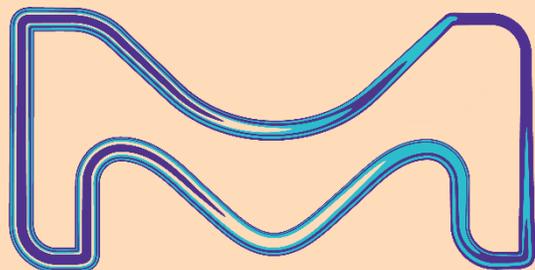


BIOCONVERGENCE

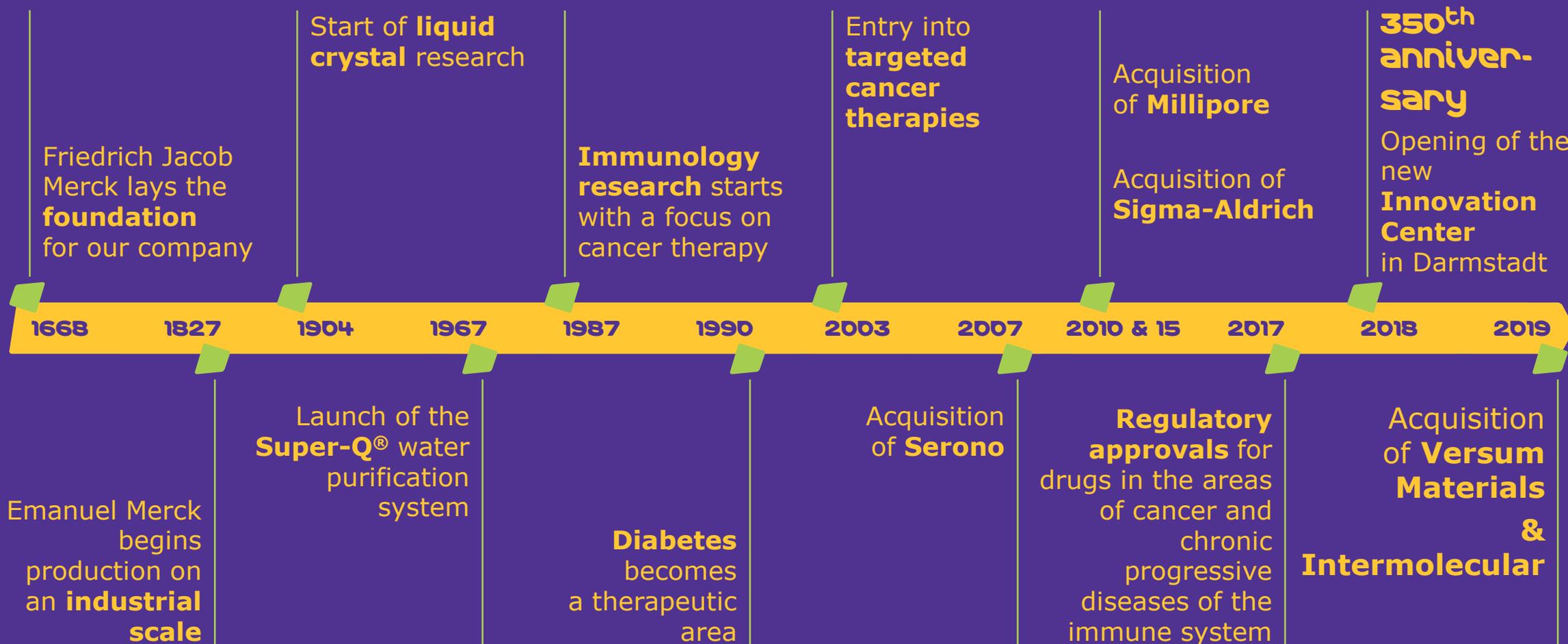
**Unlocking the full potential of data & digital
for a better future**

Steven Johnston, Ph.D.
Vice President
Head of Technology Transformation and Enablement



Merck KGaA
Darmstadt, Germany

over 350 YEARS of curiosity



Merck KGaA, Darmstadt, Germany holds the rights to the name and trademark "MERCK" internationally, except for the United States and Canada



We are unique

Since our founding over 350 years ago, we've become truly global with more than **58,000 employees** in **66 countries** working on breakthrough solutions and technologies.

EMD
SERONO

MILLIPORE
SIGMA

EMD
ELECTRONICS

In the U.S. and Canada we operate as EMD Serono in the Healthcare business, MilliporeSigma in the Life Science business, and EMD Electronics in the high-tech materials business.



We have **3 high-tech business sectors** competing in attractive markets



Healthcare

Leading in specialty pharma markets

- Biologics and small-molecule **prescription medicines** against cancer, multiple sclerosis, infertility
- **Research** focus: Oncology, Immunology & Immuno-Oncology



Life Science

Leading in life sciences

- Tools and services for **biotech research & production**
- **Tools and laboratory supply** for academic research and industrial testing



Electronics

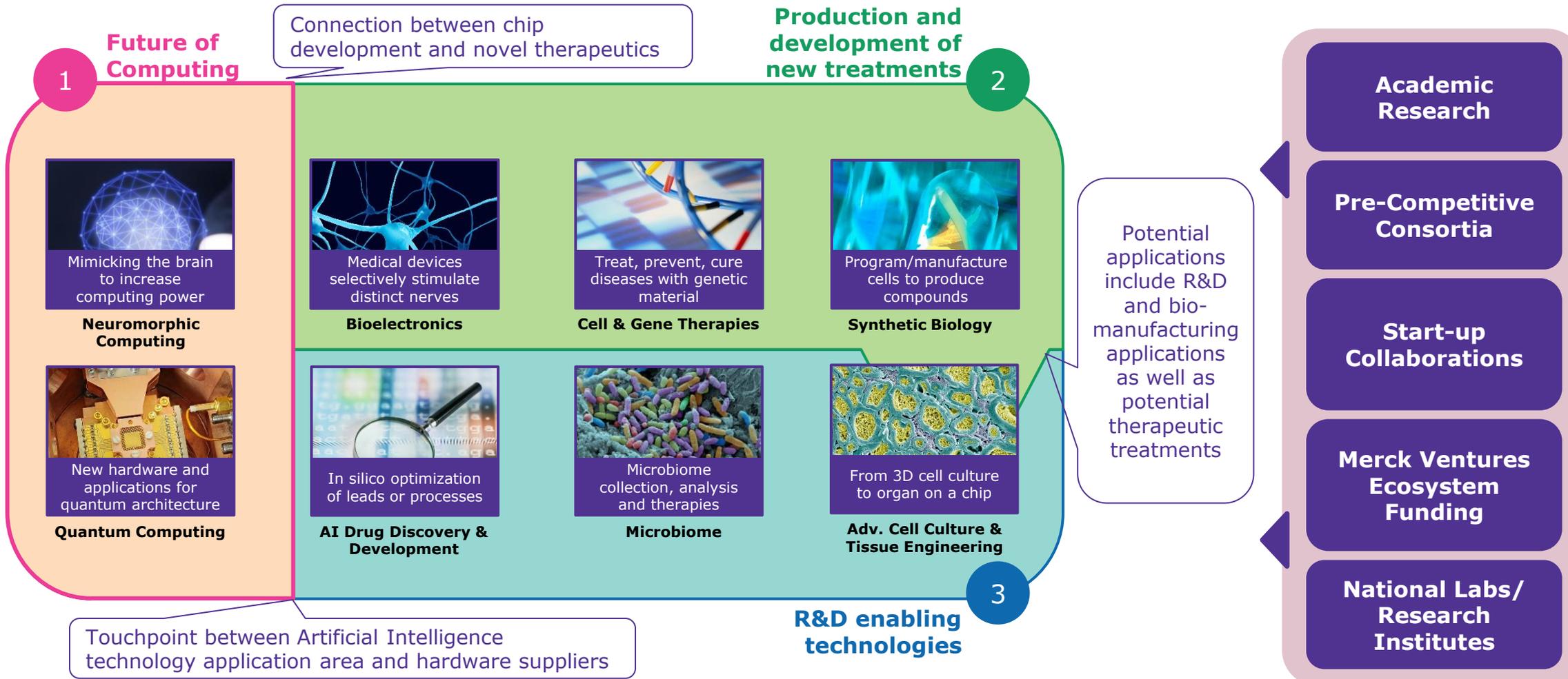
Leading in high-tech solutions

- High-tech solutions and materials for **electronics**
- Broad portfolio of **decorative and functional solutions**





Megatrends change the game and offer opportunities for Merck KGaA within and beyond our core business





BIOCONVERGENCE

Multidisciplinary approach harnessing the synergies across **digital and material science** as well as **biotechnology** aiming to improve the **speed** and **impact** of scientific discovery.

personalized Medicine

tailored to our own molecular
signature

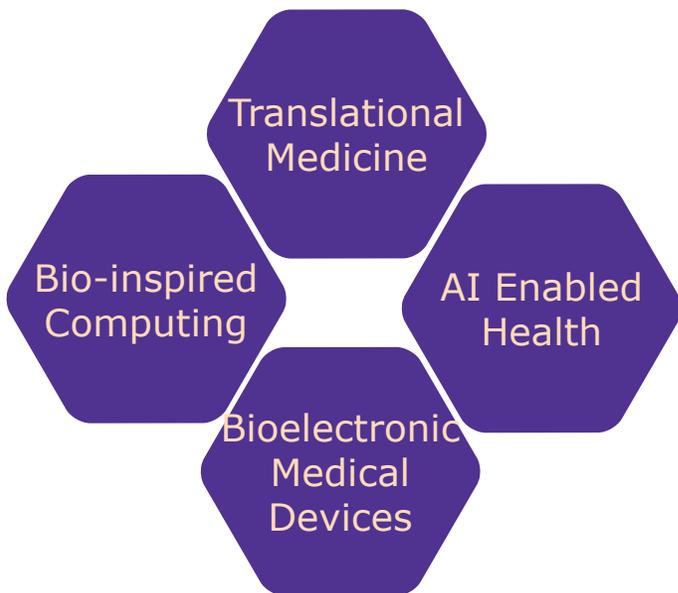


unprecedented connectedness

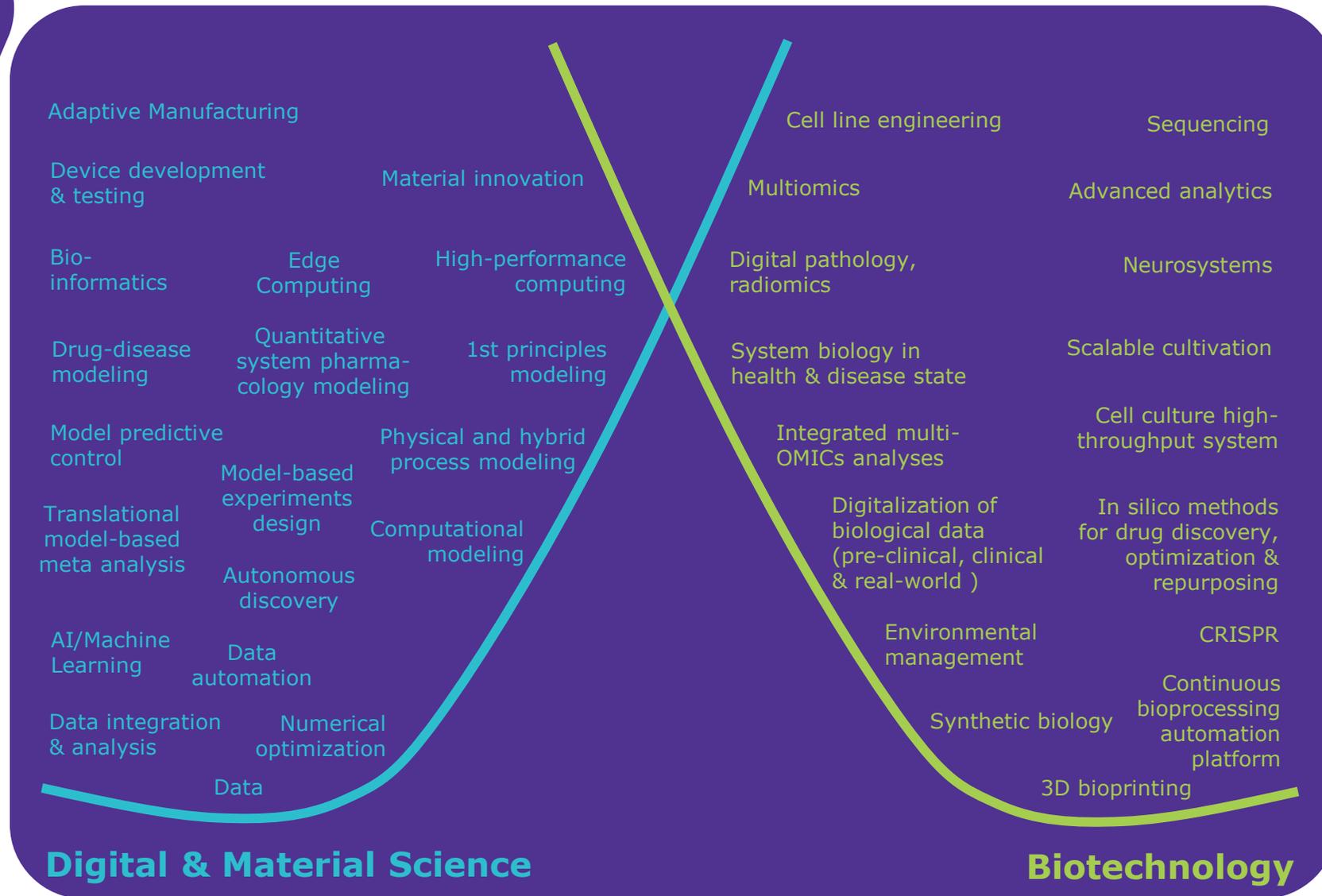
to everything and everybody



Broad spectrum of technologies are converging



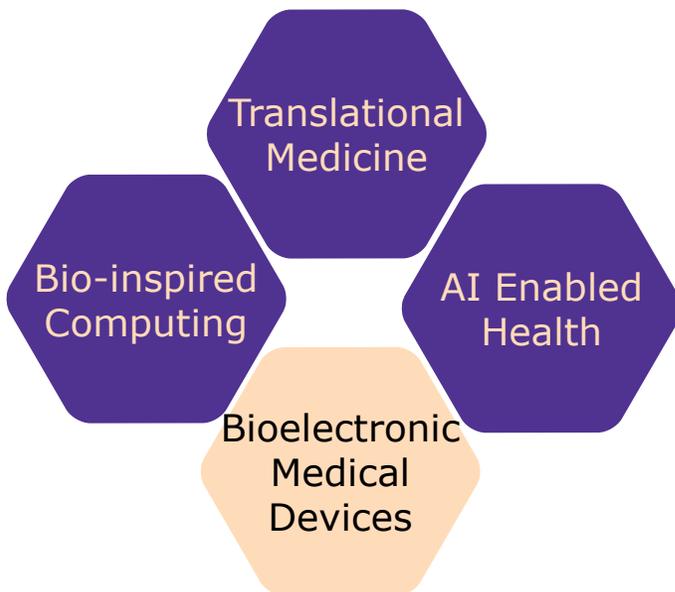
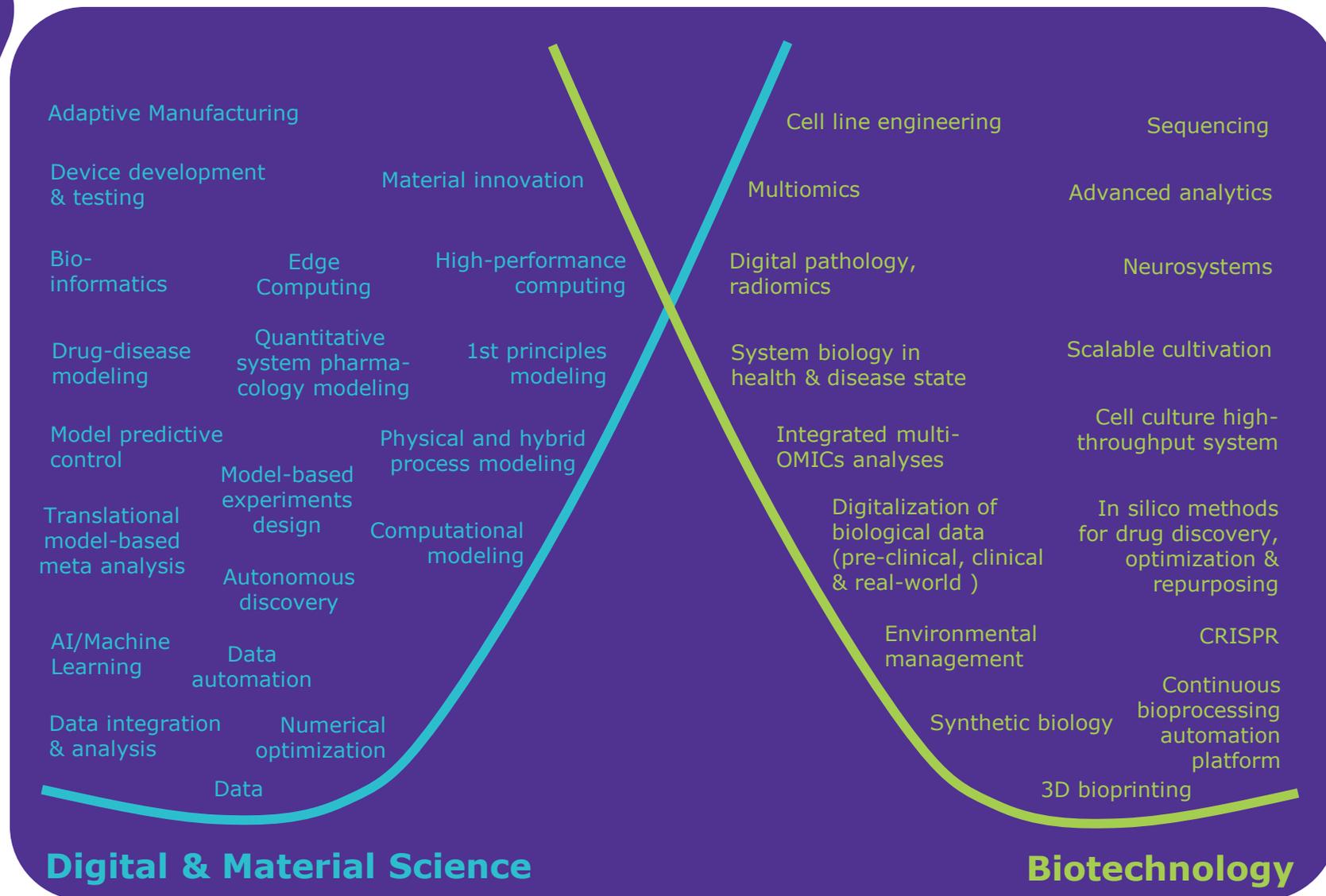
4 Example Areas for Bioconvergence



* Non exhaustive overview of competencies



Broad spectrum of technologies are converging



4 Example Areas for Bioconvergence

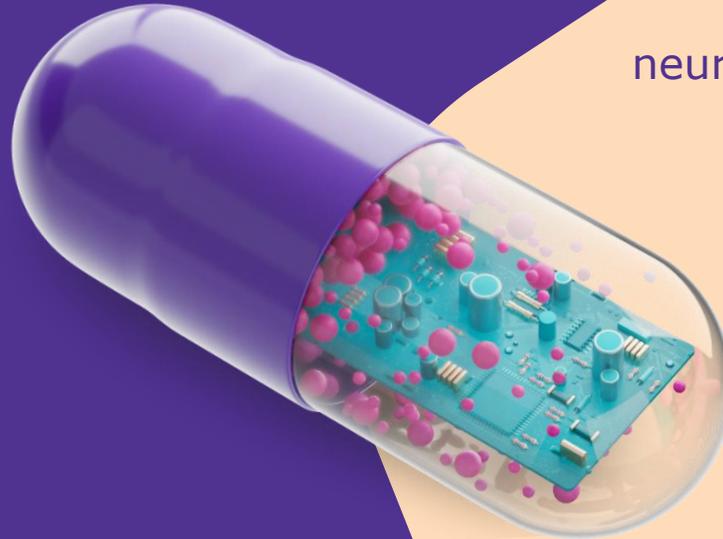
* Non exhaustive overview of competencies



Bioelectronic Medical devices

Millions of people's quality of life is severely impacted by diseases. While for many of them pharmaceuticals are of great help, for others they cause side effects or do not achieve satisfying therapeutic outcomes.

Bioelectronic medical devices may become a paradigm shift. By selectively stimulating distinct nerves they will enable targeted treatment of indications with high unmet medical needs and the reduction of side effects.



We are working to enable innovative neurostimulation treatments building on our Electronics and Healthcare capabilities

Aspects of our work include:

- Bioelectronic treatment regimes in Merck's therapeutic areas
- Next generation neuro-recording and -stimulation technologies
- Precise disease targeting leads to personalized medicine
- Continuous data gathering & analysis allows AI powered solutions for improved patient outcomes



Highly selective vagus nerve recording and stimulation by novel multichannel electrode design

Despite clinical data showing efficacy of bioelectronic treatments and approved treatments, today's devices show limited stimulation selectivity resulting in low efficacy & responder rates

We are working on solving this challenge together with the leading external startup Neuroloop GmbH

Collaboration with Neuroloop

- Development of a neurostimulator using a differentiated multichannel electrodes that allow personalized treatments of severe chronic patients.
- Combining signals from the peripheral nervous system with other physiological datasets for novel digital healthcare solutions



Boost energy efficiency to enable new treatments or minimize devices

Bioelectronic devices are continuously requiring more power (higher computing power, data communication, stimulation) yet at the same time, the devices are expected to miniaturize further.

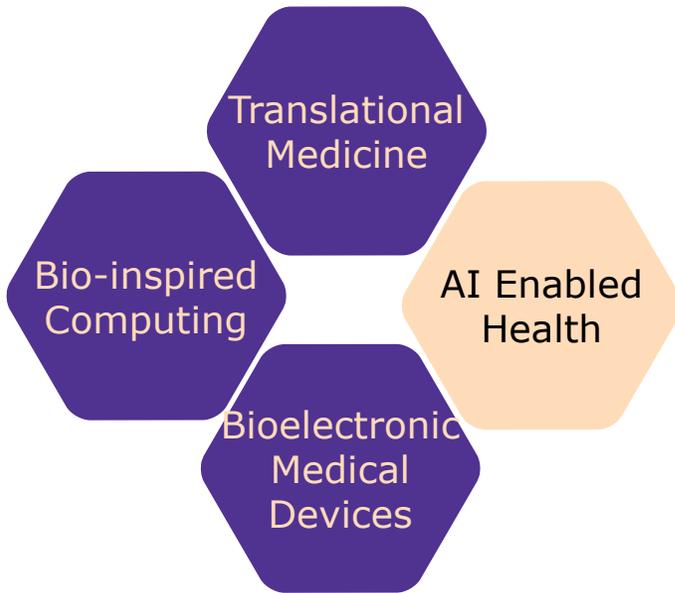
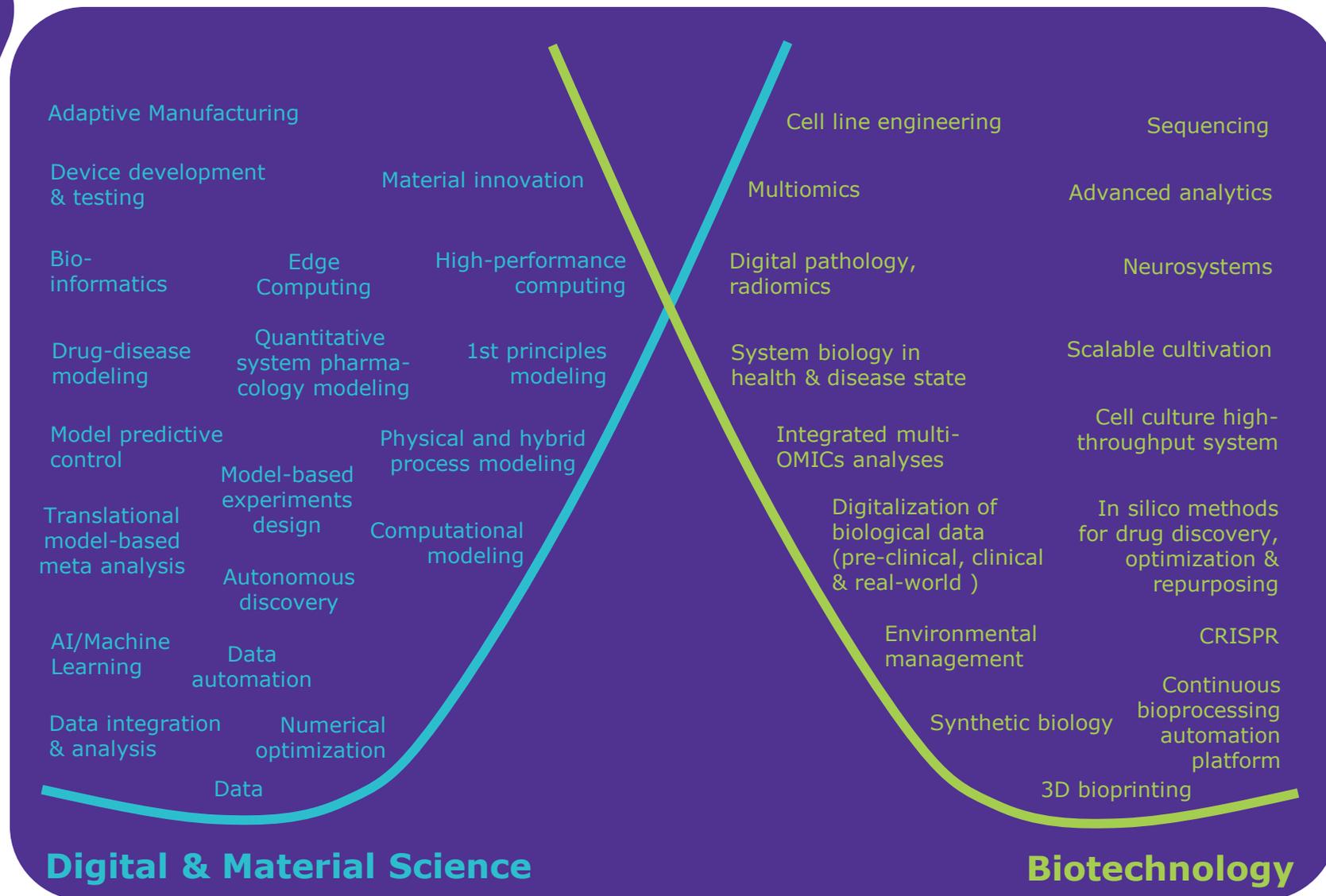
We are collaborating with startup company Innervia Bioelectronics, to solve this energy dilemma.

Collaboration with Innervia

- Introducing graphene oxide electrodes for significantly decreasing power consumption while maintaining stimulation efficacy
- Development of this technology for the bioelectronic treatment of chronic diseases which would require energy amounts current technologies are unable to satisfy



Broad spectrum of technologies are converging



4 Example Areas for Bioconvergence

* Non exhaustive overview of competencies



AI-enabled health

Caring for patients by unlocking the value of data along the pharma value chain

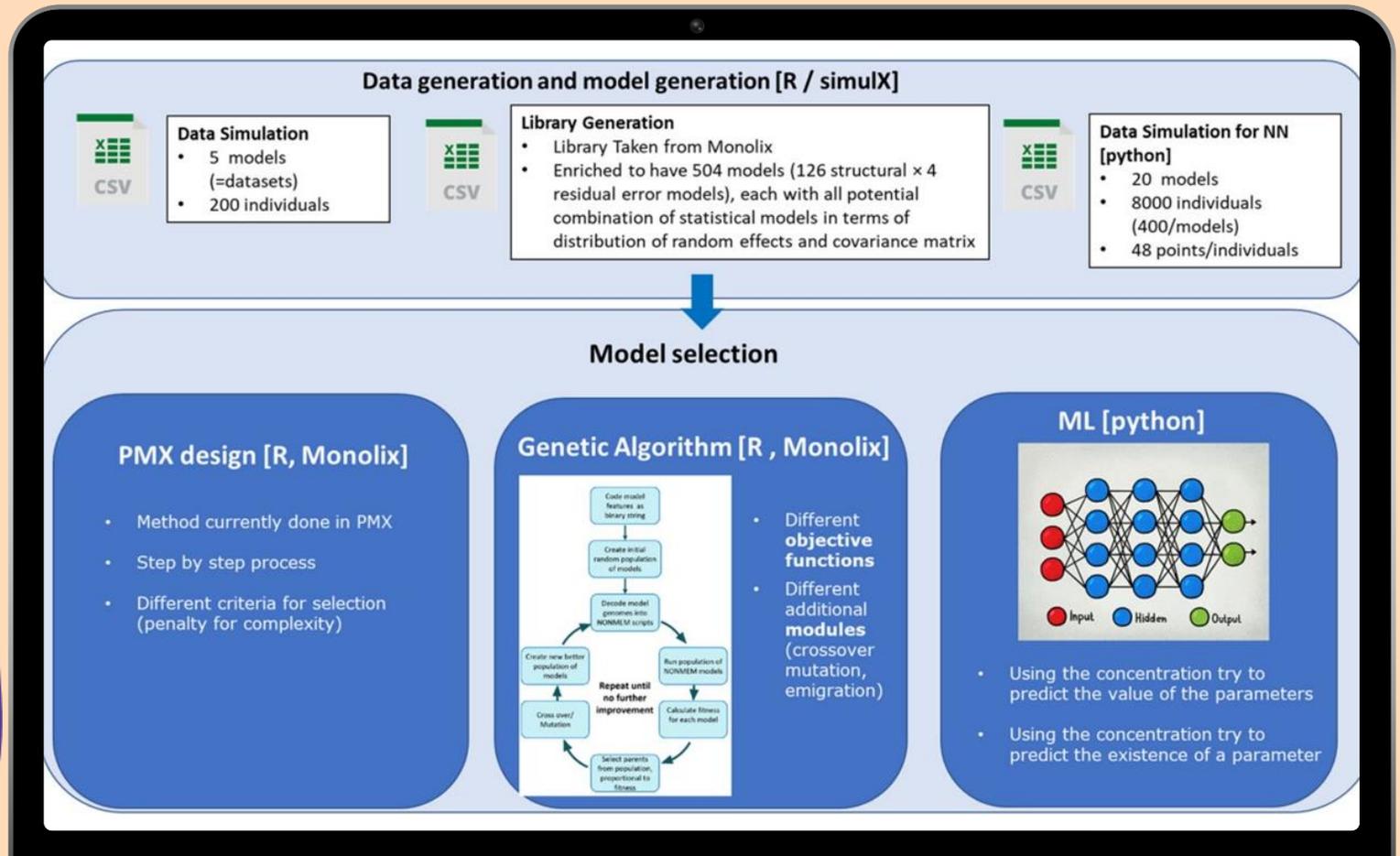


Model selection

Population pharmacokinetic model selection assisted by machine learning

Model-informed drug discovery and development (MID3)

- Key role at each stage of drug development
- Large range of applications, including:
 - characterizing the drug concentration-pharmacodynamic (PD) response relationships, explaining drug variability by identifying clinically relevant factors which impact on desired outcomes, predicting the consequences of formulation changes on drug performance



Natural language processing (NLP)

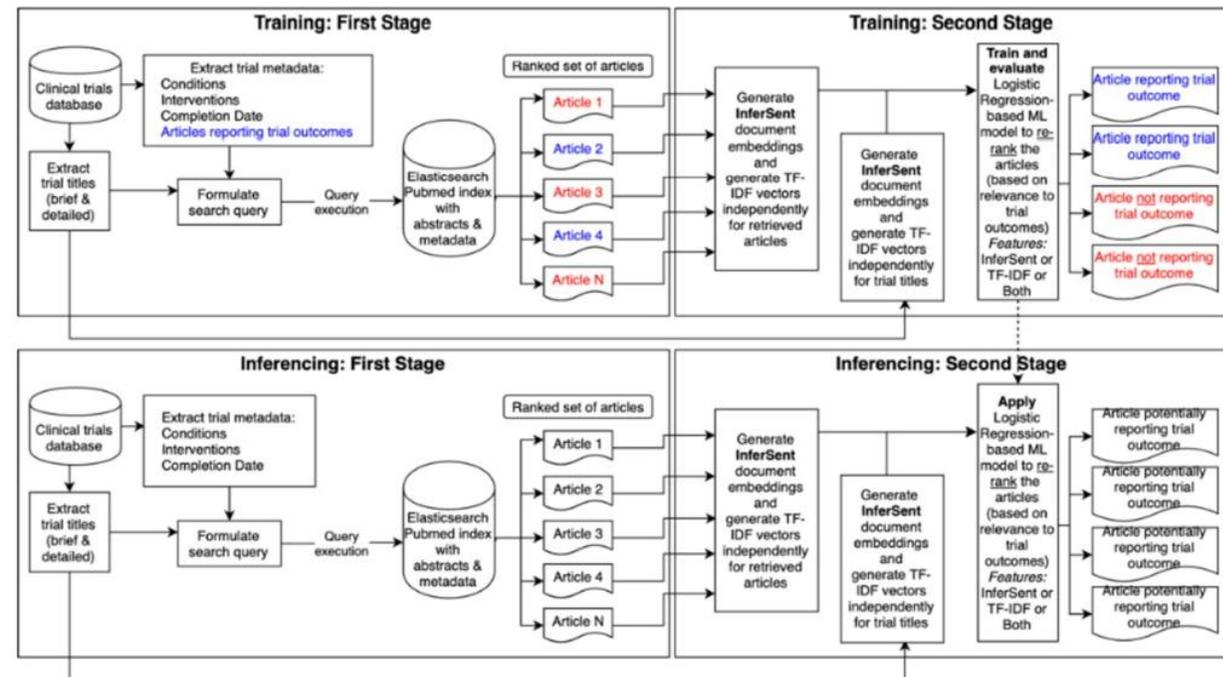
Evidence synthesis and decision support through Natural Language Processing (NLP)

Challenge

Missing links between large portions of trials registered in clinical trial registries and their reported outcomes published in scientific journals ->

Solution

Novel natural language processing-based system to establish links between clinical trials and their published outcomes in literature



Tapping into the drug discovery potential of AI



Successful pioneer: Exscientia

First two molecules designed with the help of AI to enter clinical trials [oncology drug for solid tumors and serotonin reuptake inhibitor (SSRI)]



Collaboration Merck KGaA<>Iktos

Iktos licenses their ML modules to pharma companies to be applied with their data and in-house expertise



collaboratively Accelerating AI Health research



Accelerating the discovery of materials and molecules needed for a sustainable future

This graphic features the text 'WE ARE AION LABS THE FUTURE OF PHARMA' in large blue letters on a black background. To the right, a white, cloud-like shape contains several partner logos: ISRAEL BIOTECH FUND, AWS, MERCK, Pfizer, teva, AstraZeneca, BioMed X, and Digital Israel. The text 'Powered by' and 'Supported by' is placed above the respective logos.



Digital Ethics Advisory Panel and Code of Digital Ethics (CoDE): setting standards in an undefined field



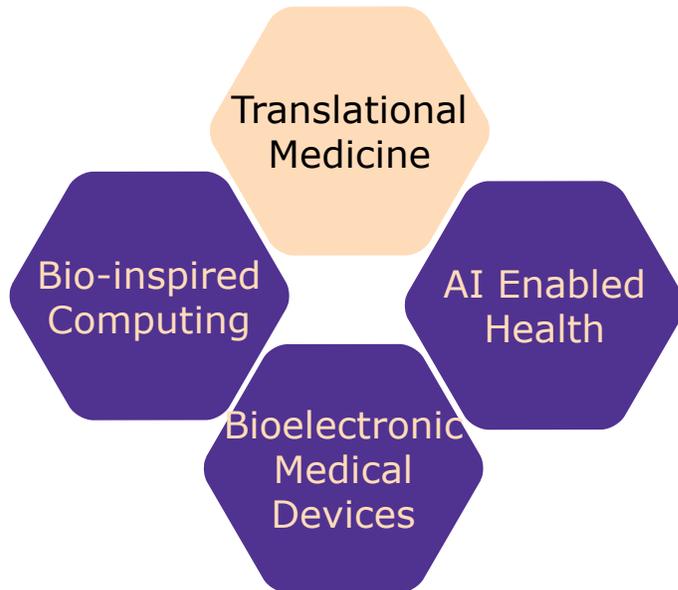
Code of Digital Ethics (CoDE)

Basing CoDE on established principles ensures applicability & acceptance

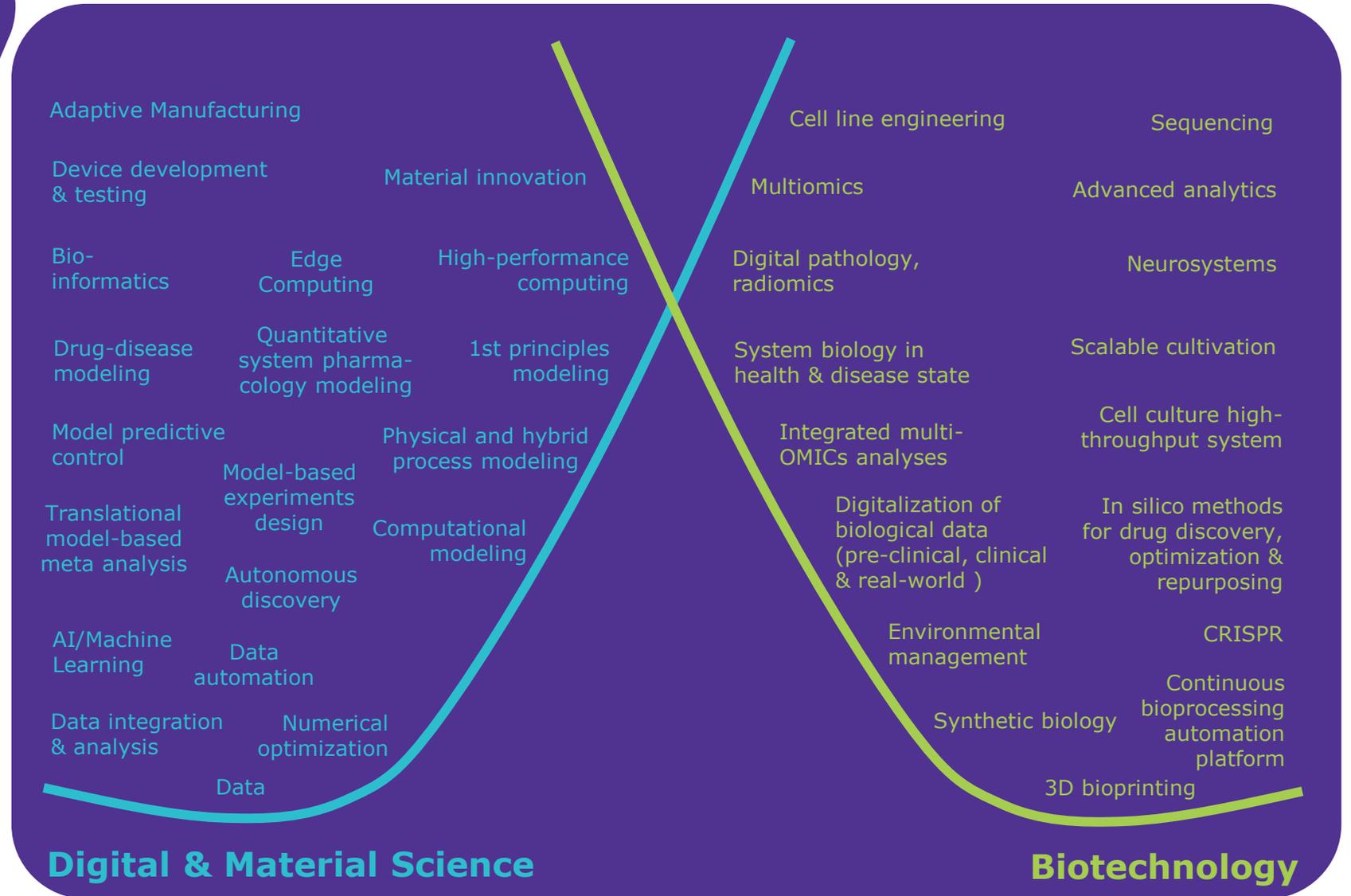
Each Principle is defined by 3 sub-principles: holistic ethical perspective for digital offerings



Broad spectrum of technologies are converging



4 Example Areas for Bioconvergence



* Non exhaustive overview of competencies



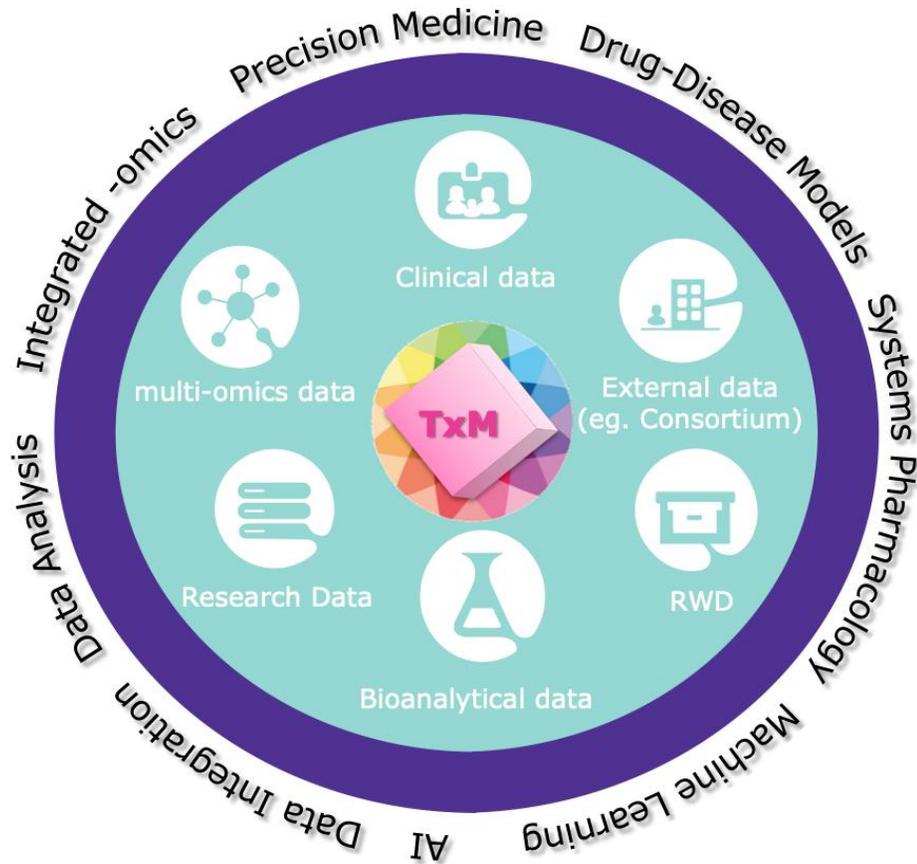


Translational Medicine

Enhance confidence in Target, Patient and Dose integrating data and novel scientific hypotheses from preclinical (bench-to-bedside) to clinical practice (bedside-to-bench) settings



Transforming data to knowledge in Translational Medicine: optimization across the dimensions of target, patient, and dose



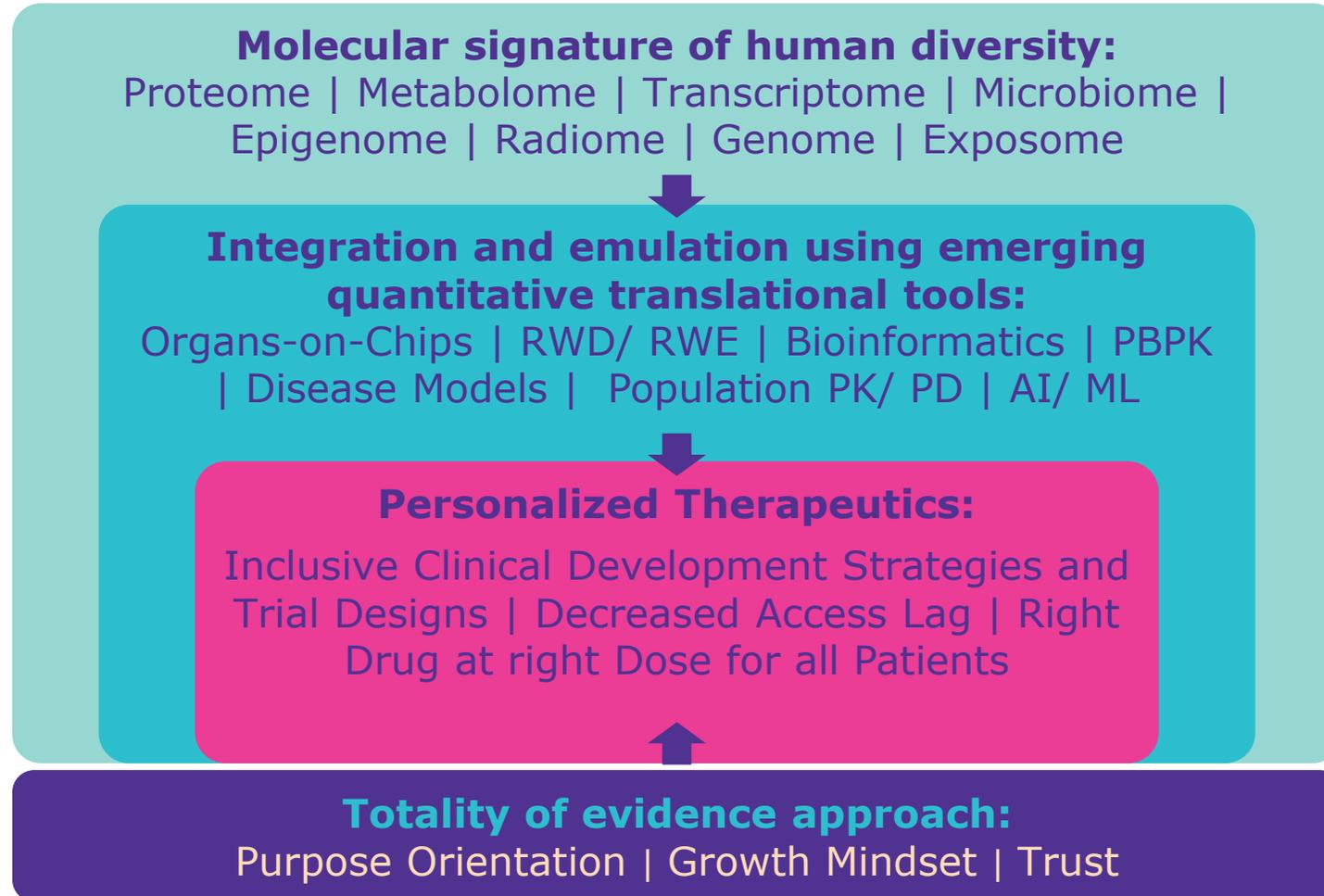
Advanced analytics as a strategic enabler of Translational Medicine:

- Quantitative integration powered by multiple advanced analytical solutions
- Innovative support for forward and reverse translation
- Strategic focus on building confidence in target, patient, and dose

Source: Terranova N, Venkatakrishnan K, and Benincosa LJ. AAPS J. 23(4):74, 2021



Tackling population diversity in human biology with translational tools and advanced analytics



Enabling

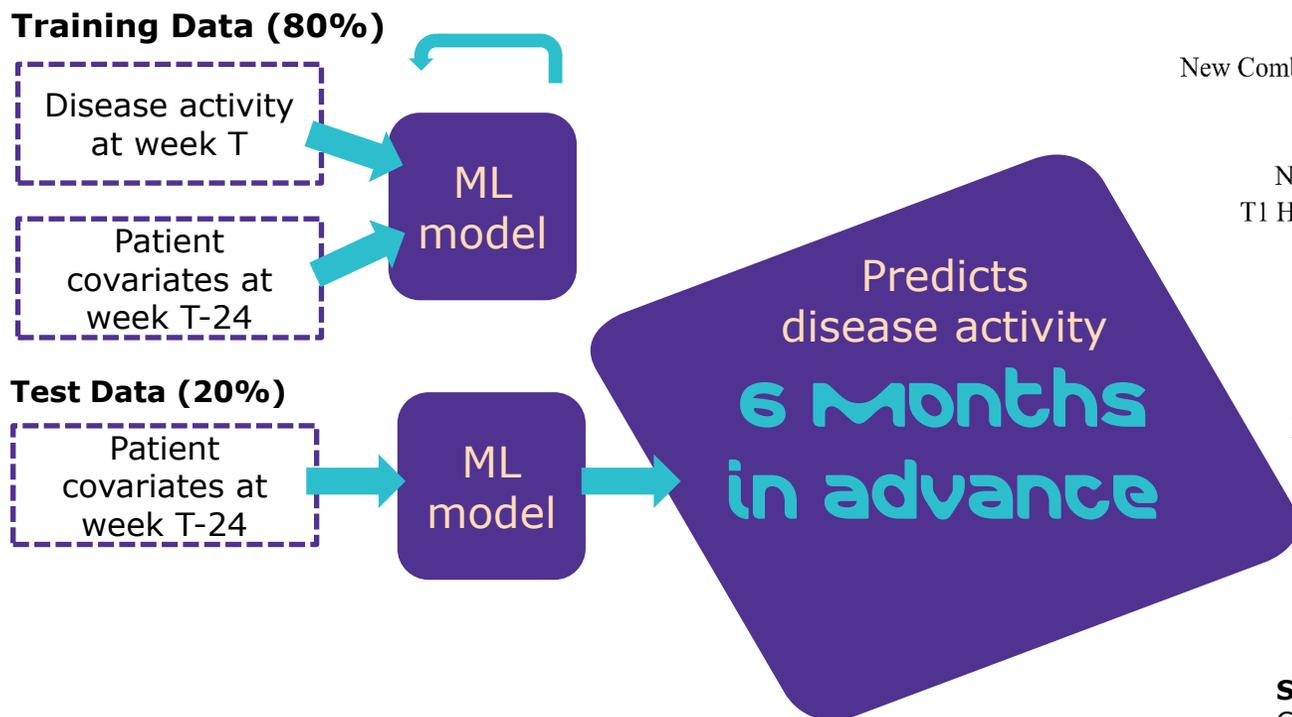
- Efficient Precision Medicine Development
- Inclusive Clinical Development

Source: Venkatakrisnan K and Benincosa LJ. Clinical Pharmacology and Therapeutics. <https://doi.org/10.1002/cpt.2416>

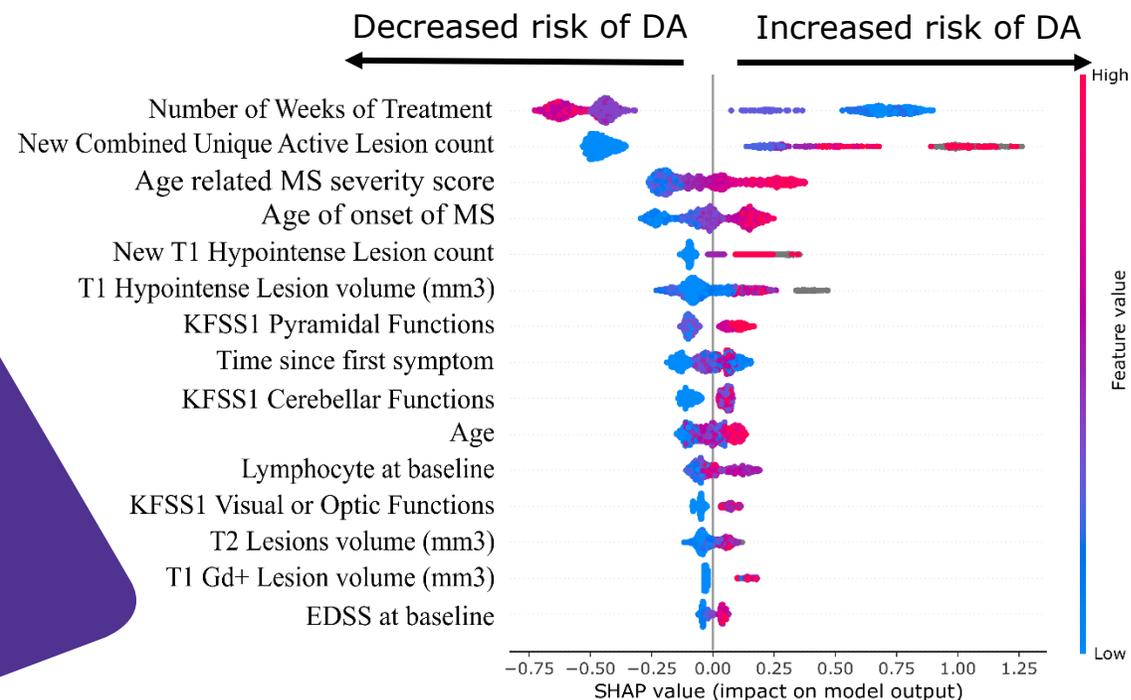


A machine learning approach in MAVENCLAD trials to find early predictors of Multiple Sclerosis disease activity

Machine Learning model predicts risk of future disease activity with 80% accuracy on unseen patient data



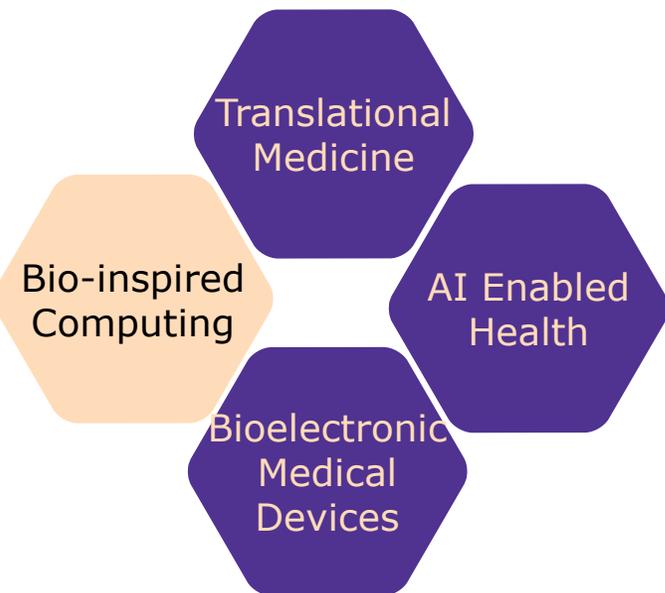
Top predictors of future disease activity (DA) identified by explainable ML methods



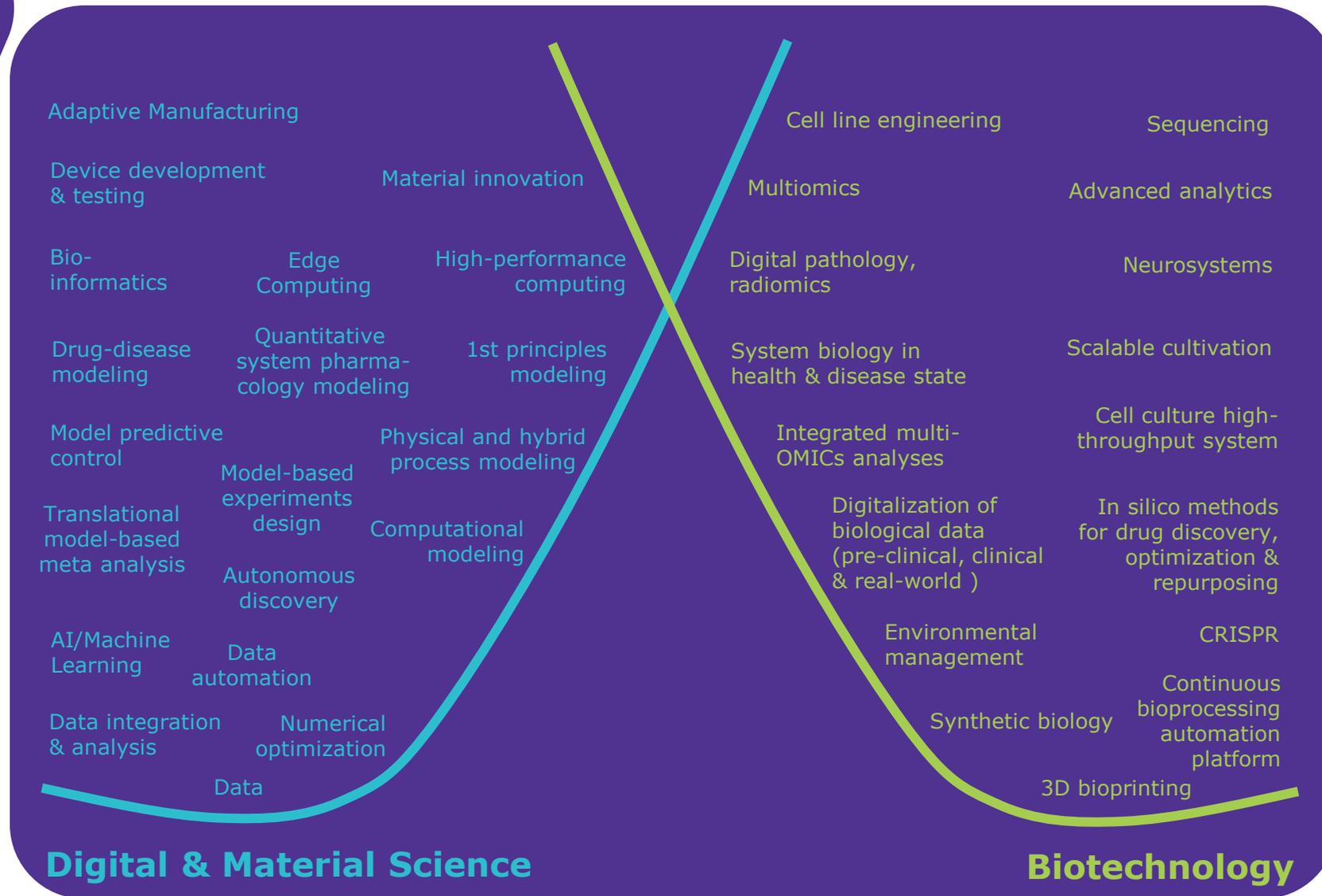
Source: S. Basu, A. Munafo, A. Ben-Amor, S. Roy, P. Girard, N. Terranova. CPT: Pharmacometrics & Systems Pharmacology (2022)



Broad spectrum of technologies are converging



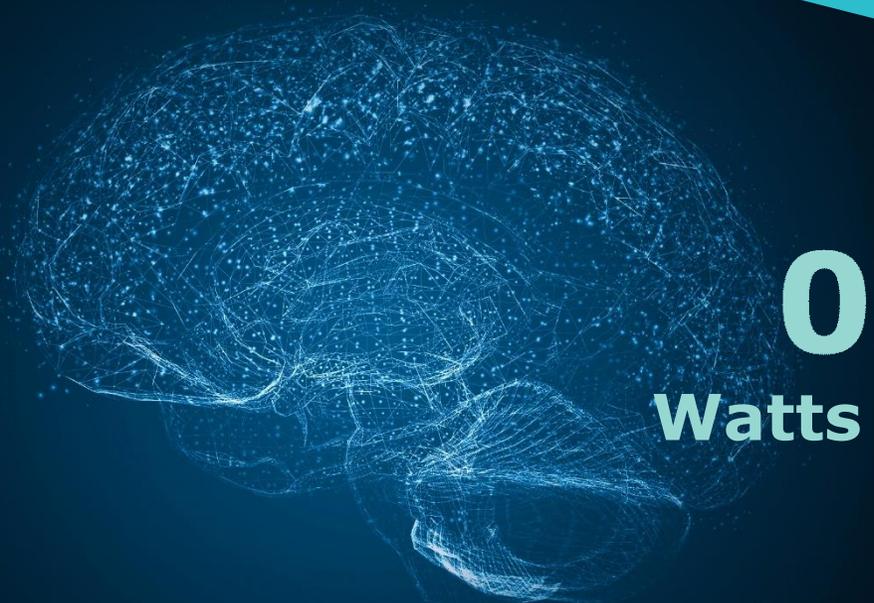
4 Example Areas for Bioconvergence



* Non exhaustive overview of competencies



HUMAN BRAIN VS. CUTTING- EDGE SUPER- COMPUTER



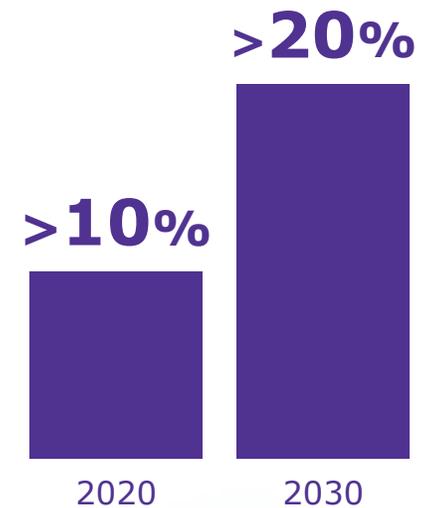
0
Watts



0,000
Watts

INFORMATION AND COMMUNICATION TECHNOLOGY

Global energy use

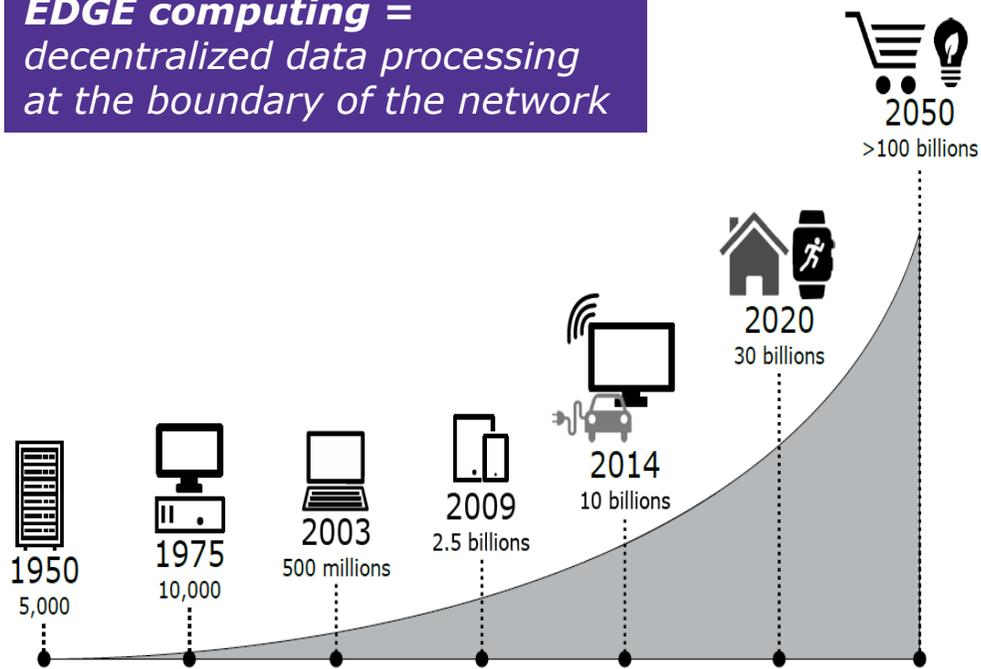


Moving from the cloud to the edge

Why do we need Edge AI?

30bn IoT devices fueling the edge 2020

EDGE computing =
decentralized data processing
at the boundary of the network



Source: Maurizio Capra, Future Internet 2019, 11, 100

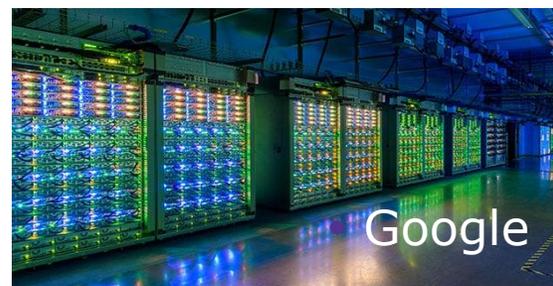
“Fundamentally because that’s where all the data is!”



Airbus A-350 jet has over 6,000 sensors and generates **2.5 terabytes** of data each day it flies



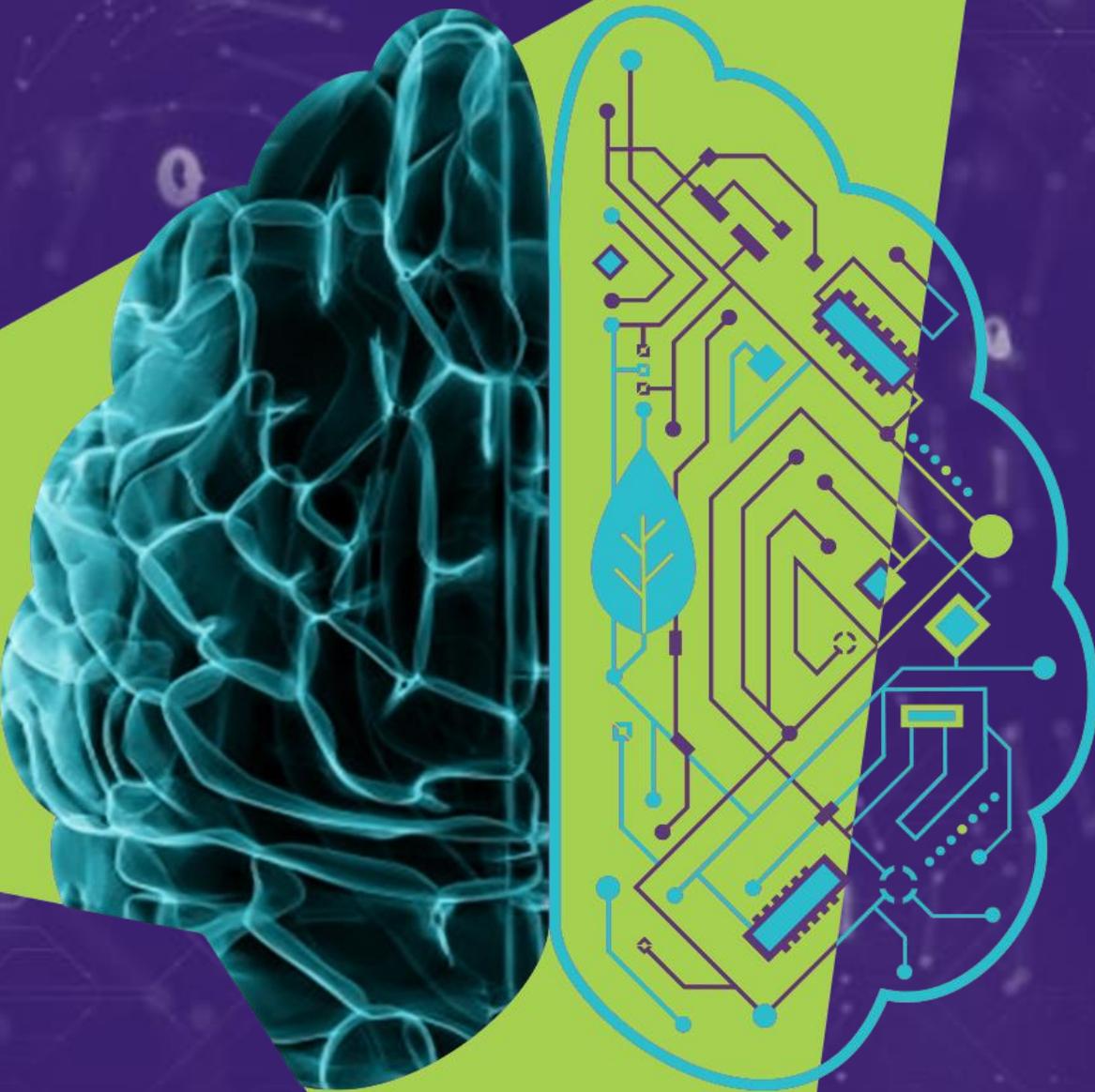
Globally security cameras create about **2,500 petabytes** of data per day



If everybody used their Android Voice Assistant for **3 min per day** they would have to **double** the number of data centers they owned.

Source: Deloitte, TMT Predictions 2020; Pete Warden, Google



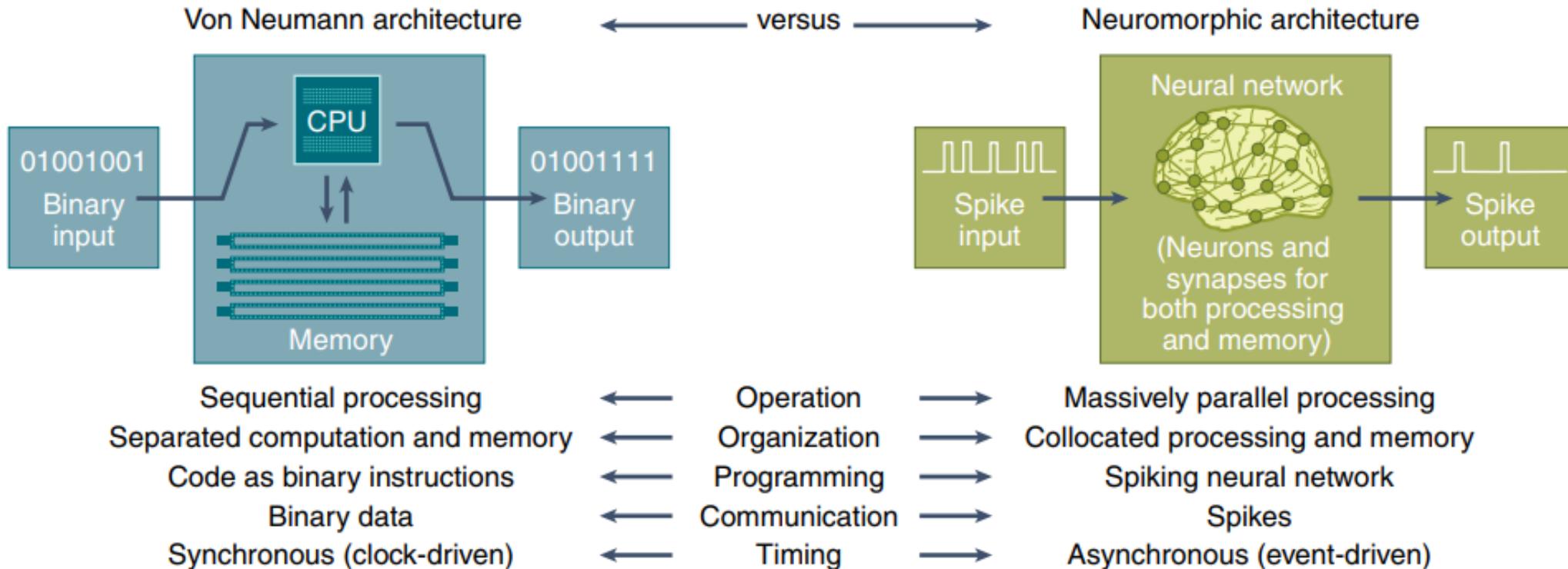


MERCK
Electronics
kicks off:

NEUROMORPHIC COMPUTING INCUBATOR

Our Silicon Valley
strategic initiative to
productize neuromorphic
synaptic memory designs
using proprietary in-house
materials

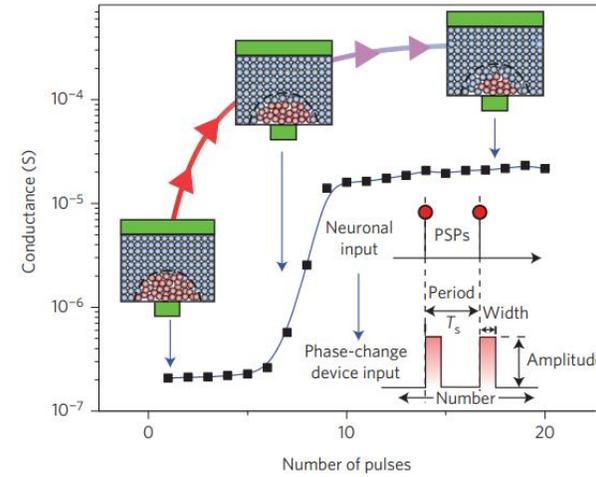
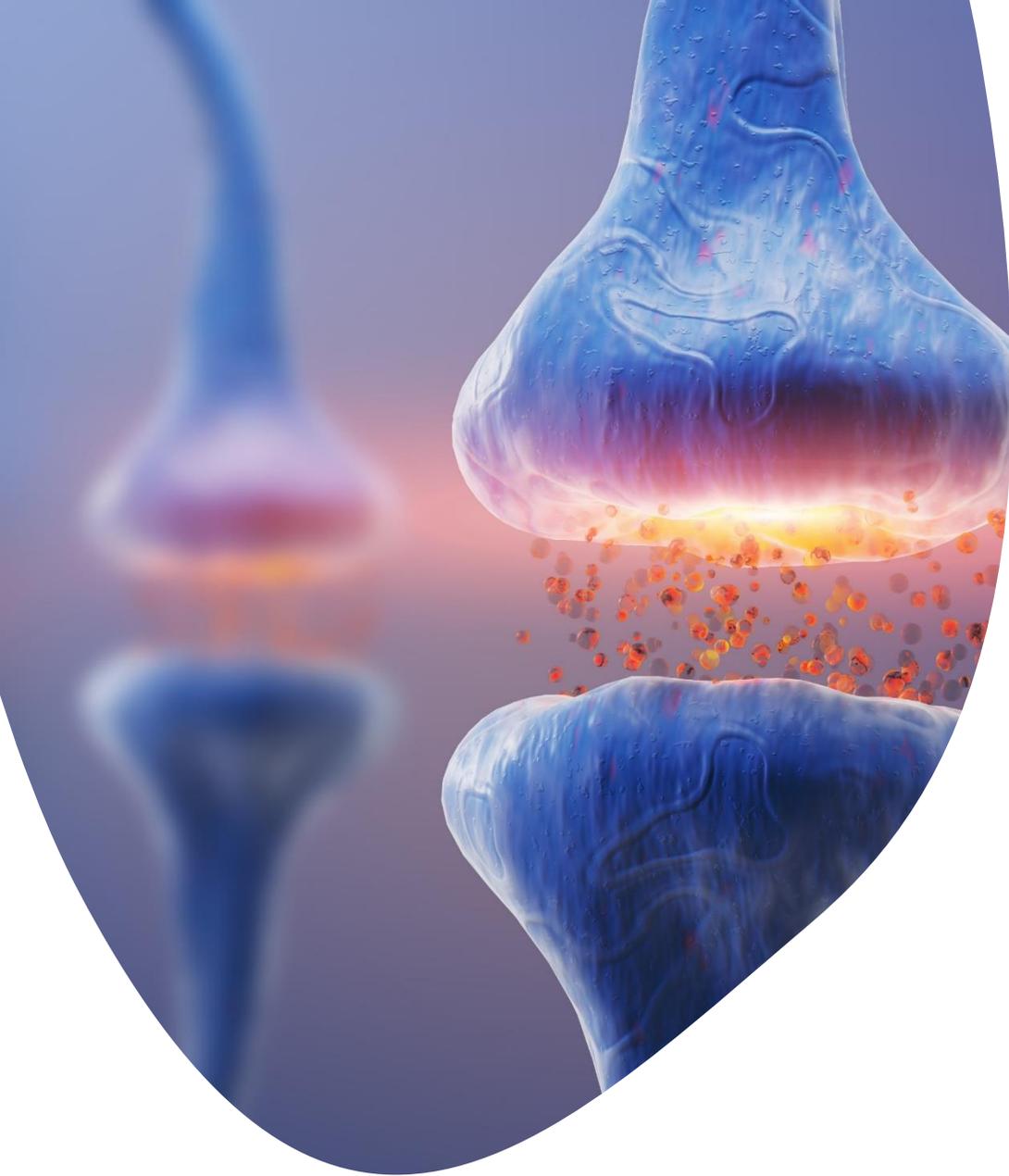
Fundamental differences between von Neumann and neuromorphic architecture



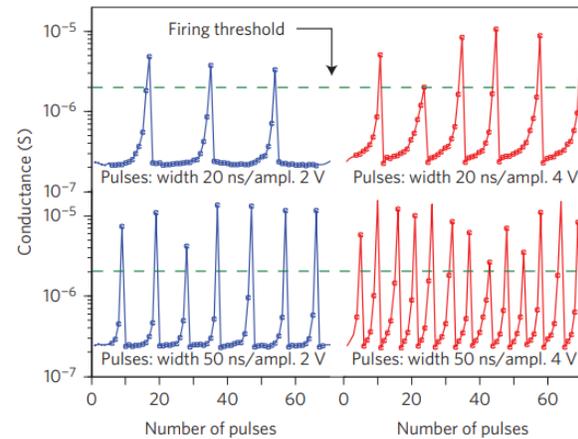
Source: Schuman, C.D., Kulkarni, S.R., Parsa, M. *et al.* Opportunities for neuromorphic computing algorithms and applications. *Nat Comput Sci* **2**, 10–19 (2022).



NEURON



Evolution of the phase-change device conductance as a function of the number of crystallizing pulses for the pulse sequence



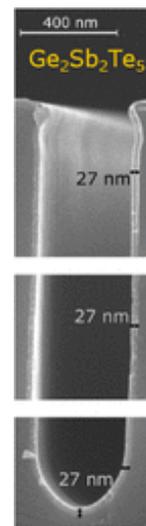
Integrate-and-fire dynamics in a phase-change **neuron**

Source: Tuma, T. et al, *Nature Nanotech*, 2016

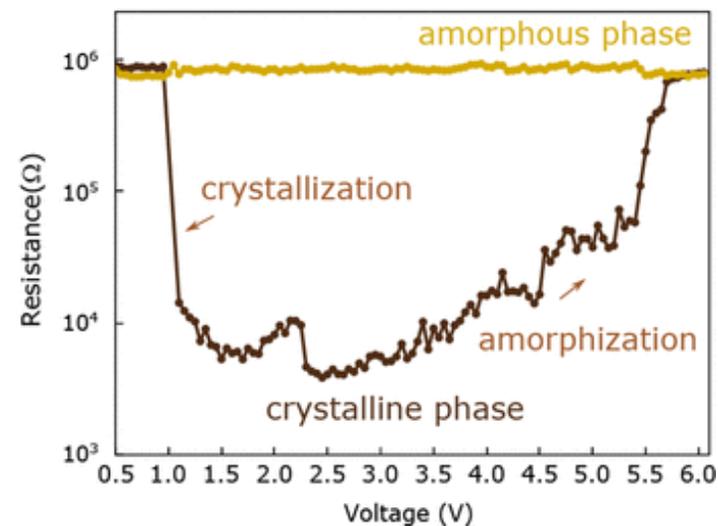


Chalcogenide compounds are the main characters in a revolution in electronic memories

Composition-Controlled Atomic Layer Deposition of Phase-Change Memories (PCM) and Ovonic Threshold Switches (OTS) with High Performance



Silicon trench Structure



Resistance-voltage characterization

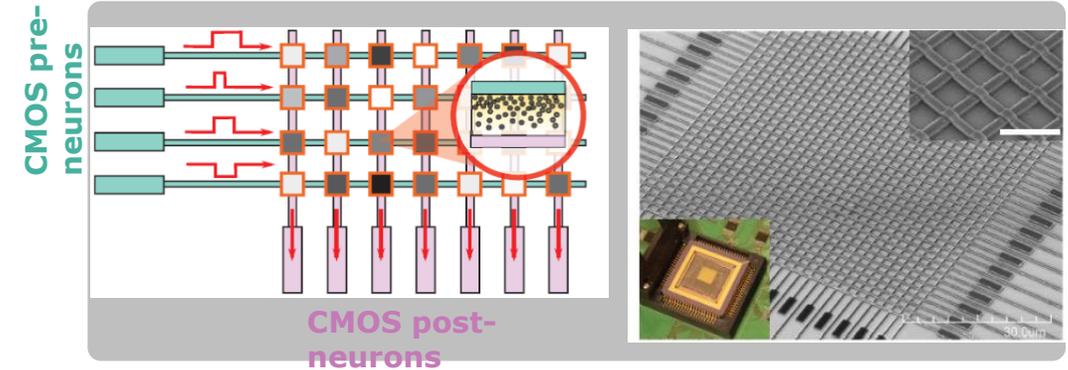
Source: DOI: 10.1021/acsnano.9b04233 ACS Nano 2019, 13, 10440–10447; US7960205B2



Seeding the ecosystem using M-Ventures Investments



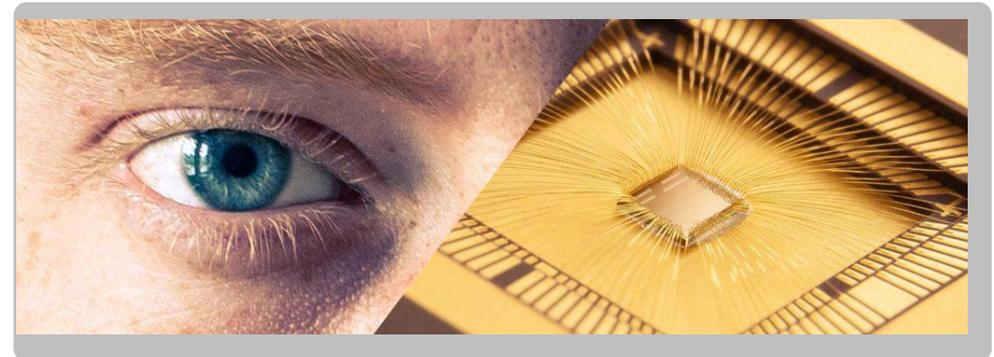
Computing and storing at the same location



Source: Nano Letters 2012, Wei Lu, University of Michigan



Dedicated event-driven neuromorphic processors for real-time vision processing

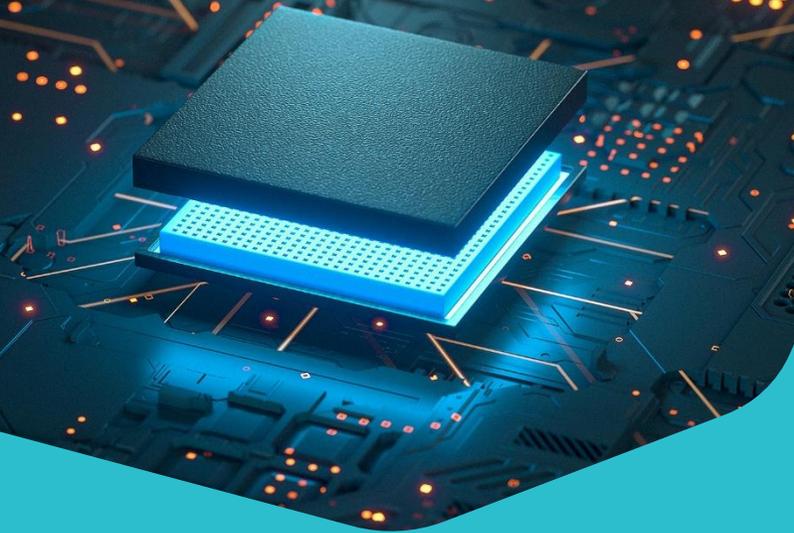


Source: <https://www.synsense-neuromorphic.com/>



DNA-based storage

The ultimate bio-convergence example?



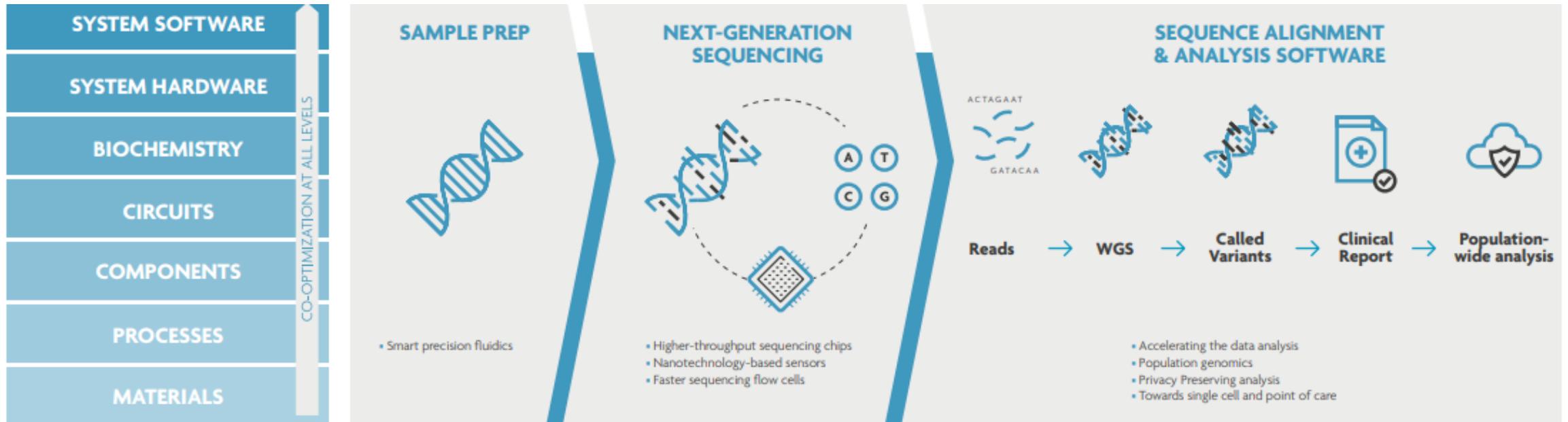
EVOLUTION

vs.

REVOLUTION



Semiconductor technology can bring value to the different steps in sequencing, from sample prep to data analysis



Source: White paper on semiconductor technologies and system concepts to revolutionize genomics, <https://www.imec-int.com/en/whitepaper-genomics>



Key Takeaways

- Bioconvergence is rapidly disrupting numerous fields, and we're just at the beginning of this inflection point
- Future technology complexity requires a multi-disciplinary solutions
- Digital is a backbone of key advancements going forward
- The challenges are numerous, the opportunities are immense, and the solutions will require deeper and broader collaboration across industries and the academic/industry pipeline





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