



BIOHYBRID NEURAL PROCESSOR



Using Living Neurons to Simulate Drug Effects and Cognitive Processing

AI in Drug Discovery & Molecular Design

AI for Clinical Pharmacy & Medication Safety

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INTRODUCTION

Central nervous system (CNS) drug discovery remains one of the most challenging areas in pharmaceutical research, with nearly 90% of candidates failing in clinical trials due to poor translational models. Conventional systems such as 2D cell cultures and animal models fail to replicate the complexity of human neural networks and dynamic signaling.

To address this gap, we propose the **BioHybrid Neural Processor (BNP)** - an innovative platform that integrates living human neurons with microelectrode arrays and artificial intelligence. This system enables real-time simulation and analysis of drug effects on functional neural networks, offering a more accurate, efficient, and ethically advanced approach to CNS drug testing.



THE PROBLEM — WHY CNS DRUG DEVELOPMENT IS FAILING

>90%

CNS drug candidates fail in clinical trials

99.6%

Alzheimer's drug attrition rate

\$2.6B

Average cost per CNS drug to market

~1B

People globally with CNS disorders (WHO)

115M+

Animals used in research/yr globally

12–15yrs

Average CNS drug development timeline

99%

CNS drugs blocked by the BBB

\$60B+

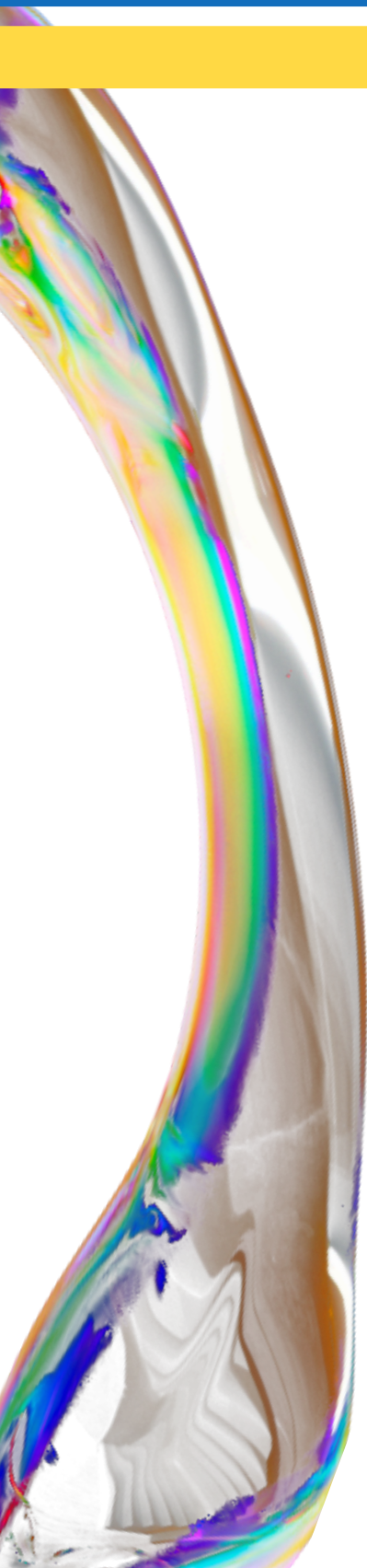
Annual economic burden of CNS drug failures

Root Cause: Preclinical models (2D cultures, animals) lack biological authenticity — failing to predict real CNS drug behaviour, wasting time, money, and 115 million animal lives every year.



WHY CURRENT MODELS FAIL — HEAD-TO-HEAD COMPARISON

Parameter	2D Cell Cultures	Animal Models	In Silico Models	BNP Platform
Human relevance	Moderate	Low (species gap)	Moderate (coded)	Direct — iPSC human
Network dynamics	None	Present but invasive	Simulated only	Real — live network
Animal use	Low	Millions killed/yr	None	Zero — fully in vitro
Energy consumption	Low	High (facility costs)	GPU-intensive	~1000× less than GPU
Self-adaptation	None	Present	Needs retraining	Neurons self-adapt
Human translatability	Partial	Species gap failure	Partial	Living human neurons
Drug trial phases	Supports Phase 0	Supports Phase 0-1	Supports Phase 0	Can compress phases
Regulatory acceptance	Standard	Standard	Emerging	FDA approved 2024



WETWARE COMPUTING — BIOLOGY MEETS SILICON

Cortical Labs - CL1 (2024)

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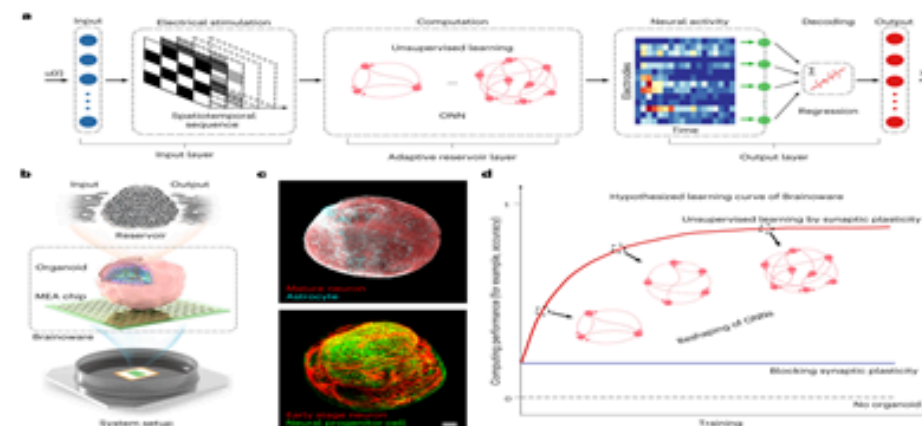
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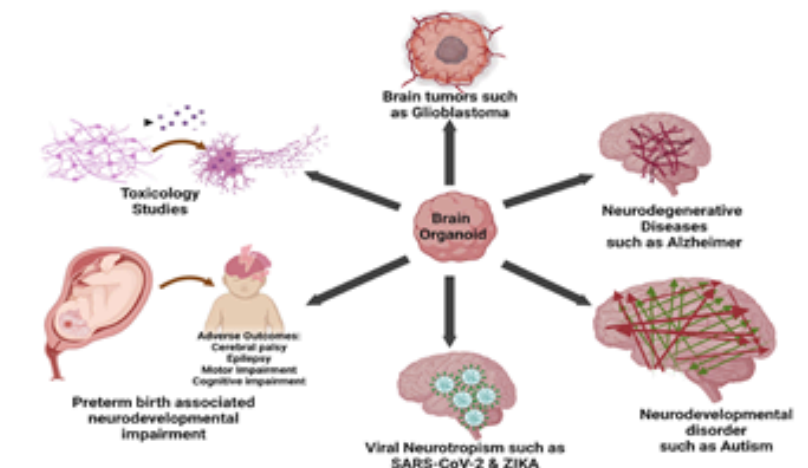
Indiana University. Brain organoid on HD-MEA chip. 78% speech recognition accuracy. Published Nature Electronics. Proof that biological neural tissue performs real computation — self-adapting with each training stimulus, no backpropagation required.



Organoid Intelligence (OI)

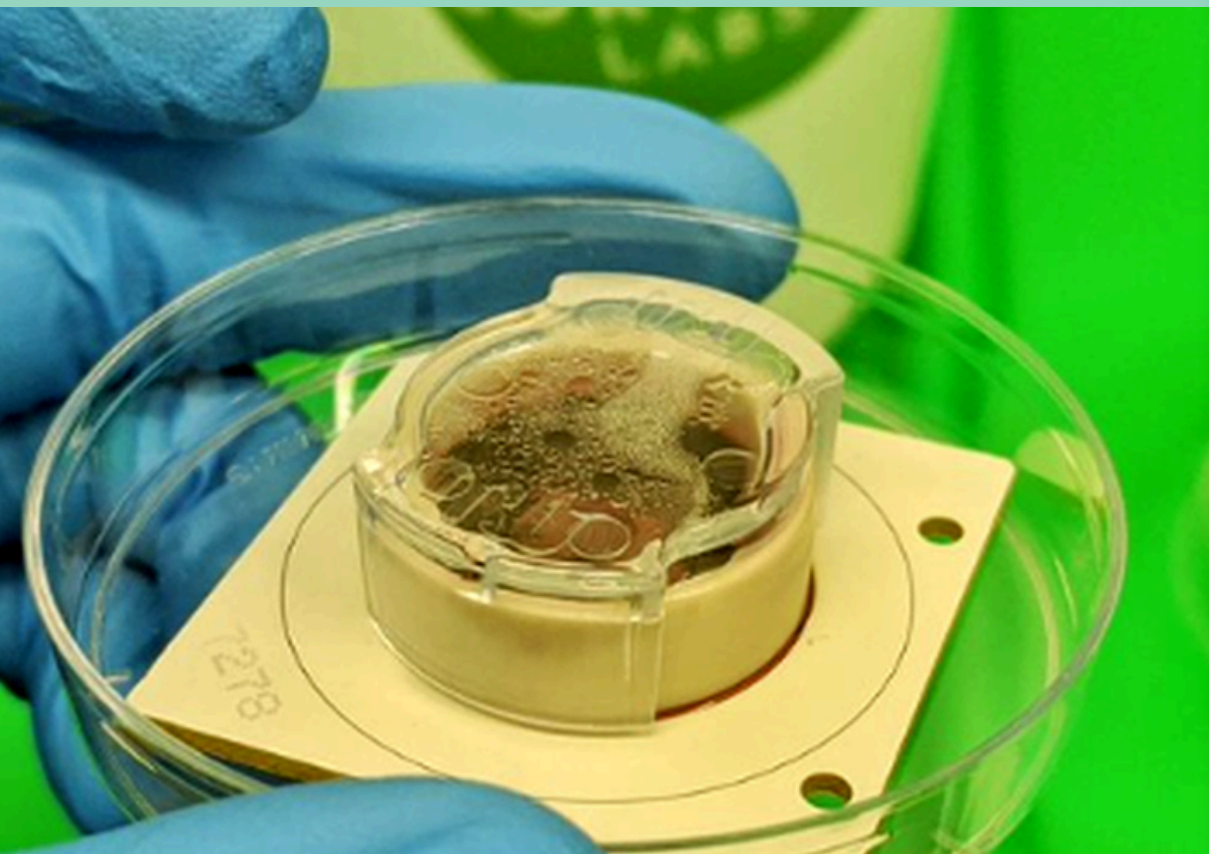
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Frontiers in Science framework (2023). Defines biocomputing using brain organoids, MEA, and AI decoding. Estimates 1mm³ organoid contains ~100,000 neurons — processing capacity exceeding many conventional neural network architectures.



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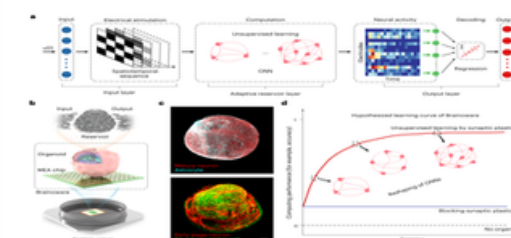
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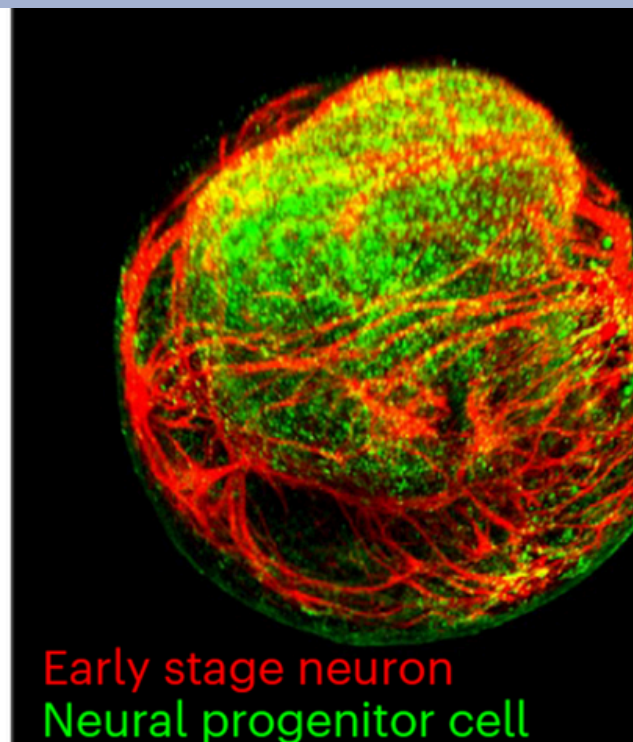
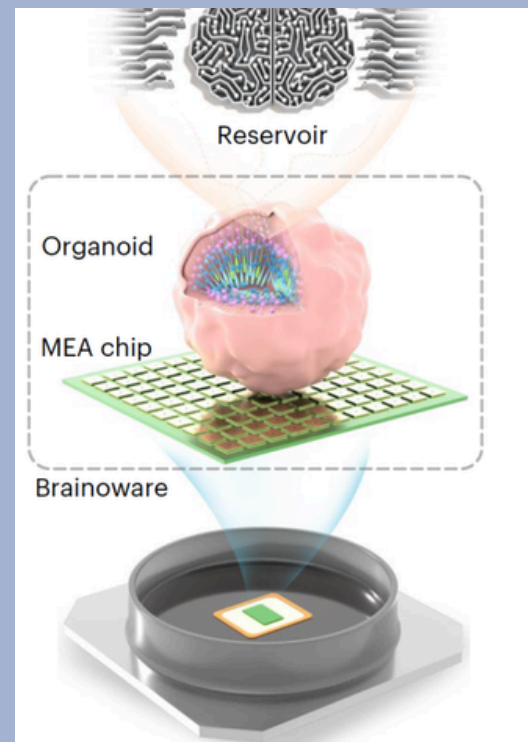
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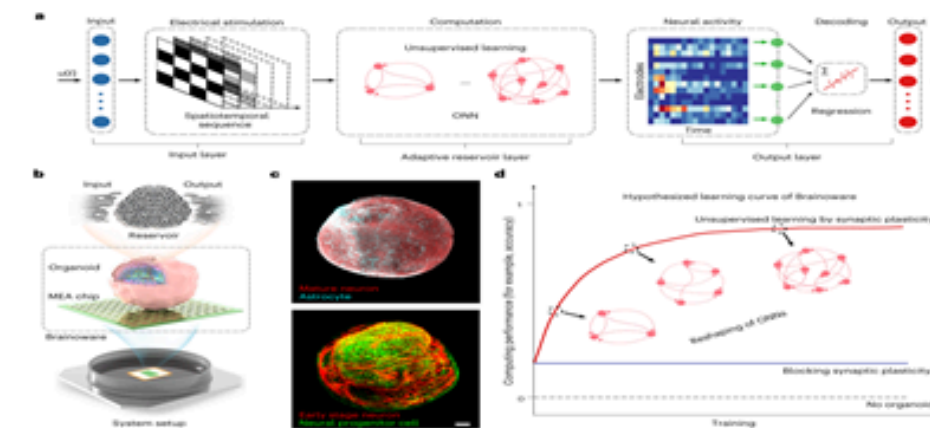


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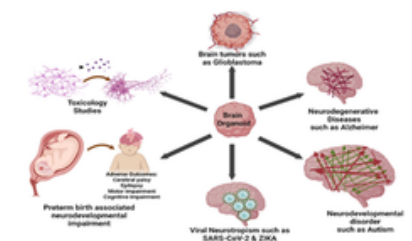
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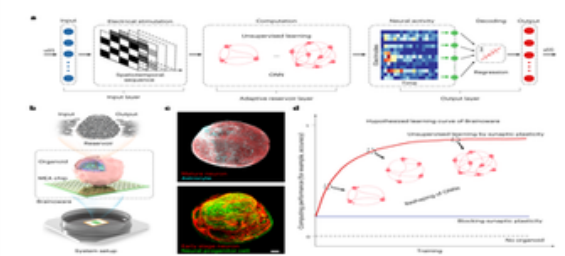
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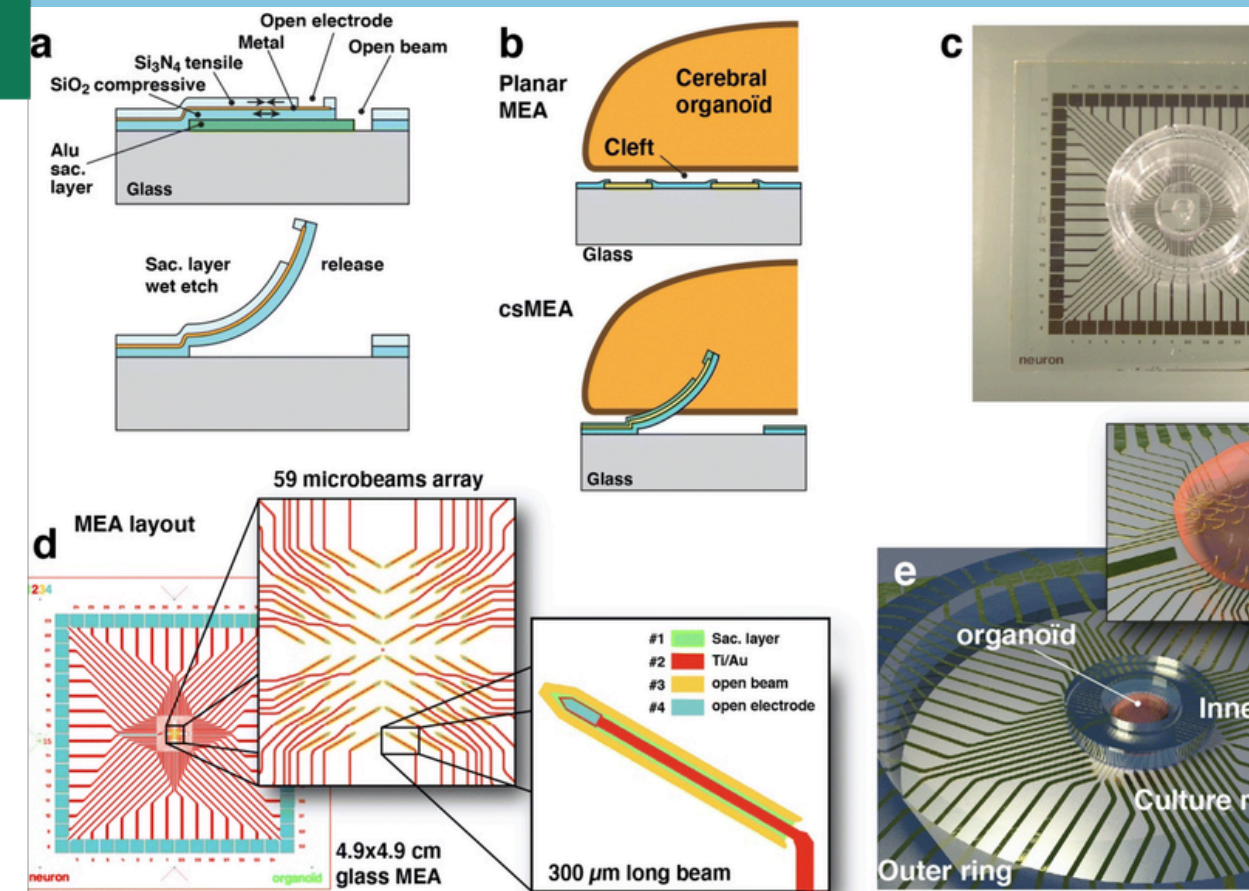
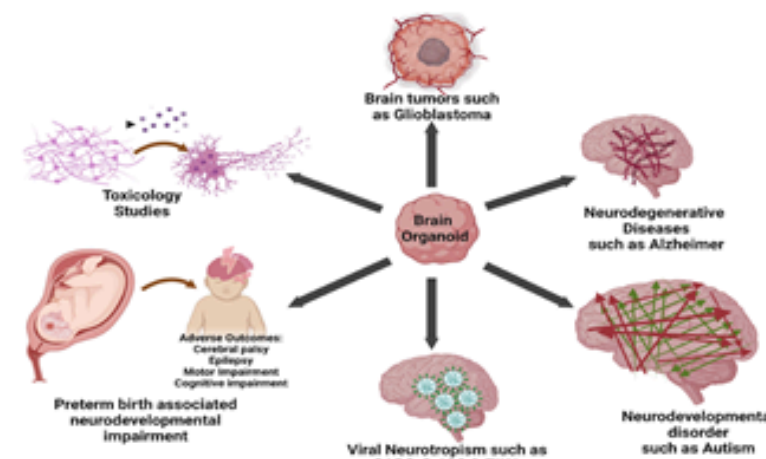
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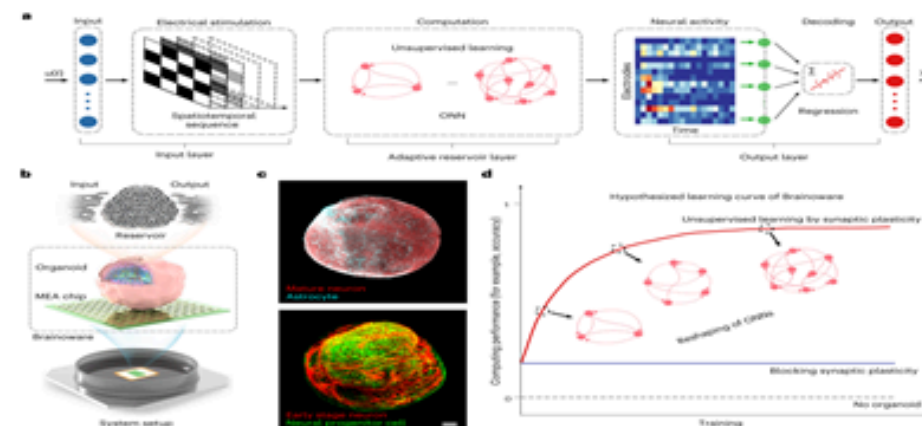
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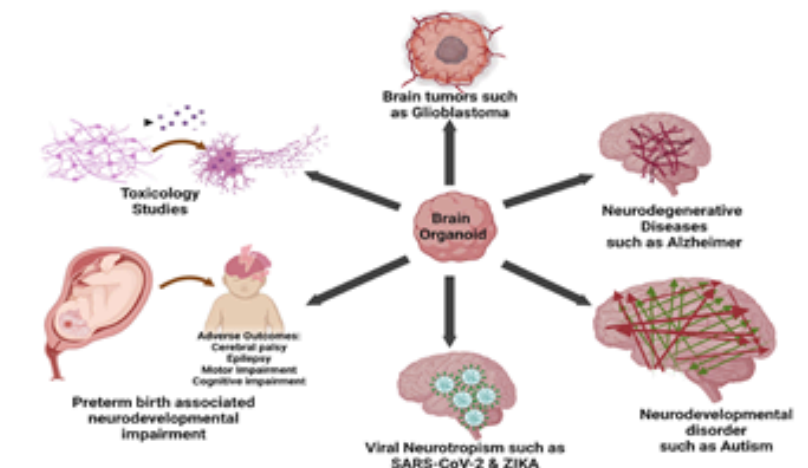
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WHY NEURONS BEAT SILICON — THE COMPUTATIONAL REVOLUTION



Conventional AI / Silicon

Energy

Massive electricity use (megawatts).
Training ~50 GWh → powers 4,500 homes/year.

Adaptability

Needs millions of labelled data + retraining cycles. No real-time adaptation.

Biological Fidelity

Simulations only. Cannot replicate true synaptic plasticity or ion channels.

Cost

\$100M+ GPU clusters. High cloud inference costs.
~284 tonnes CO₂ per model training.

BioHybrid Neural Processor (BNP)

Energy

Runs on glucose & ATP. ~20W efficiency.
Near-zero electrical cost.

Adaptability

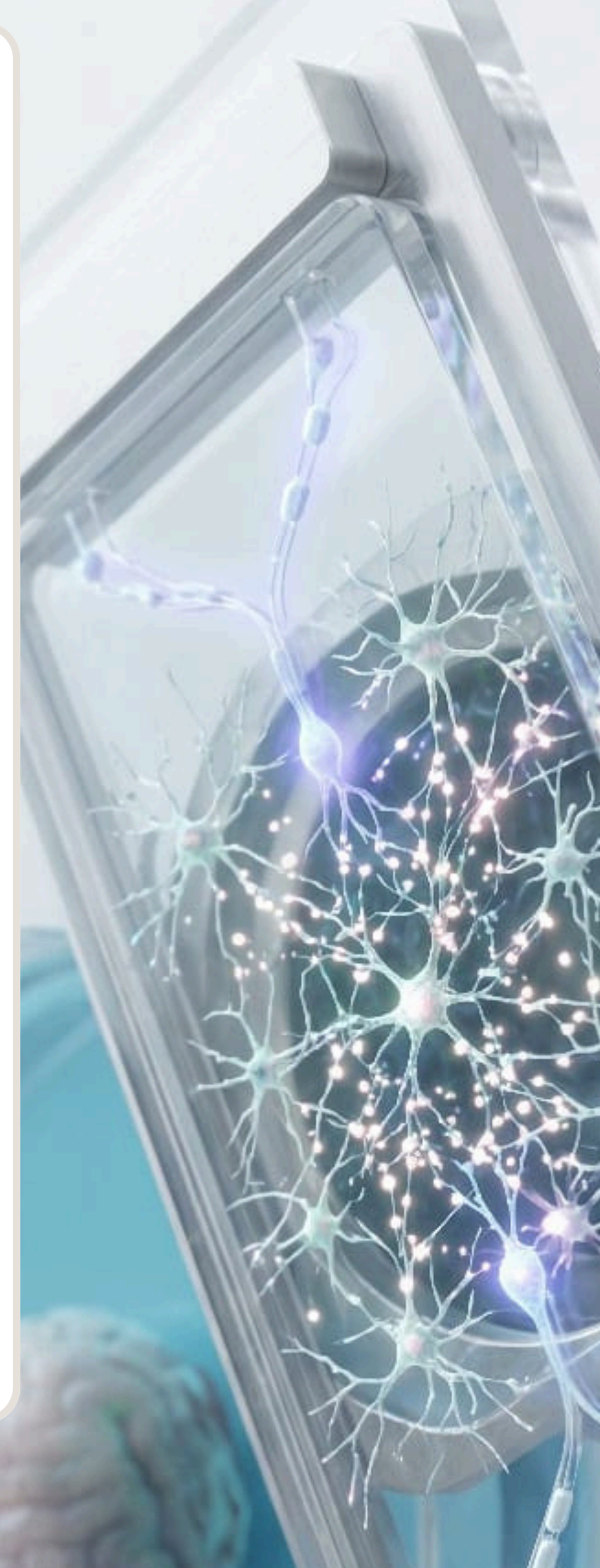
Self-learning neurons. Real-time synaptic updates (LTP). No retraining needed.

Biological Fidelity

Real neurons. True ion channels, plasticity & drug response modeling.

Sustainability

~\$200-500 setup. Runs for months.
Highly efficient biology-driven computation.



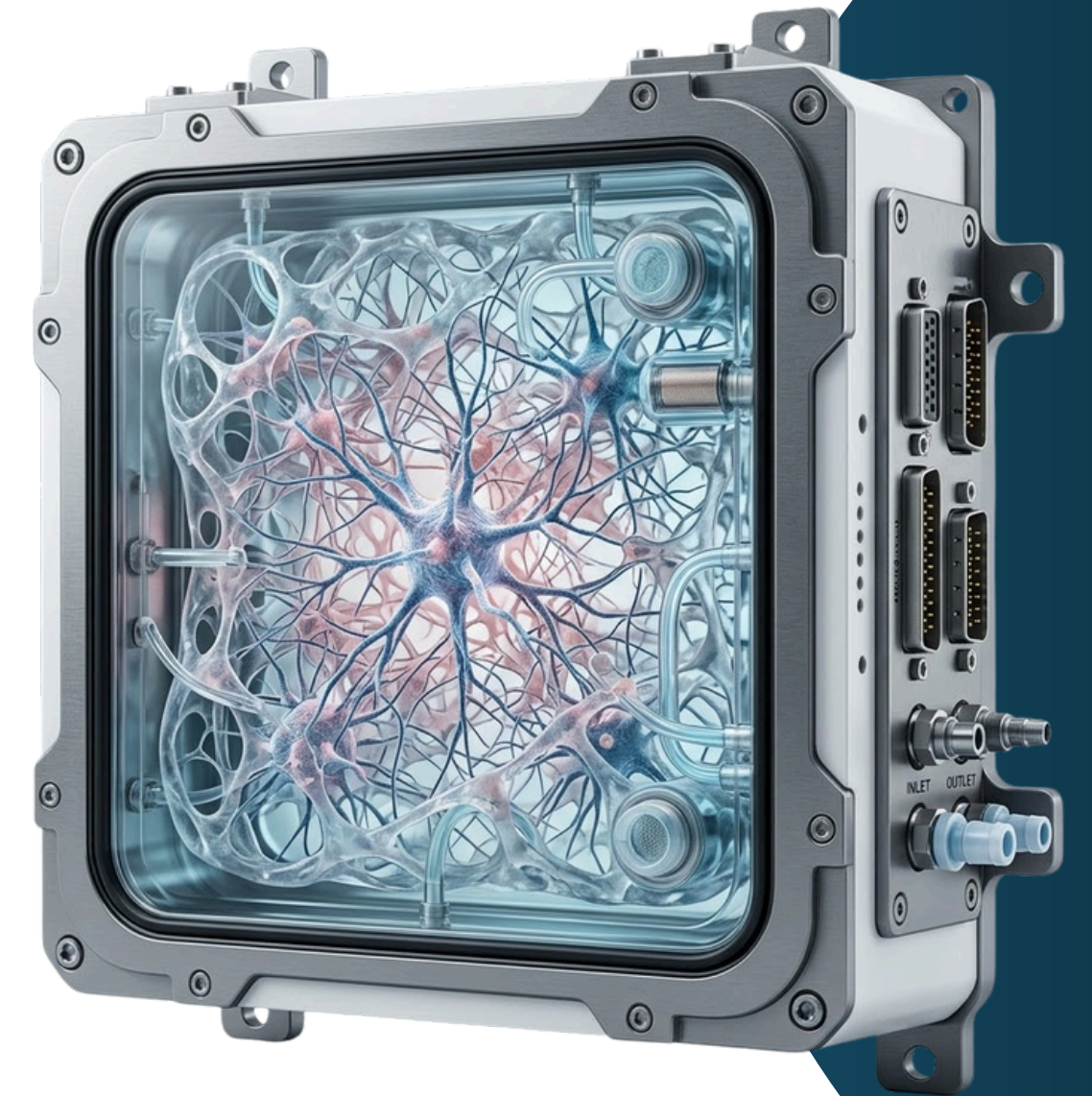
★ BNP's edge over conventional AI & computing



Layer 1: Living Neuronal Substrate Module

Engineered Human Neural Network for Real-Time Biological Simulation

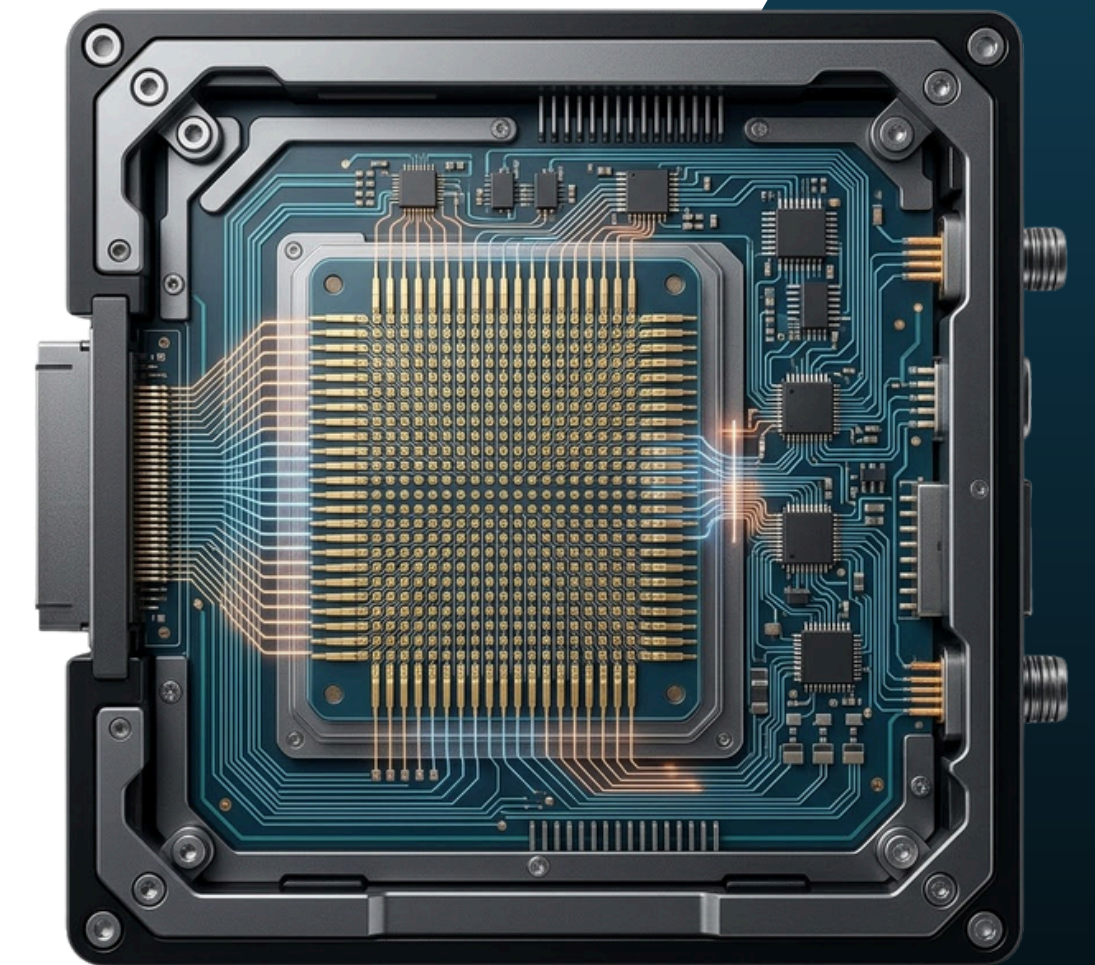
Human iPSC-derived neurons are cultured within a controlled bioreactor environment to form a dense, synaptically active 3D neural network. Supported by glial cells and maintained through microfluidic nutrient and environmental regulation, this system mimics real human neuronal signaling. It serves as a biologically relevant platform for studying drug interactions and enables patient-specific neural modeling for personalized CNS drug testing.



Layer 2: Neural Signal Acquisition & Interface Module

High-Precision Electrophysiological Recording and Bioelectronic Integration

A high-density microelectrode array (MEA) is integrated beneath the neuronal network to enable real-time acquisition of electrophysiological signals. This interface captures extracellular neural activity, including firing patterns, burst dynamics, and network synchrony. Advanced signal amplification and conditioning circuits process these signals with high sensitivity and resolution. By converting biological neural activity into structured electrical data, this module serves as the critical bridge between the living neuronal system and computational analysis.



Layer 3: AI Computational & Analysis Module

Intelligent Decoding and Prediction of Drug-Induced Neural Responses

Electrophysiological signals are analyzed using AI and machine learning to identify patterns in neural activity. Techniques such as spike sorting and network modeling enable interpretation of drug-induced changes. This module generates pharmacodynamic profiles, predicting therapeutic effects and neurotoxicity for accurate CNS drug evaluation.



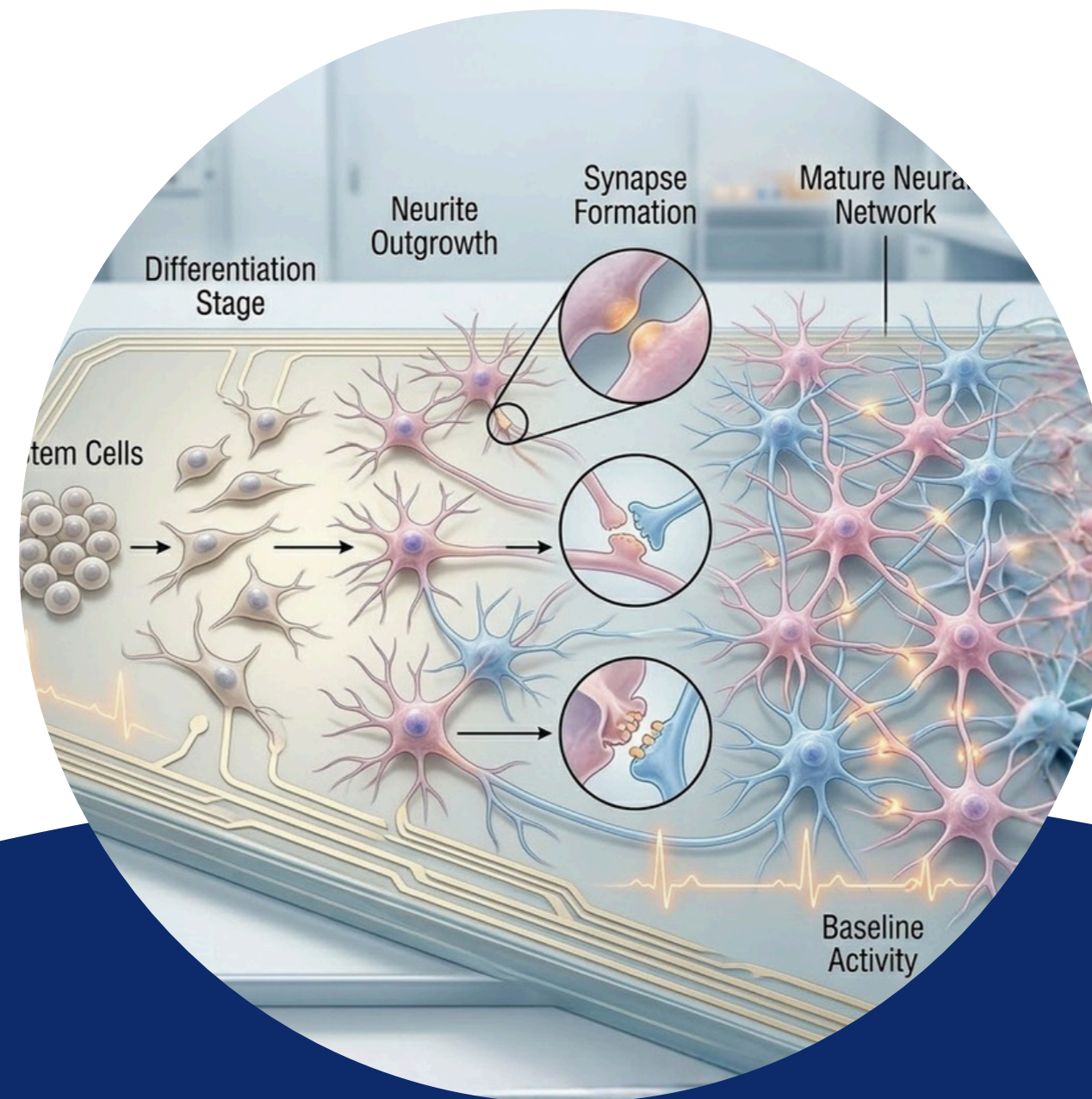
Final: BioHybrid Neural Drug Assay System

Integrated Platform for Real-Time CNS Drug Simulation and Analysis

The BioHybrid Neural Drug Assay System integrates living neuronal networks, electrophysiological interfaces, and AI into a unified platform. Neuroactive compounds are applied to the biological chamber, where real-time neural responses are recorded via microelectrode arrays. These signals are analyzed using machine learning to generate pharmacodynamic profiles, enabling prediction of drug efficacy, neurotoxicity, and pathway-specific effects in a human-relevant system.



Step 1 — Neural Network Formation

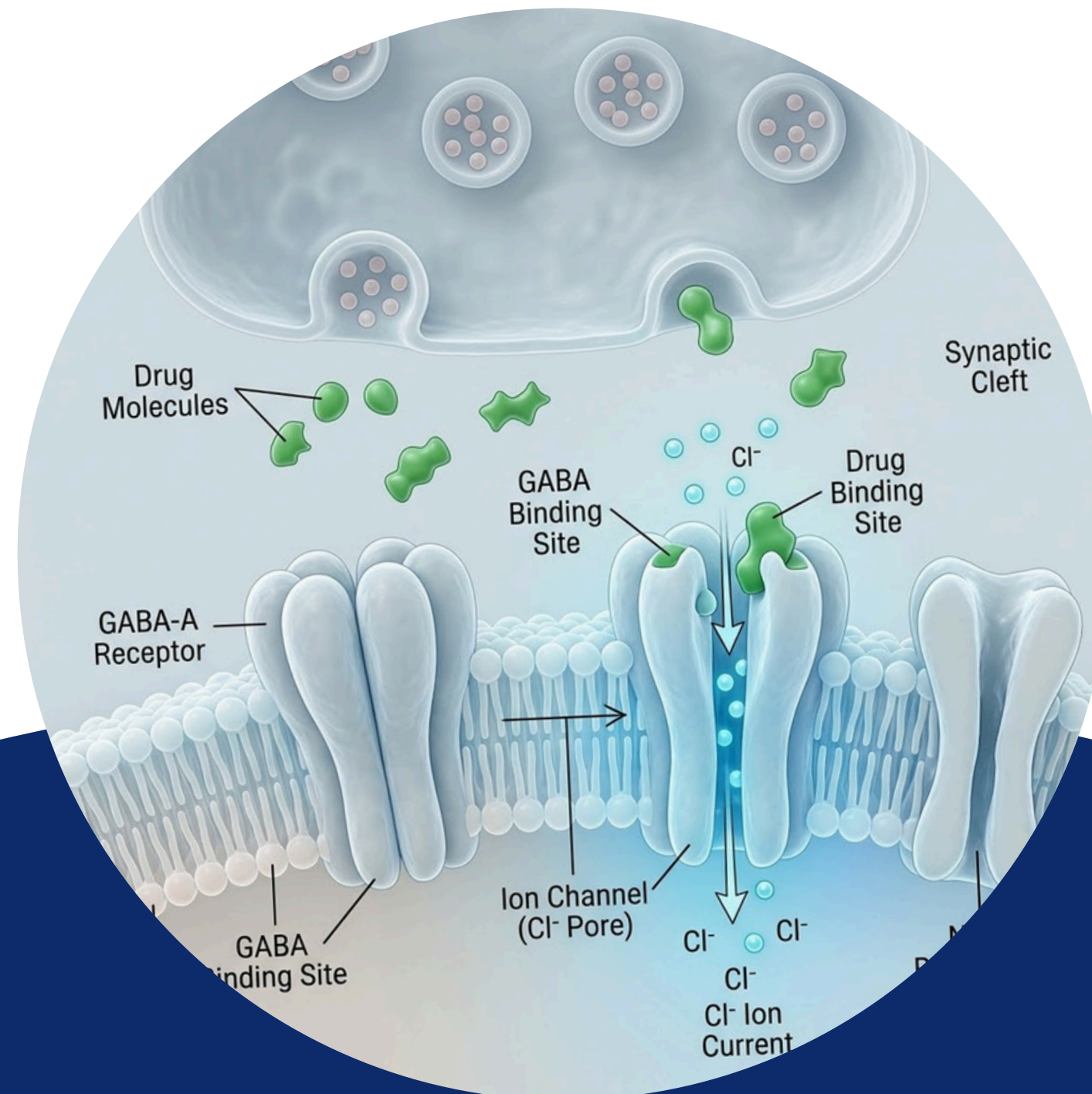


Human iPSC-derived cells differentiate into neurons and establish synaptic connections on a structured interface.

A functional 3D neural network is formed, capable of baseline electrophysiological activity.



Step 2 — Drug–Receptor Interaction

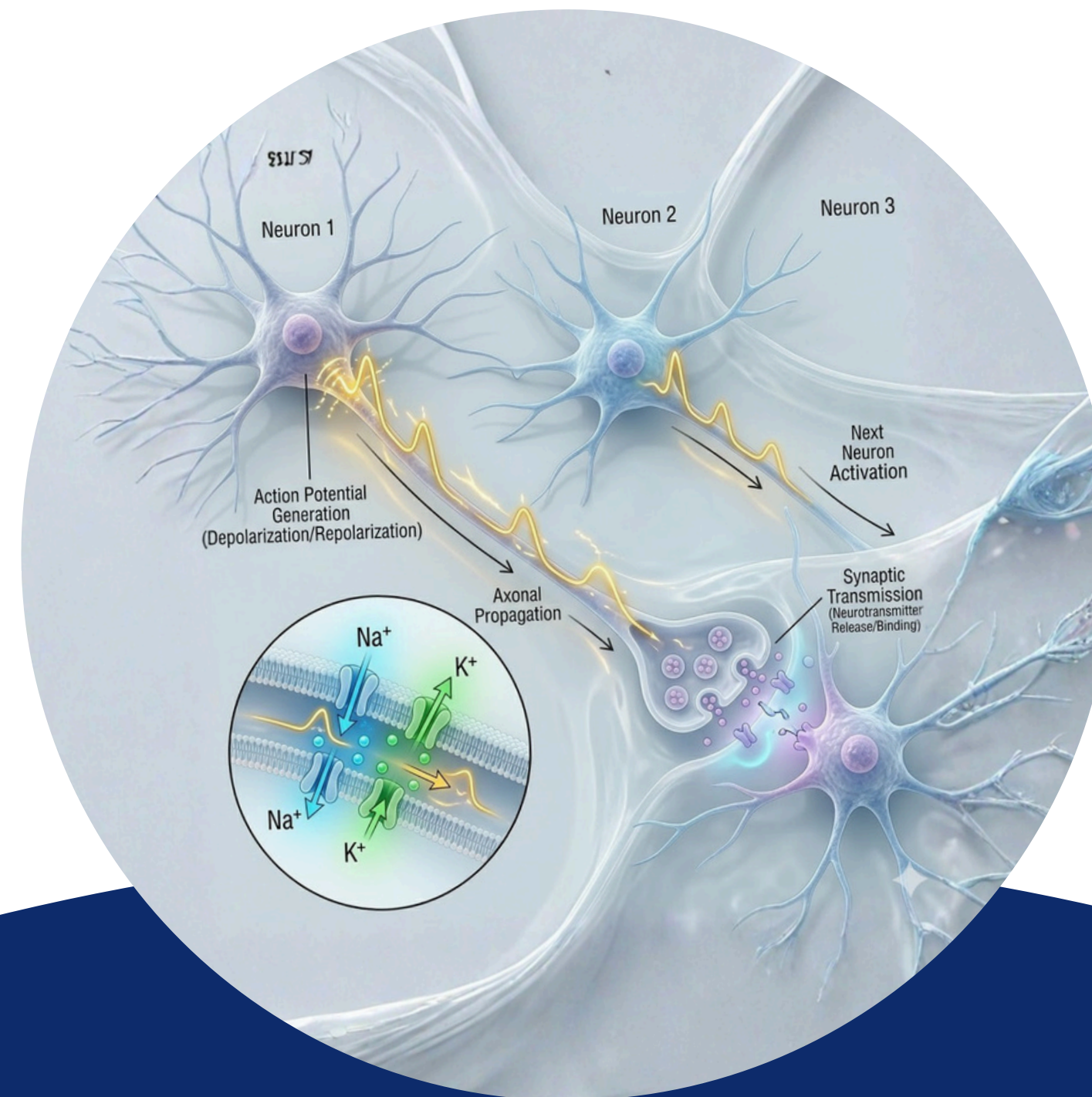


Neuroactive compounds bind to specific neuronal receptors such as GABA, NMDA, or dopamine receptors.

This interaction modulates ion channel activity, altering membrane potential and cellular signaling.



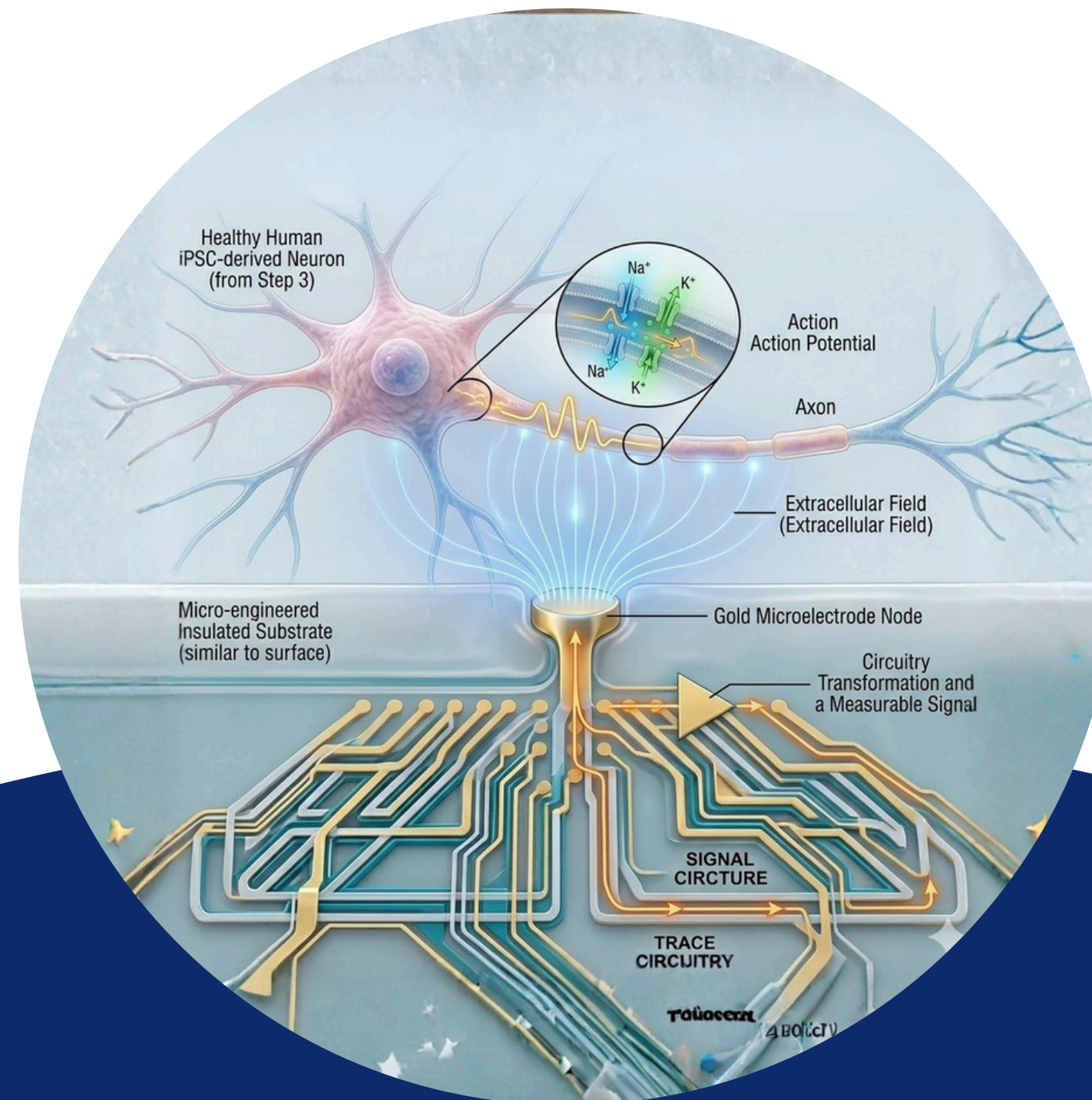
Step 3 — Signal Propagation



Drug-induced changes trigger action potentials that propagate along axons and across synapses. This results in dynamic network-level communication and altered neuronal firing patterns.

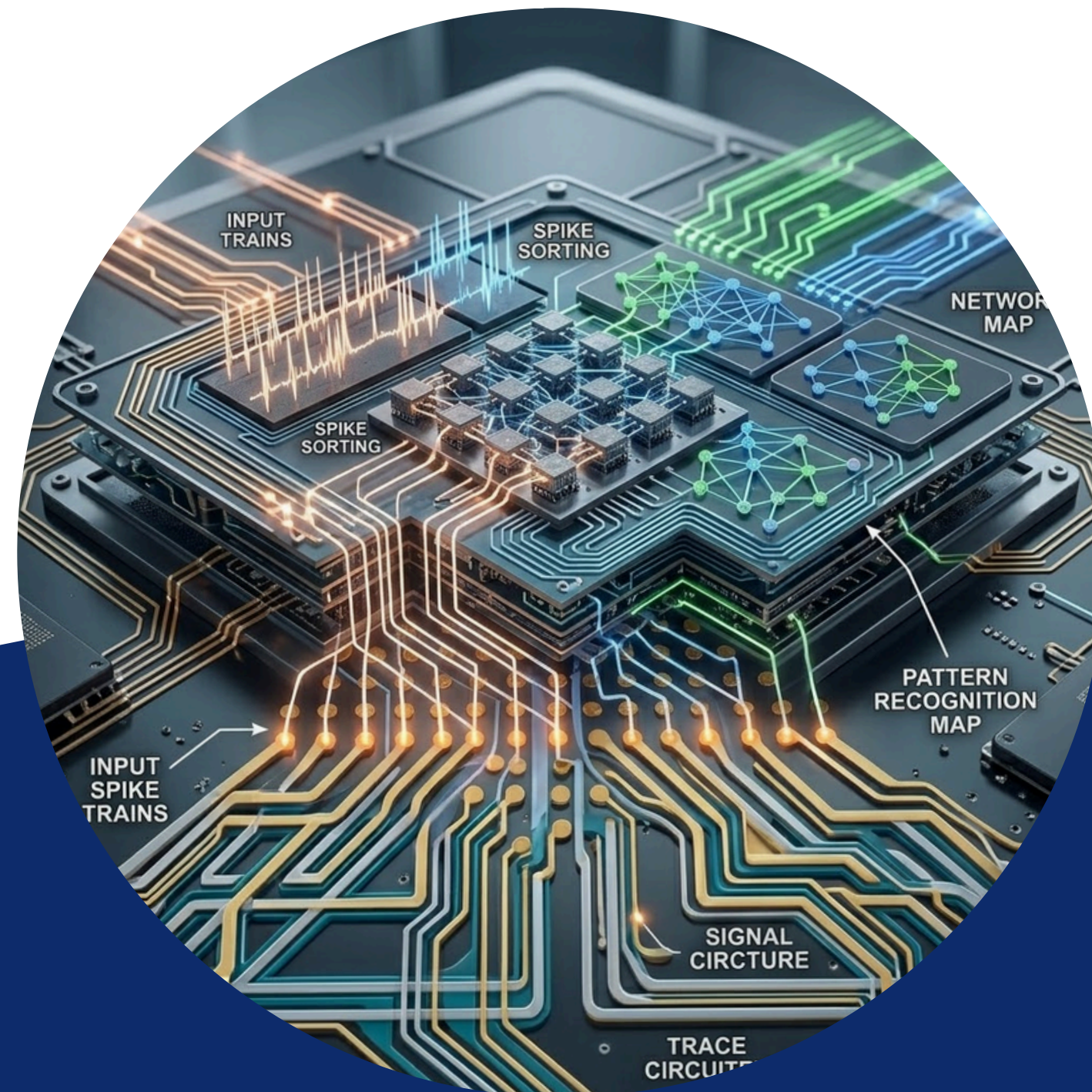


Step 4 — Electrophysiological Detection



Extracellular neural activity is captured by high-density microelectrode arrays positioned beneath the network. Biological signals are converted into measurable electrical data through precise electrode interfaces.

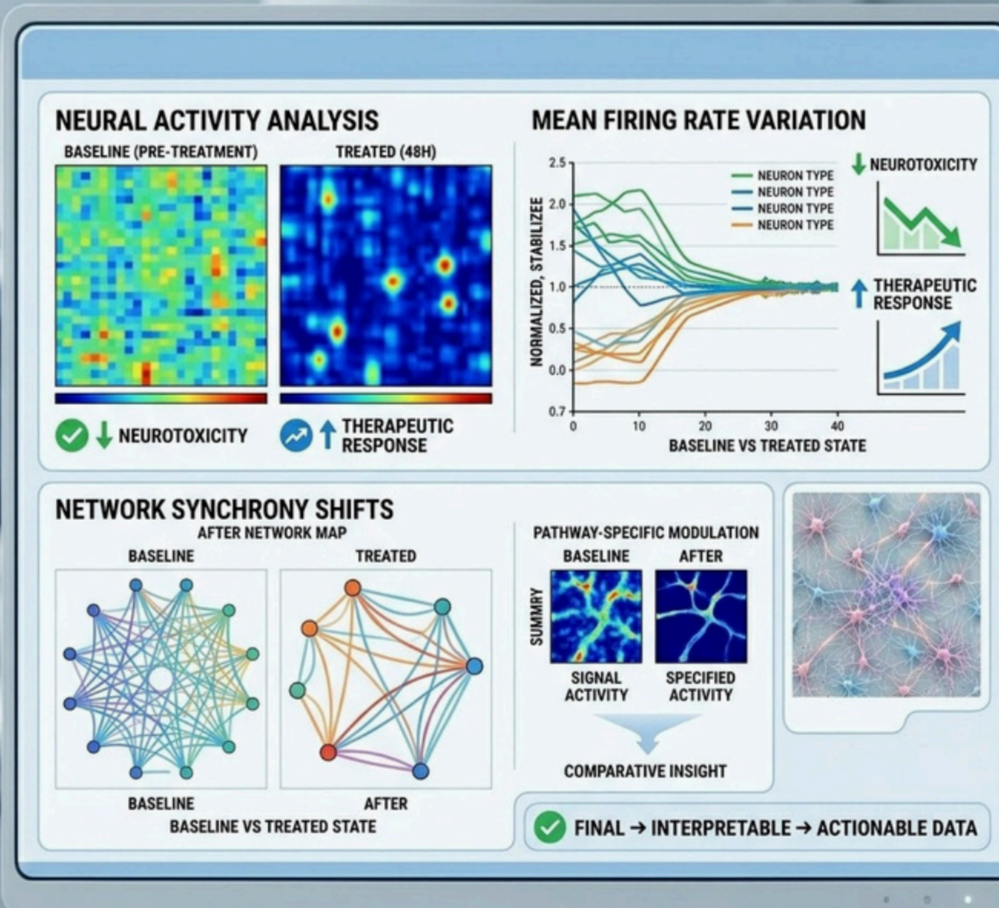
Step 5 — Computational Decoding



Recorded signals are analyzed using AI algorithms to identify patterns and neural activity signatures. Techniques such as spike sorting and network modeling enable interpretation of drug-induced effects.



Step 6 — Pharmacodynamic Output







Processed data is translated into pharmacodynamic profiles reflecting drug efficacy and neurotoxicity. This enables prediction of therapeutic outcomes in a human-relevant neural system.



APPLICATION 1 – CNS DRUG SCREENING & NEUROTOXICITY

CNS Drug Screening – BNP Signatures & Validated Outputs

BNPs detect pharmacological signatures in human neurons, replicating key animal models of CNS effects.

Drug Class	Primary MEA Signature	Animal Model Replaced	Clinical Advantage
 Diazepam / GABA _A Modulators	↑ Synchrony, ↓ MFR, ↑ Burst duration	✓ Rodent EEG / PTZ model	• Sub-therapeutic detection
 Ketamine / NMDA Antagonists	Disrupted γ oscillations, ↓ network coherence	✓ Rat anaesthesia model	• Earlier than cytotoxicity assays
 L-DOPA / Dopaminergic Agents	↑ Burst frequency, ISI normalization	✓ MPTP Parkinson's model	• Circuit-level pathway mapping
 Amyloid-β (1-42) Synaptic toxicity	Progressive MFR decline	✓ APP/PS1 transgenic mouse	• Early neuro- degeneration detection



APPLICATION 2 — NEURODEGENERATIVE DISEASE MODELLING

01. Alzheimer's Disease

Model: iPSC neurons from AD patients
+ amyloid- β (1–42) peptide challenge

MEA Signature: Progressive MFR decline →
network desynchrony → complete firing

Drugs Tested: BACE inhibitors, γ -secretase
modulators, tau aggregation inhibitors

02. Parkinson's Disease

iPSC dopaminergic & alpha-synuclein aggregates

MEA Signature: ↓ Dopaminergic burst frequency →
progressive network silence

Drugs Tested: L-DOPA, MAO-B inhibitors,
 α -synuclein clearance compounds

03. Epilepsy

GABA-blockade iPSC cortical networks

Real-time seizure electrophysiology without
animal models.

Animal Toxicology Phases

Rodent/primate neurotoxicity studies replaced by
BNP NAM assay — FDA accepted since 2024.

Species Translation Delay

No conversion of rodent pharmacology to human equivalents. BNP uses human neurons directly — zero translation step.

Phase 0 / Phase 1 Compression

PD fingerprint data supports early regulatory review, fast-tracking Phase 0 / 1 studies.

Cost & Timeline Reduction

Estimated 3–5 year reduction in preclinical timeline.
\$200–500 per assay vs \$50,000+ for in vivo study.



REGULATORY & MARKET LANDSCAPE

FDA – October 2024

Officially approved organoid-on-chip efficacy data for new drug indications. BNP output now constitutes valid regulatory evidence. Eliminates need for some animal study phases.

China CDE Guidelines

Guidelines accepting organoid-on-chip as quantitative pharmacology data source for rare disease drug development – setting precedent for full CNS drug applications.

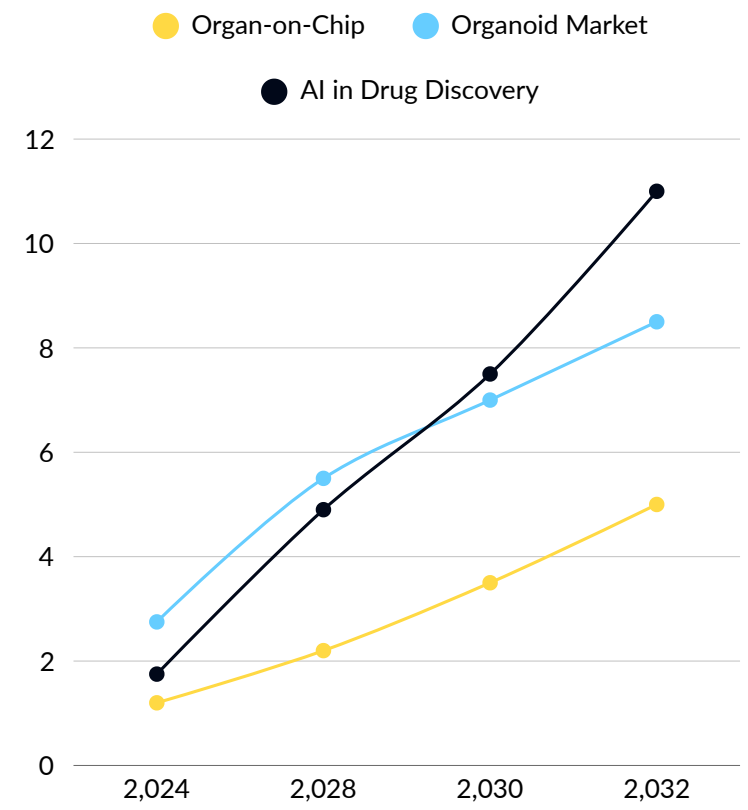
EU REACH Framework

New Approach Methodologies (NAMs) integrated into EU toxicology frameworks. MEA-based assays replace mandated animal tests under updated REACH 3Rs obligations.

INDIA FIRST-MOVER ADVANTAGE

India's \$50B pharma sector has zero BNP-class domestic platforms. UIPS is positioned to pioneer this technology in South Asia – a clear first-mover opportunity.

Year	Organ-on-Chip	Organoid Market	AI in Drug Discovery
2024	1.2	2.75	1.75
2028	2.2	5.5	4.9
2030	3.5	7	7.5
2032	5	8.5	11



Organ-on-Chip “~317% growth by 2032 (1.2→5B)”

Organoid Market “~210% growth, fastest growing segment”

AI in Drug Discovery “~530% growth, exponential industry expansion”



THE ETHICAL & PHARMA REVOLUTION — WHY THIS CHANGES EVERYTHING



Why BNP Matters

- **115M+** animals/year used in research
- **~80%** failure rate translating animal → human trials
- BNP uses **human iPSC-derived neurons** → eliminates species gap



Key Advantages

- **~\$500** vs **\$50K+** per assay
- Cuts preclinical time by **3–4 years**
- More accurate human drug response prediction
- Enables direct human neuron testing (no animals)



Challenges & Ethics

- **Consciousness risk** → monitor organoid complexity
- **Donor consent & data privacy** (DPDP Act, GDPR)
- **Standardisation** needed (protocols, MEA, analysis)



Impact on Drug Development

- **FDA supports** organ-on-chip data (2024)
- BNP can compress or bypass early trial phases
- → **Faster, safer, more reliable** drug approval



EVIDENCE BASE — KEY PUBLISHED STUDIES

Cai et al., Nature Electronics (2023)

Brainware: Brain organoid on HD-MEA chip achieved 78% speech recognition after training. Self-adapted with each stimulus – no GPU retraining. Proved living neural tissue can function as a reservoir computer.

Cortical Labs CL1 (2024)

First commercial biological computer. Human neurons on silicon learned Pong. ~1000× more energy-efficient than GPU equivalents. Commercially available today – not theoretical.

Smirnova et al., Front. Science (2023)

Organoid Intelligence (OI) framework: defines biocomputing using brain organoids + MEA + AI. Establishes scientific and ethical roadmap for BNP-class systems globally.

Beaubois et al., Nat. Comm. (2024)

Closed-loop organoid-neuromorphic hardware system. Automated bidirectional real-time communication between cortical organoids and hardware SNN emulator. Models BNP feedback architecture

Hartmann et al., Arch. Toxicol. (2025)

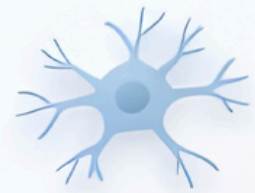
3D iPSC BrainSpheres MEA assay validated as New Approach Methodology (NAM) for neurotoxicity screening. First regulatory-accepted platform as an alternative to animal neurotoxicity models.

FDA – October 2024

FDA officially approved organoid-on-chip efficacy data for new drug indications. Landmark regulatory milestone – BNP outputs now constitute valid evidence for drug approval submissions



EXPECTED RESULTS — LITERATURE-VALIDATED BNP OUTPUTS



A Functional Biohybrid Platform Achieved

- Successfully integrates living neurons + MEA + AI
- Enables real-time neural response analysis
- Mimics human CNS drug behavior with high fidelity



Superior to Conventional Models

- Eliminates limitations of 2D cultures & animal models
- Captures true electrophysiological responses
- Provides patient-specific and biologically relevant data



Transforming Drug Development

- Early prediction of drug efficacy & neurotoxicity
- Reduces clinical trial failure rates
- Supports personalized CNS therapeutics
- Aligns with FDA & NAM regulatory frameworks



Next-Generation Pharma & Computing

- Foundation for Organoid Intelligence & wetware computing
- Scalable for drug discovery, disease modeling, AI integration
- Positions India as a first-mover in BNP technology



FUTURE DIRECTIONS & CONCLUSION

Assembloid Circuits

Multi-organoid assembloids replicating cortico-striatal and cortico-limbic circuits — capturing inter-regional drug dynamics impossible in single-region cultures.

Personalised BNP

Patient iPSC BNPs enable individual CNS pharmacology — test a drug on your patient's own neurons before prescribing. True precision medicine.

Post-GPU Computing

As AI energy demands hit planetary limits, BNPs offer a ~1000× more efficient alternative. Self-adapting biological processors may replace entire GPU clusters for specific tasks.

Full ADMET Platform

Integration with gut-liver-BBB organ-on-chip for complete ADMET profiling of CNS drugs — entire human drug journey simulated without a single animal or patient.

"From a petri dish of living neurons — no electricity, no animals, no species gap — to a regulatory-grade pharmacodynamic dataset. This is the BioHybrid Neural Processor."





THANK YOU

for your time &
attention



WORKING OF PROPOSED BIOHYBRID NEURAL PROCESSOR



<https://mrnatherapeutics.in/#layman>

Biohybrid Neural Processor

Biohybrid Neural Processor combines living neurons, electrophysiology, and AI to simulate drug effects and cognitive processing in real time.

mrnatherapeutics.in



ABBREVIATIONS USED

BNP – BioHybrid Neural Processor

CNS – Central Nervous System

iPSC – Induced Pluripotent Stem Cells

MEA – Microelectrode Array

HD-MEA – High-Density Microelectrode Array

AI – Artificial Intelligence

ML – Machine Learning

GPU – Graphics Processing Unit

AP – Action Potential

GABA-A – Gamma-Aminobutyric Acid Type A Receptor

NMDA – N-Methyl-D-Aspartate Receptor

D2R – Dopamine D2 Receptor

MFR – Mean Firing Rate

ISI – Inter-Spike Interval

E/I Balance – Excitatory/Inhibitory Balance

PD – Pharmacodynamics

ADMET – Absorption, Distribution, Metabolism, Excretion, Toxicity

