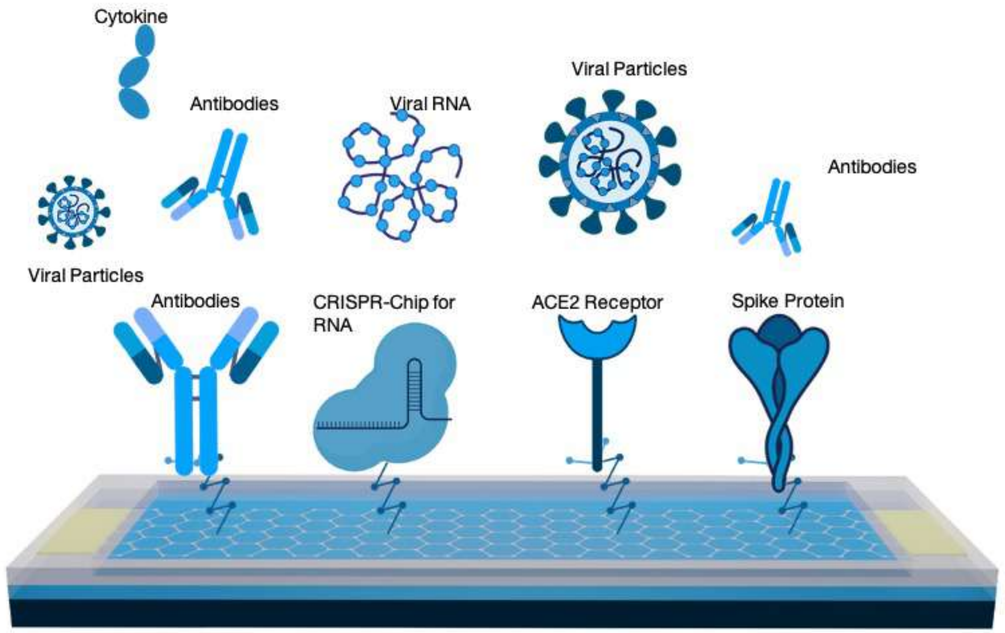


Press Release: Cardean Transistors™ Made Available to Companies and Government Agencies Willing to Build Handheld Coronavirus Detection Devices

Case example 3 of 100s: Enabling a Testing Revolution for Coronavirus

A multi-analyte reconfigurable approach:

- 1st Generation: Direct viral direction (Antigen 2.0) test via electronics and multiple antigen targets.
- 2nd Generation: Very accurate viral testing with both Viral RNA and antigens, removing doubt about precision/errors
- 3rd Generation: Combined viral detection & immunity test
- 4th Generation: Any customized product for different use cases – e.g. Cytokine storm monitoring or screening of offices, nursing homes, airports, airplane screening etc.



The Cardea Co-founder Team

Michael Heltzen

Co-Founder & **Chief Executive Officer**

Michael spearheads Digital Biology leadership and strategy at Cardea. Michael has an extensive background in tech business development in Bioinformatics, Next-Gen Sequencing, Genomics, and Intercellular communication.

He has held leadership positions at CLC bio, BGI, EXO Incubator, Nanosens and BlueSEQ before heading up the leadership team at Cardea Bio Inc.

Brett Goldsmith, PhD

Co-Founder, **Chief Technology Officer**

Brett's passion is applying nanoelectronics technology to products that change people's lives. Brett was a post-doc at the University of Pennsylvania, from one of the world's leading graphene labs.

Brett was an Intelligence Community Fellow and is the lead researcher on landmark Field Effect Biosensing papers in Science and Nature Nanotechnology.

Kiana Aran, PhD

Co-Founder, **Chief Scientific Officer**

Kiana received her PhD in Biomedical Engineering at the Rutgers University. She then continued her postdoctoral studies in bio-engineering at the UC Berkeley. She is a recipient of the National Institutes of Health postdoctoral training fellowship at the Buck Institute for Age Research and is a consultant for the Gates Foundation.

Kiana runs the Cardea Innovation lab at the Keck Graduate Institute of Applied Life Sciences.

Ross Bundy

Co-Founder & **Chief Entrepreneur**

Ross is responsible for new expansions and key projects at Cardea including scaling up the chip production for Cardea and help setting up partnerships. With an MBA from San Diego State University, Ross has held positions in supply chain, operations, and finance at companies such as General Dynamics and UBC Financial Services.

Ross brings precision execution and implementation to the company.

Thank you

Questions?

Feel free to contact CEO Michael Heltzen
michael@cardeabio.com

*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