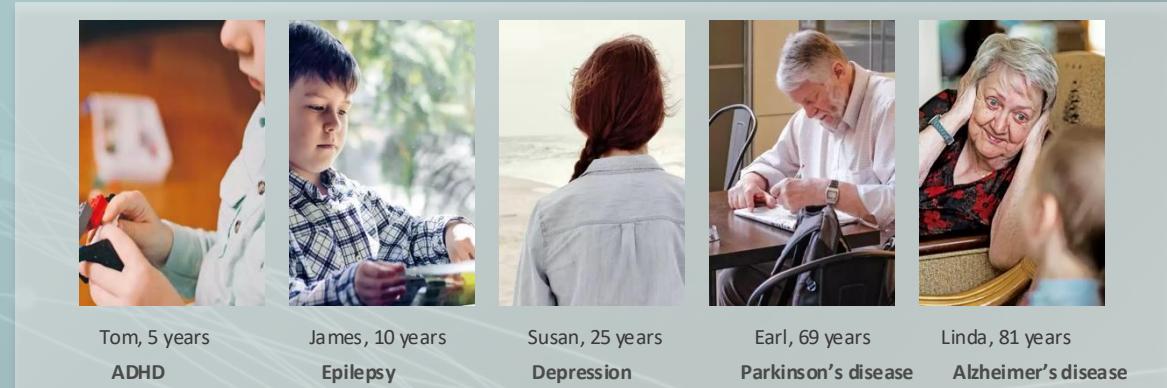


# From Kolmogorov Theory to Computational Modeling and Brain Stimulation

Dr. Giulio Ruffini  
Co-founder & CTO Starlab /Neuroelectrics

Barcelona, July 7, 2025



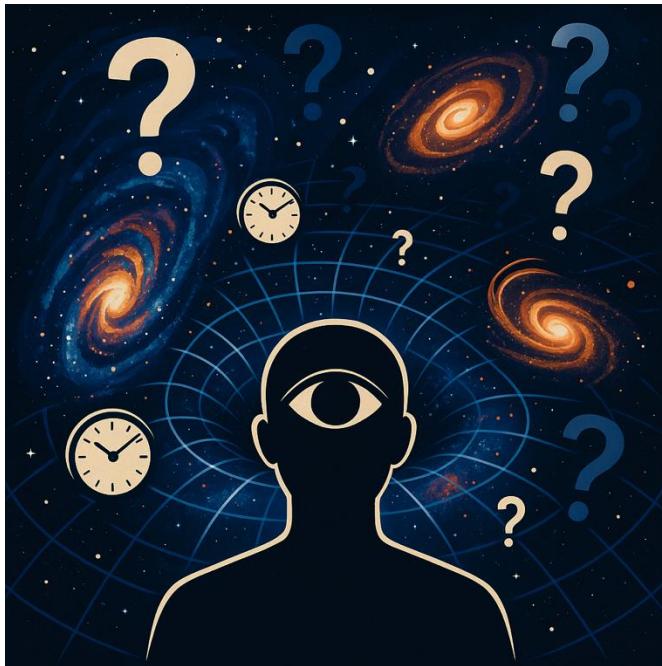


## OUR MISSION

To deliver life-changing therapies that empower patients and families living with neuropsychiatric disorders.

Treat patients with Epilepsy, Major Depressive Disorder, and other neuropsychiatric disorders with our novel breakthrough-designed personalized medical technology: **Neurotwin-powered Transcranial Electrical Stimulation (tES)**.

# Physics and the big questions



What is mass, space, time?

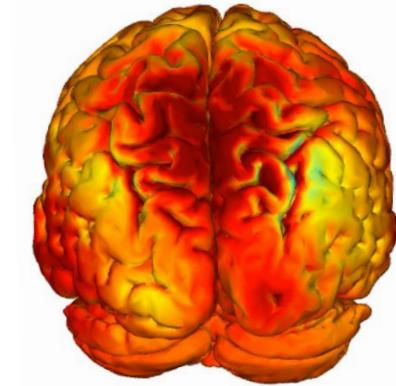
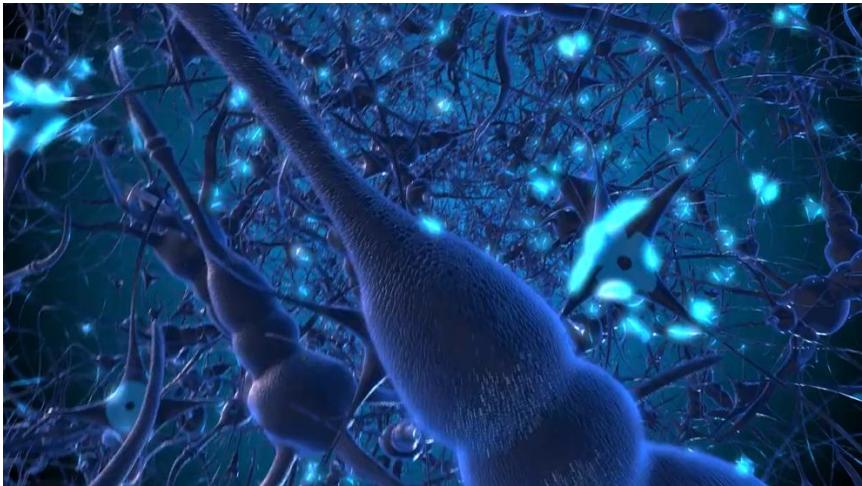
What is, indeed, **Reality**?

Why is math so powerful?

And who is this famous

**Observer**? Who am I?

# The Electric Brain



The brain appears to **compute electrically**. What do electric field patterns have to do with **mind**?  
Can we harness them for **communication or therapy**?



Read EEG



Write tES

Easy-to-use, non-invasive, portable  
device for monitoring and treatment  
of the brain diseases *at home*

# How do you stimulate a brain?

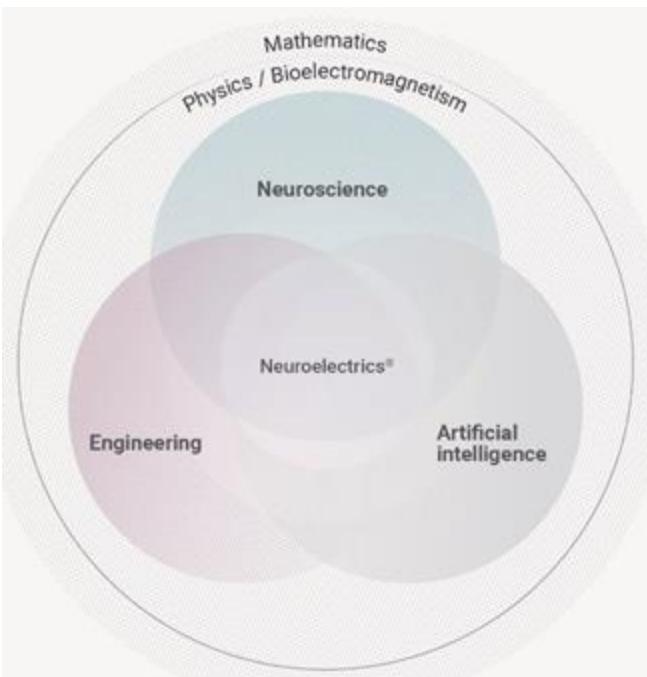


The brain is a  
plastic network, a  
large dynamical  
system

# A Solid Foundation with Robust Modeling



Leveraging expertise across mathematics, physics, and neuroscience, unique models can be developed to provide novel insights



## PHYSIOLOGICAL BRAIN MODELING

Dynamical brain network models can be used to simulate brain activity for each patient



## BIPHYSICAL BRAIN MODELING

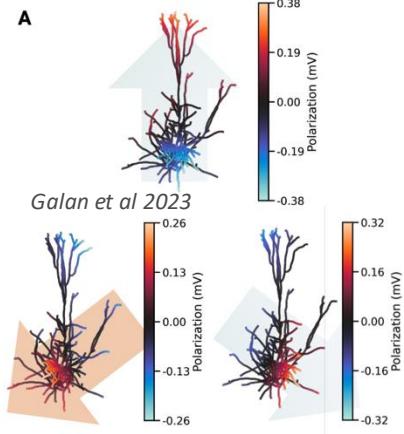
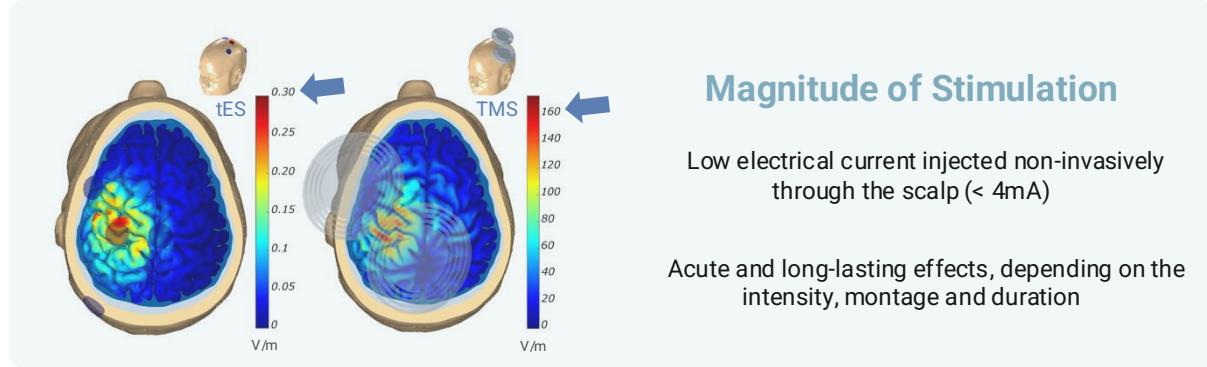
The physical interaction between the brain and the world (measurements or brain stimulation) requires a physical layer.



## COMPLETE NEUROTWIN

Complete digital twin of the brain of a patient ready for optimization of stimulation protocol or analysis

# Mechanism of Action Transcranial Electrical Stimulation (tES)



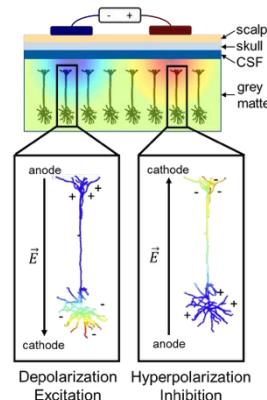
## Mechanism of Action

Introduction of current generates electric field in the brain

Electric field couples with neurons, altering their membrane potential

Modulates neuronal firing patterns  
→ heightening/reducing excitability or entraining oscillations

Leads to synaptic remodeling  
→ “rewiring” the brain



*J Physiol.* 2000 Sep 15; 527(PI 3): 633-639.  
doi: 10.1111/j.1469-7793.2000.t01-1-00633.x

PMCID: PMC2270089  
PMID: 10990547

Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation

**M A Nitsche and W Paulus**

**Review** > *Nat Neurosci.* 2018 Feb;21(2):174-187. doi: 10.1038/s41593-017-0054-4.  
Epub 2018 Jan 8.

**Studying and modifying brain function with non-invasive brain stimulation**

Rafael Polania <sup>1</sup>, Michael A Nitsche <sup>2 3</sup>, Christian C Ruff <sup>4</sup>

**Review** > *Clin Neurophysiol.* 2016 Feb;127(2):1031-1048. doi: 10.1016/j.clinph.2015.11.012.  
Epub 2015 Nov 22.

**A technical guide to tDCS, and related non-invasive brain stimulation tools**

A J Woods <sup>1</sup>, A Antal <sup>2</sup>, M Bikson <sup>3</sup>, P S Boggio <sup>4</sup>, A R Brunoni <sup>5</sup>, P Celinkin <sup>6</sup>, L G Cohen <sup>7</sup>,  
F Fregni <sup>8</sup>, C S Hermann <sup>9</sup>, E S Kappelen <sup>10</sup>, H Knotkova <sup>11</sup>, D Liebetanz <sup>12</sup>, C Minussi <sup>12</sup>,  
P C Miranda <sup>13</sup>, W Paulus <sup>14</sup>, A Priori <sup>14</sup>, D Reato <sup>3</sup>, C Stagg <sup>15</sup>, N Wenderoth <sup>16</sup>, M A Nitsche <sup>17</sup>

**> Brain Stimul.** 2020 Mar-Apr;13(2):287-301. doi: 10.1016/j.brs.2019.10.014. Epub 2019 Oct 18.

**Direct current stimulation boosts hebbian plasticity in vitro**

Greg Kronberg <sup>1</sup>, Asif Rahman <sup>2</sup>, Mahima Sharma <sup>2</sup>, Marom Bikson <sup>2</sup>, Lucas C Parra <sup>2</sup>

**Review** > *Neurophysiol Clin.* 2016 Dec;46(6):319-398. doi: 10.1016/j.neucli.2016.10.002.  
Epub 2016 Nov 17.

**A comprehensive database of published tDCS clinical trials (2005-2016)**

Jean-Pascal Lefaucher <sup>1</sup>

# Epilepsy



Boston  
Children's  
Hospital

Until every child is well™

*Co-Principal Investigator*  
Dr. Alexander Rotenberg



Beth Israel Deaconess  
Medical Center

MASSACHUSETTS  
LIFE SCIENCES CENTER



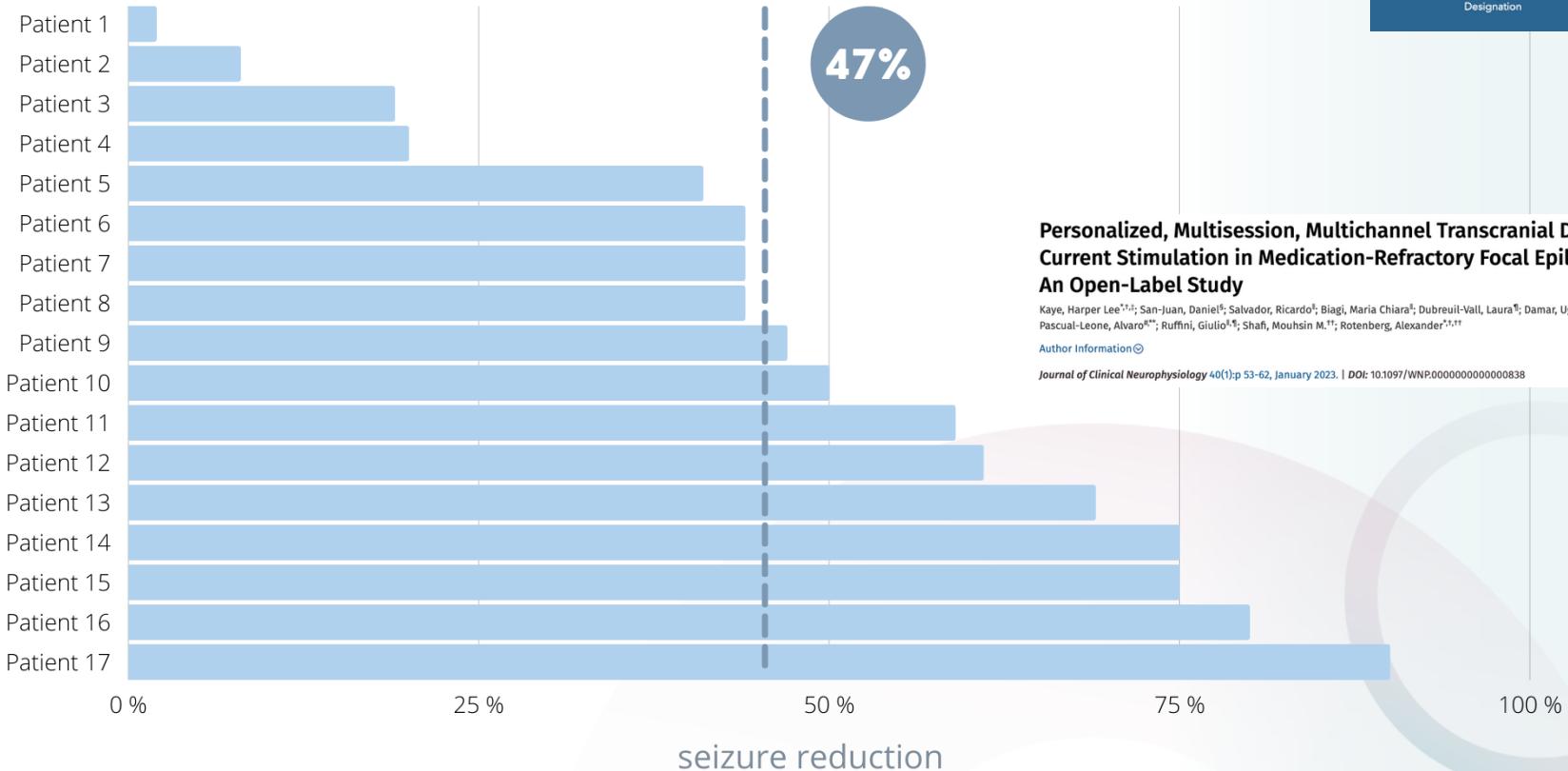
Breakthrough Designation

NE  
neuroelectrics®

NE®



# REDUCING SEIZURES BY 47%

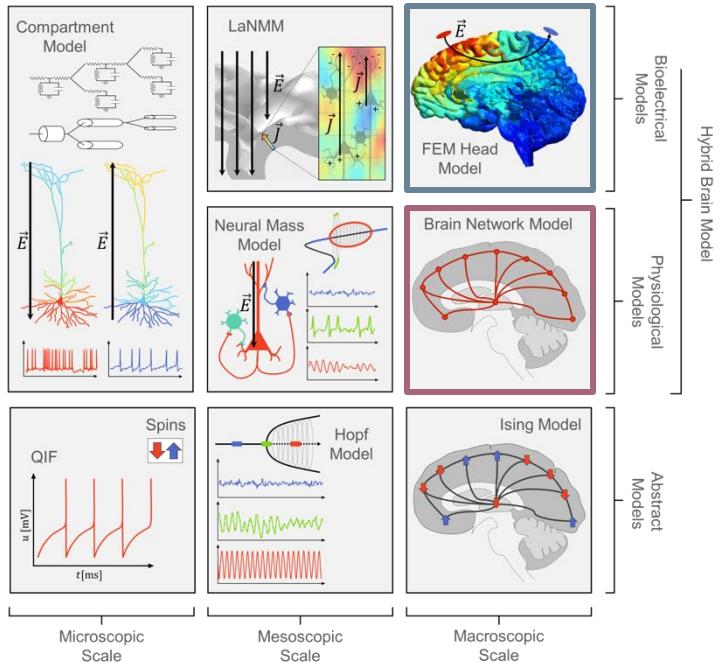


# Neurotwins in Epilepsy



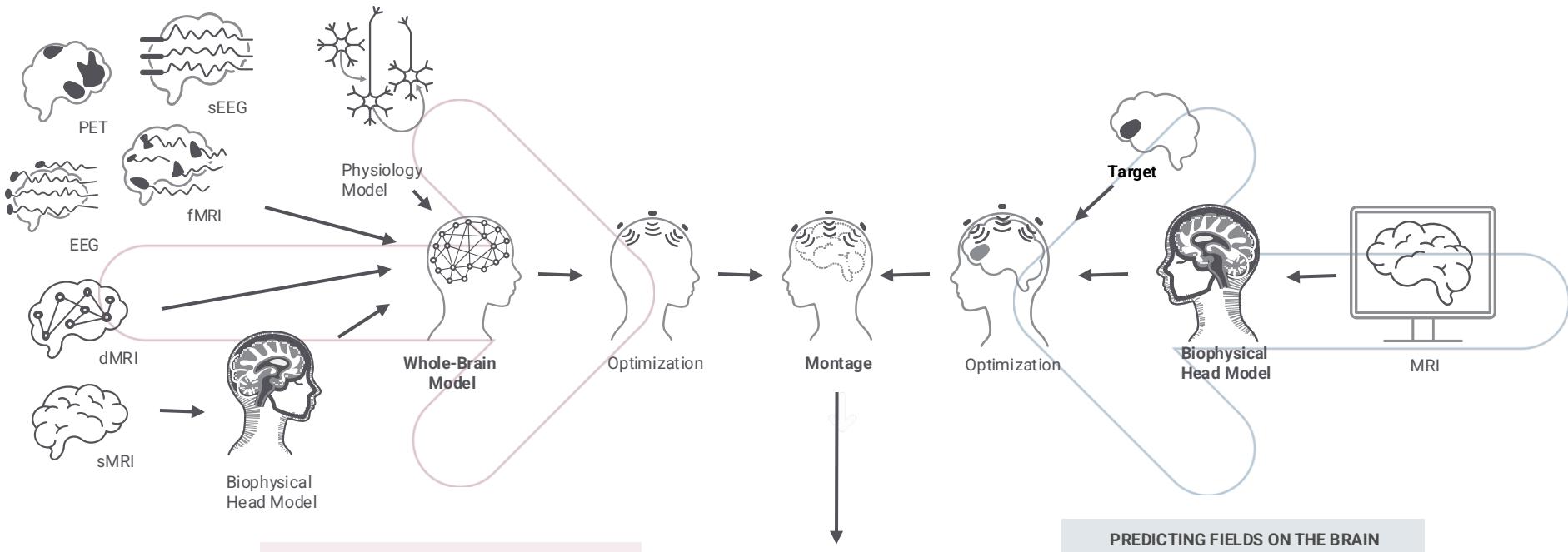
## AIM

1. Develop advanced individualized whole-brain models that predict the physiological effects of tES
2. Use them to design optimal stimulation protocols in the context of neuropsychiatric disorders



**Neurotwin:** Mathematical model of the human brain comprising either or both physical and physiological aspects in the context of a disorder for the purpose of optimizing therapy.

# Neurotwin Technology



## WHOLE-BRAIN MODELS

Whole Brain Models represent cortical dynamics by simulating the collective activity of neuron populations.

## PREDICTING FIELDS ON THE BRAIN

We can predict the electric field in the cortex using biophysical head models that represent the **brain geometry**, and its passive **electrical properties** based on neuroimaging structural data.



- Whole-brain Personalization Methods
- Whole-brain Optimization methods
- Clinical study design and analysis

The project is investigating the impact **weak electric fields** have on the physiology of neurons and neural networks. The key objective is to understand if these electric pulses can improve the patient-specific **epileptogenic network**.



## Multicenter Clinical Epilepsy

Sept 2024-27

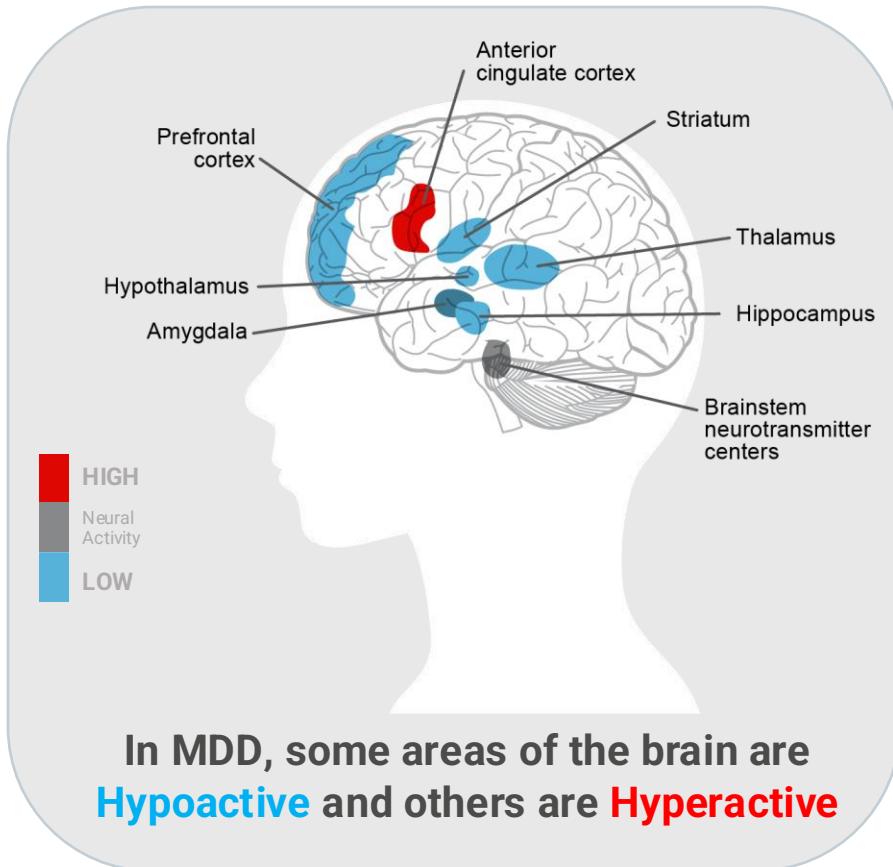


*Neurotwins for advanced tDCS in focal epilepsy*



How can we help  
patients with  
psychiatric conditions?

# Major Depressive Disorder (MDD)



## Target indication: refractory MDD

- >28M patients globally
- Therapeutic alternatives include TMS, VNS, ECT

## Mechanistic rationale

- MDD is characterized by reduced left vs right neuronal activity in the dorsolateral prefrontal cortex (**DLPFC**)
- Application of tDCS on left **DLPFC** stimulates neuronal activity in this region, restoring electrophysiological function
- Plasticity from repeated application is to lead to healthy rewiring of frontolimbic network

## Clinical evidence

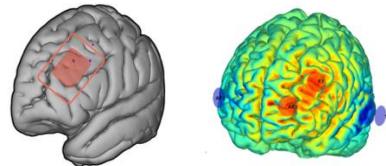
- >20 RCTs conducted to date; >1,000 patients studied
- LeFaucheur (2017) meta-analyses supports Level B recommendation – probable efficacy – for anodal TES of the left DLPFC in MDD patients with drug resistance

# MDD Open Label Pilot Study Results

Montages, biotypes and etiology matter

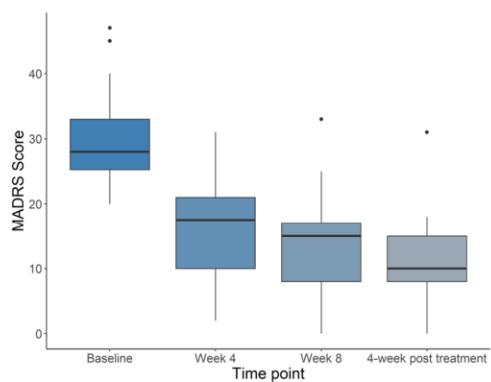


## Neuroelectrics Home pilot MDD1



### PRIMARY ENDPOINT: MADRS

(gold standard depression severity assessment)

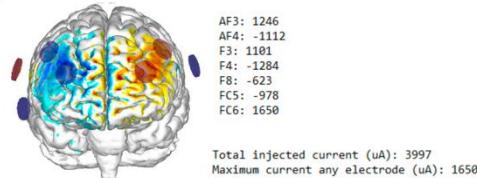


- Avg Baseline: **30.1 (ITT)**
- Avg Improvement @ Week 4 Post-treat: **19.8 pts**
- Min. Clinical-Important Difference (MCID): **3-5 pts**

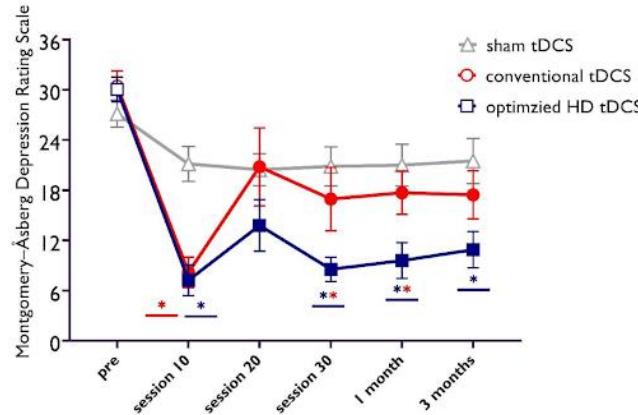
### Optimized HD-tDCS protocol for clinical use in patients with major depressive disorder

Mohammad Ali Salehinejad, Marzieh Abdi, Mohsen Dadashi, Reza Rostami, Ricardo Salvador, Giulio Ruffini, Michael A. Nitsche

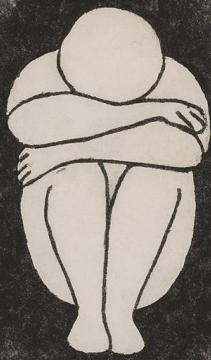
#### Protocol:



### Results – MADRS



# Can we do better?



## What is Depression?

MDD is not a single condition.

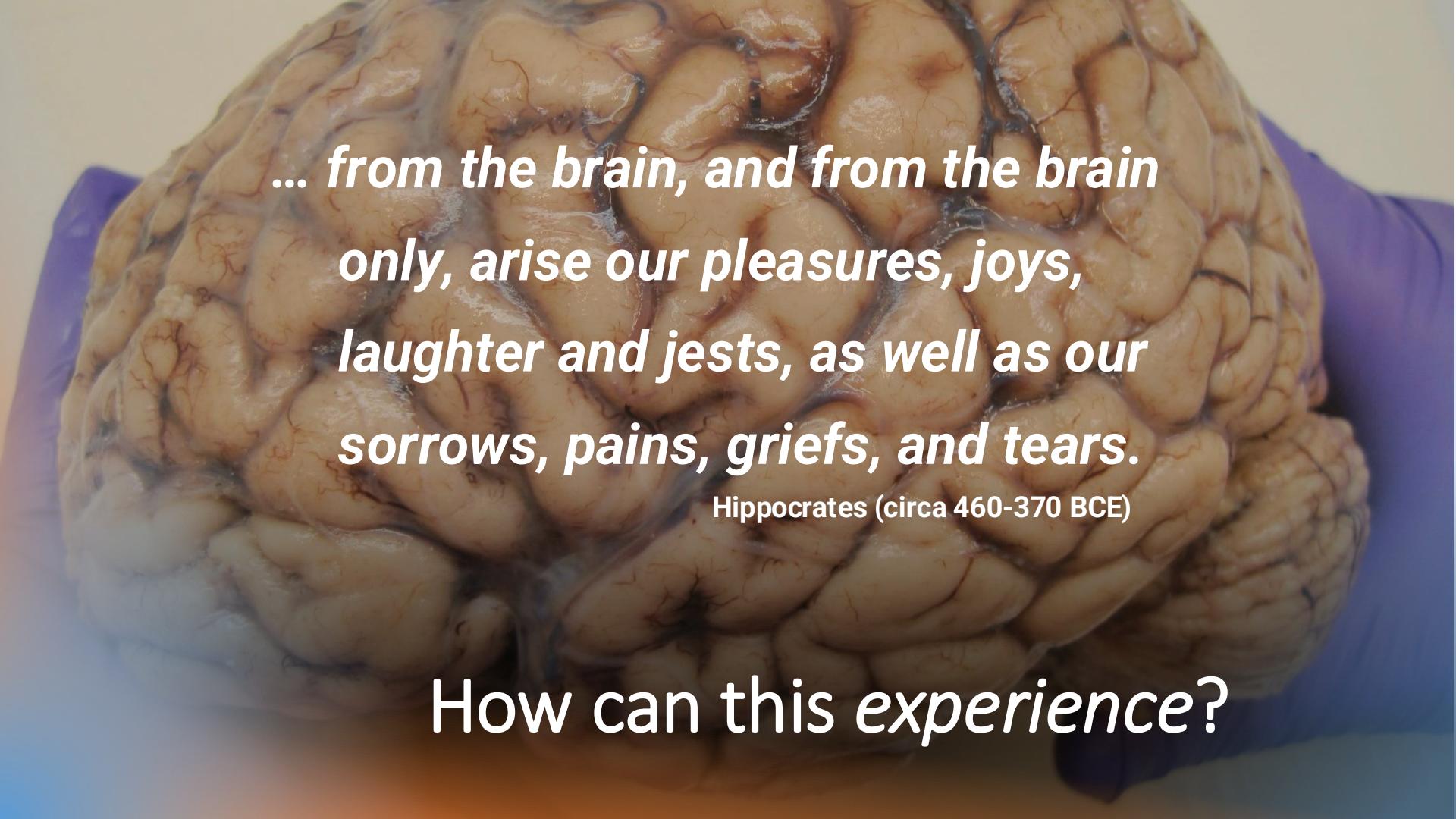
Etiology is diverse.

MDD is characterized by a persistent **first-person experience** of sadness, hopelessness, and a lack of interest or pleasure in activities.

**Neurology** is primarily concerned with the **physical and structural** aspects of the nervous system and its diseases.

**Psychiatry** focuses on the **mental, emotional, and behavioral** aspects of well-being.

The ***experience machine!***



*... from the brain, and from the brain  
only, arise our pleasures, joys,  
laughter and jests, as well as our  
sorrows, pains, griefs, and tears.*

Hippocrates (circa 460-370 BCE)

How can this *experience*?

# The Challenge



We are missing a principled, unifying framework to define and operationalize **what** we want to model and understand what its physiological signatures are – **how** to measure it.

# Defining Experience/Consciousness



1. A brief intro to Kolmogorov theory (KT)
2. Emotion, depression, and the role of valence

# Kolmogorov Theory (KT)

arXiv > physics > arXiv:0704.1147

Physics > General Physics

[Submitted on 9 Apr 2007]

## Information, complexity, brains and reality (Kolmogorov Manifesto)

Giulio Ruffini

arXiv > physics > arXiv:0903.1193

Physics > General Physics

[Submitted on 6 Mar 2009 (v1), last revised 19 Jun 2009 (this version, v3)]

## Reality as Simplicity

Giulio Ruffini

arXiv > cs > arXiv:1612.05627

Computer Science > Machine Learning

[Submitted on 13 Dec 2016]

## Models, networks and algorithmic complexity

Giulio Ruffini

## An algorithmic information theory of consciousness

Giulio Ruffini

Neuroscience of Consciousness, Volume 2017, Issue 1, 2017, nix019,

Journal of Artificial Intelligence and Consciousness | Vol. 09, No. 02, pp. 153-191 (2022)

## AIT Foundations of Structured Experience

Giulio Ruffini and Edmundo Lopez-Sola

Open Access Perspective

## Neural Geometrodynamics, Complexity, and Plasticity: A Psychedelics Perspective

by Giulio Ruffini 1,\* , Edmundo Lopez-Sola 1,2 , Jakub Vohryzek 2,3  and Roser Sanchez-Todo 1,2 

Open Access Perspective

## The Algorithmic Agent Perspective and Computational Neuropsychiatry: From Etiology to Advanced Therapy in Major Depressive Disorder

by Giulio Ruffini 1,\* , Francesca Castaldo 1,\* , Edmundo Lopez-Sola 1,2 , Roser Sanchez-Todo 1,2  and Jakub Vohryzek 2,3 

## Cross-Frequency Coupling as a Neural Substrate for Prediction Error Evaluation: A Laminar Neural Mass Modeling Approach

 Giulio Ruffini,  Edmundo Lopez-Sola,  Raul Palma,  Roser Sanchez-Todo,  Jakub Vohryzek,  Francesca Castaldo,  Karl Friston

doi: <https://doi.org/10.1101/2025.03.19.644090>

## Restoring Oscillatory Dynamics in Alzheimer's Disease: A Laminar Whole-Brain Model of Serotonergic Psychedelic Effects

 Jan C. Gendra,  Edmundo Lopez-Sola,  Francesca Castaldo,  Élia Leal-Custey,  Roser Sanchez-Todo,  Jakub Vohryzek,  Ricardo Salvador,  Ralph G. Andzejak,  Giulio Ruffini, the Alzheimer's Disease Neuroimaging Initiative

doi: <https://doi.org/10.1101/2024.12.15.628565>

A physical neural mass model framework for the analysis of oscillatory generators from laminar electrophysiological recordings

Roser Sanchez-Todo <sup>a,f</sup>, André M. Bostan <sup>b</sup>, Edmundo Lopez-Sola <sup>c</sup>, Borja Mercadal <sup>d</sup>, Emiliiano Santoromechi <sup>e</sup>, Earl K. Miller <sup>d,1</sup>, Gustavo Deco <sup>e,g,1</sup>, Giulio Ruffini <sup>a,f</sup> 

## LSD-induced increase of Ising temperature and algorithmic complexity of brain dynamics

Giulio Ruffini , Giada Damiani, Diego Lozano-Soldevilla, Nikolas Deco, Fernando E. Rosas, Narsis A. Kiani, Adrián Ponce-Alvarez, Morten L. Kringlebach, Robin Carhart-Harris, Gustavo Deco

Open Access Article

## Structured Dynamics in the Algorithmic Agent

by Giulio Ruffini 1,\* , Francesca Castaldo 1  and Jakub Vohryzek 2,3 

Navigating Complexity: How Resource-Limited Agents Derive Probability and Generate Emergence

Giulio Ruffini\*  
Neuroelectrics

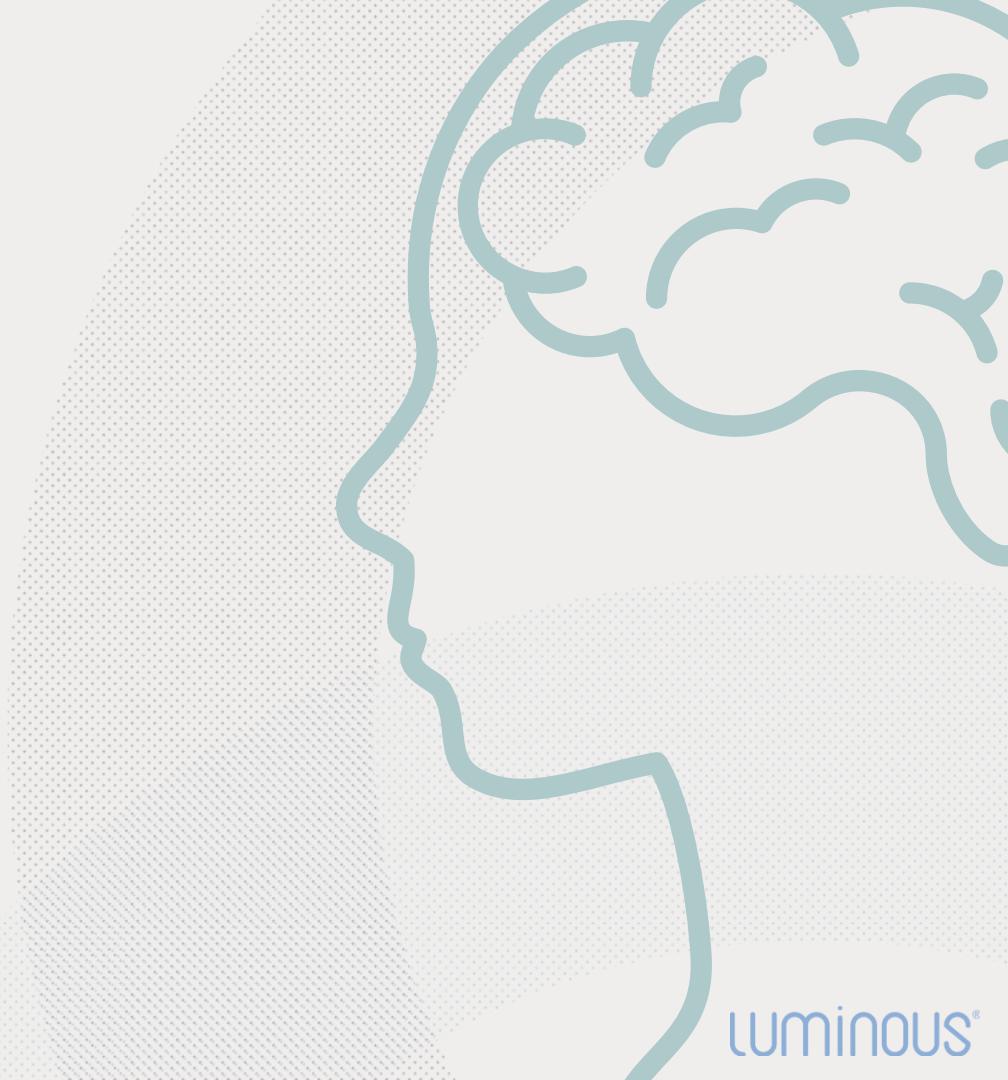
## Fast Interneuron Dysfunction in Laminar Neural Mass Model Reproduces Alzheimer's Oscillatory Biomarkers

 Roser Sanchez-Todo,  Borja Mercadal,  Edmundo Lopez-Sola,  Maria Guasch-Morgades,  Gustavo Deco,  Giulio Ruffini

doi: <https://doi.org/10.1101/2025.03.26.645407>

# Kolmogorov Theory of Consciousness

1. Postulate: There is Experience
2. Focus on Structured Experience





## There is *Pure Experience*

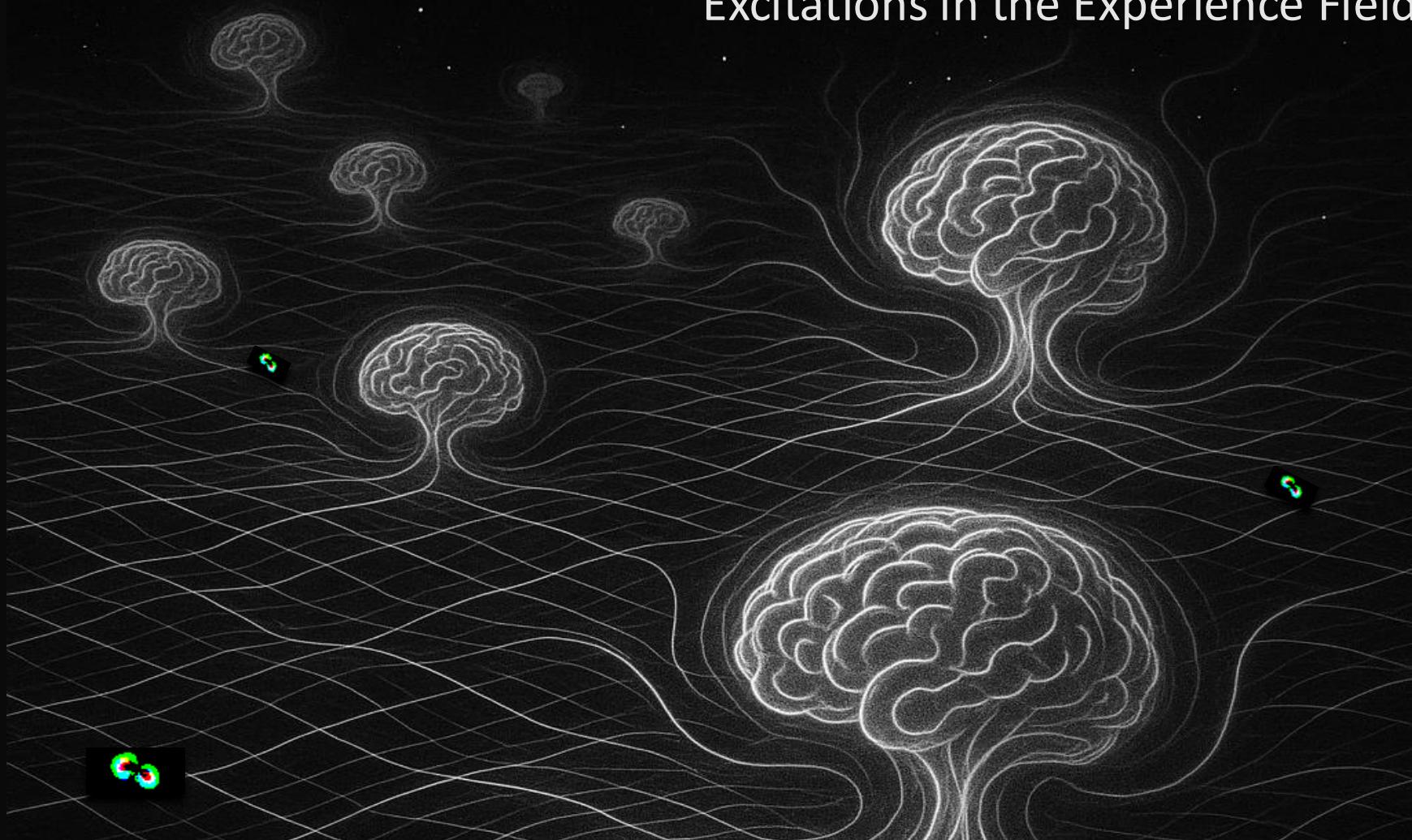
The immediate, subjective sense of “what it feels like” to be oneself at any given moment.

What is it like to be you?

What is it like to be a bat? (Thomas Nagel 1974)



# Excitations in the Experience Field



# What is *structured* experience?

The spatial, temporal, and conceptual organization of our first-person experience of the world and of ourselves as agents in it.



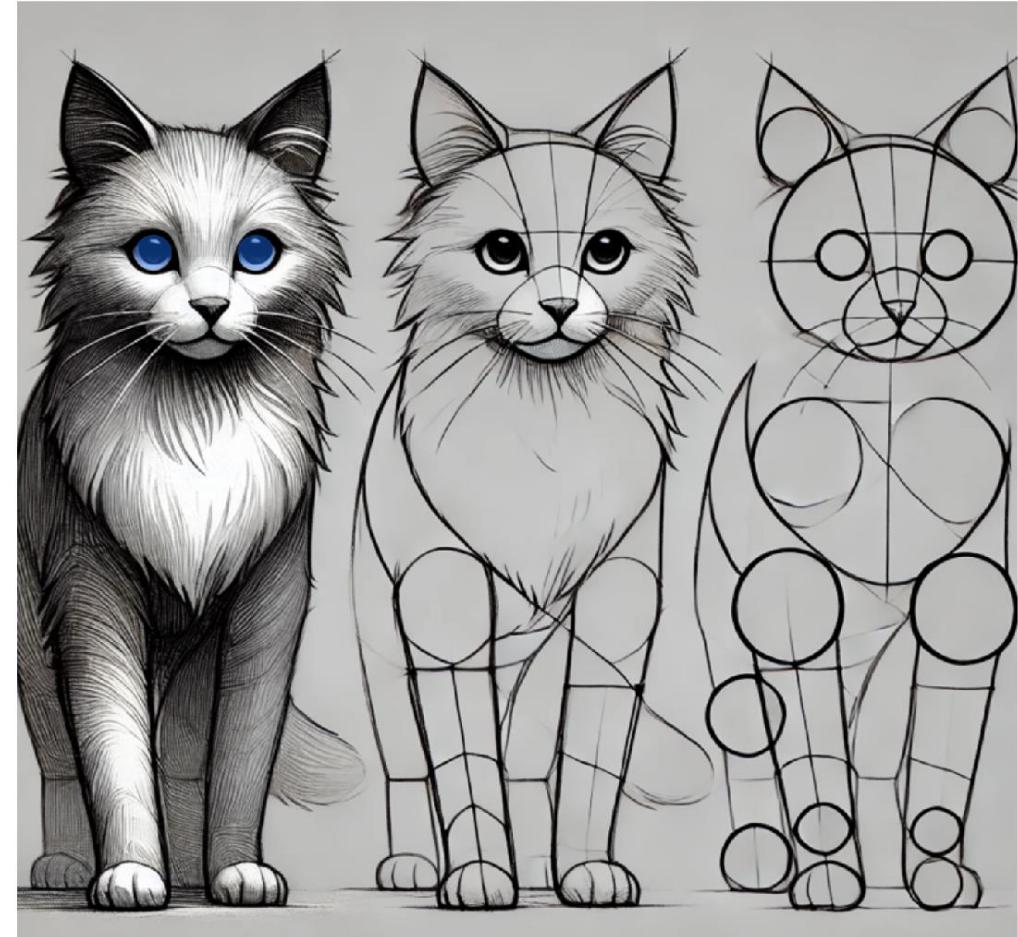
An algorithmic information theory of consciousness 

Giulio Ruffini 

Neuroscience of Consciousness, Volume 2017, Issue 1, 2017, nix019,  
<https://doi.org/10.1093/nco/nix019>

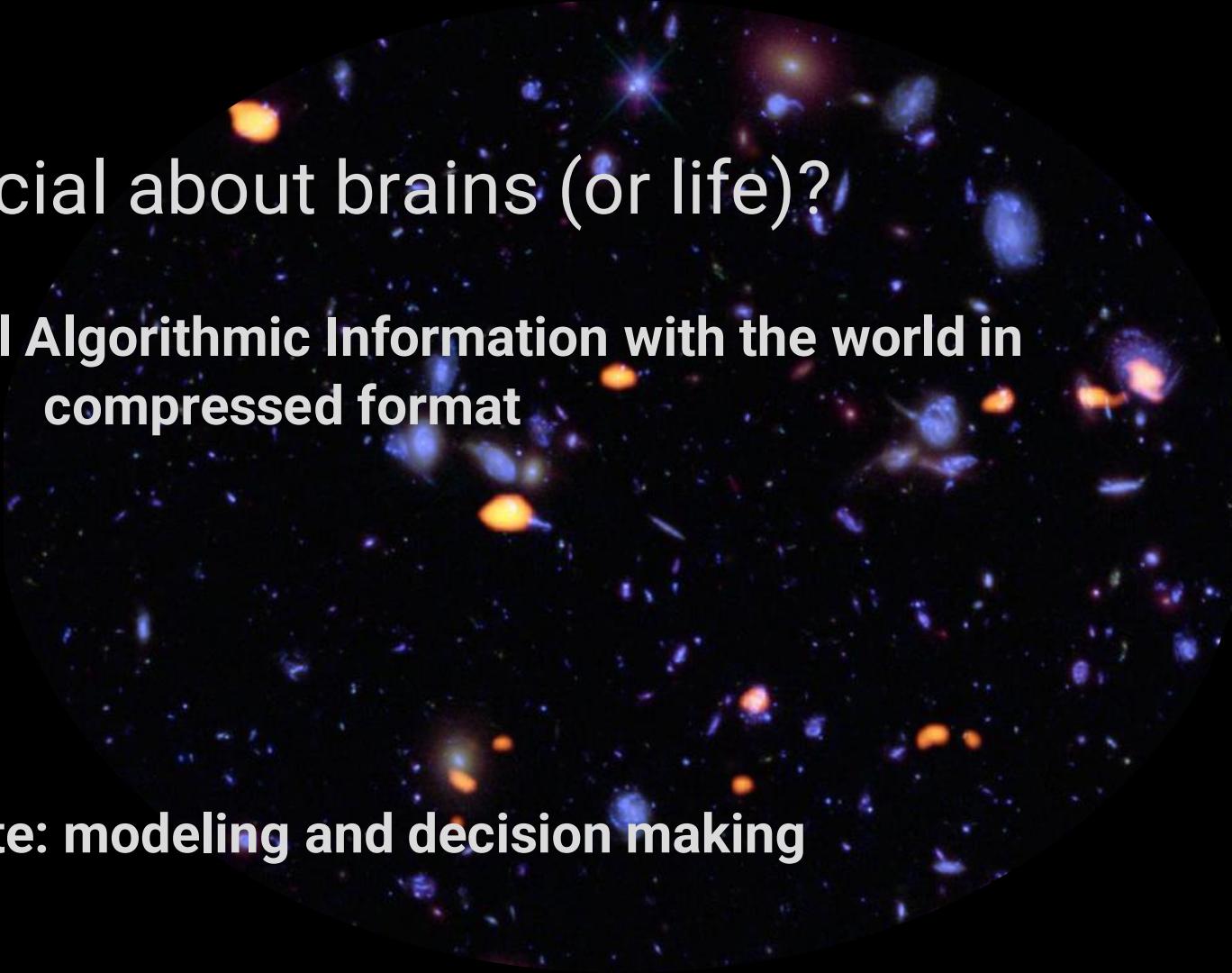
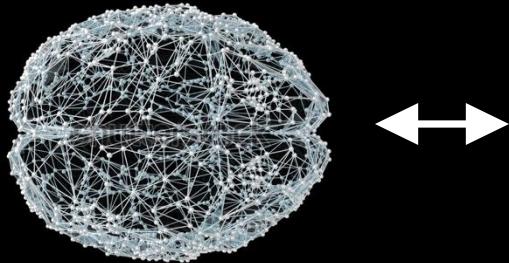
Coarse-  
grained  
modeling,  
lossy  
**compression**  
to extract  
useful  
structure

*Kolmogorov  
Complexity is the limit!*



# What is special about brains (or life)?

**#1 High Mutual Algorithmic Information with the world in compressed format**

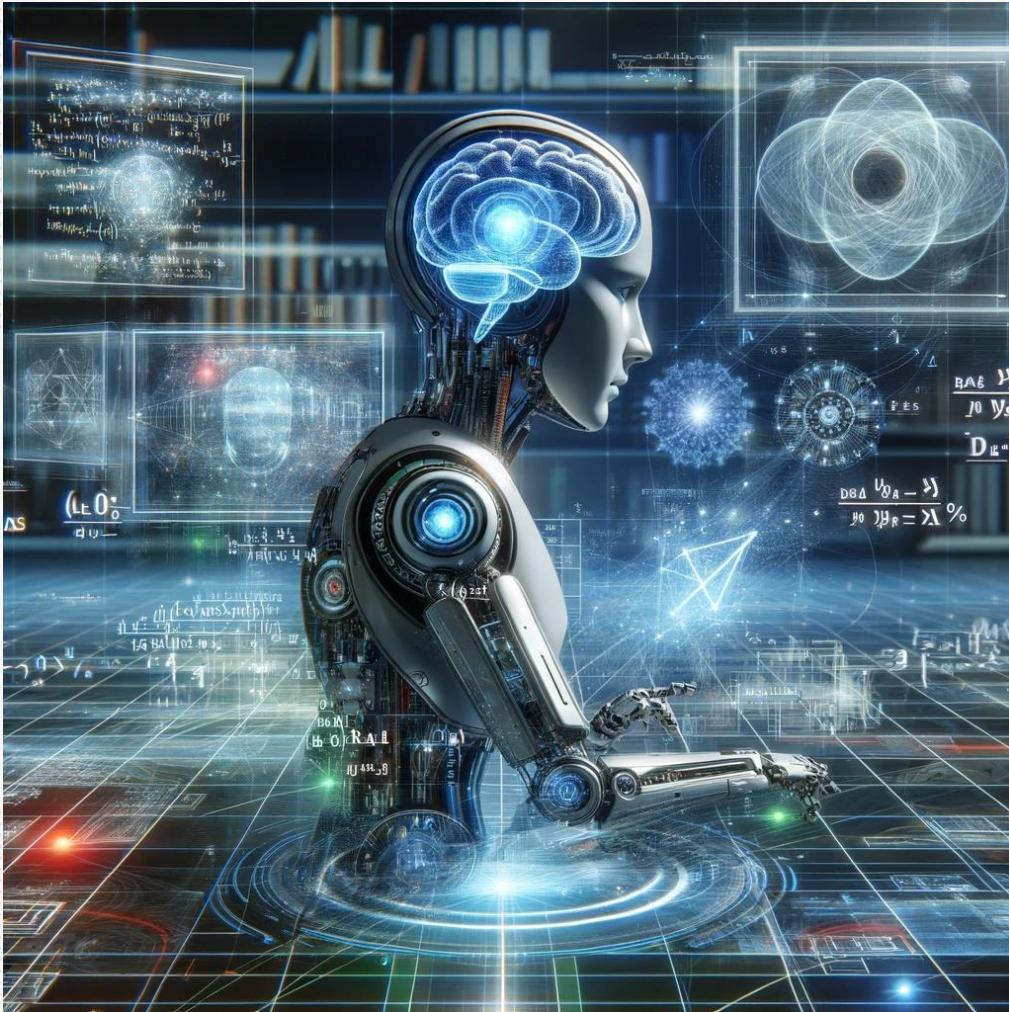


**#2 The compute: modeling and decision making**

# KT in a Nutshell

Ask what creates *structured experience* in an *algorithmic context*

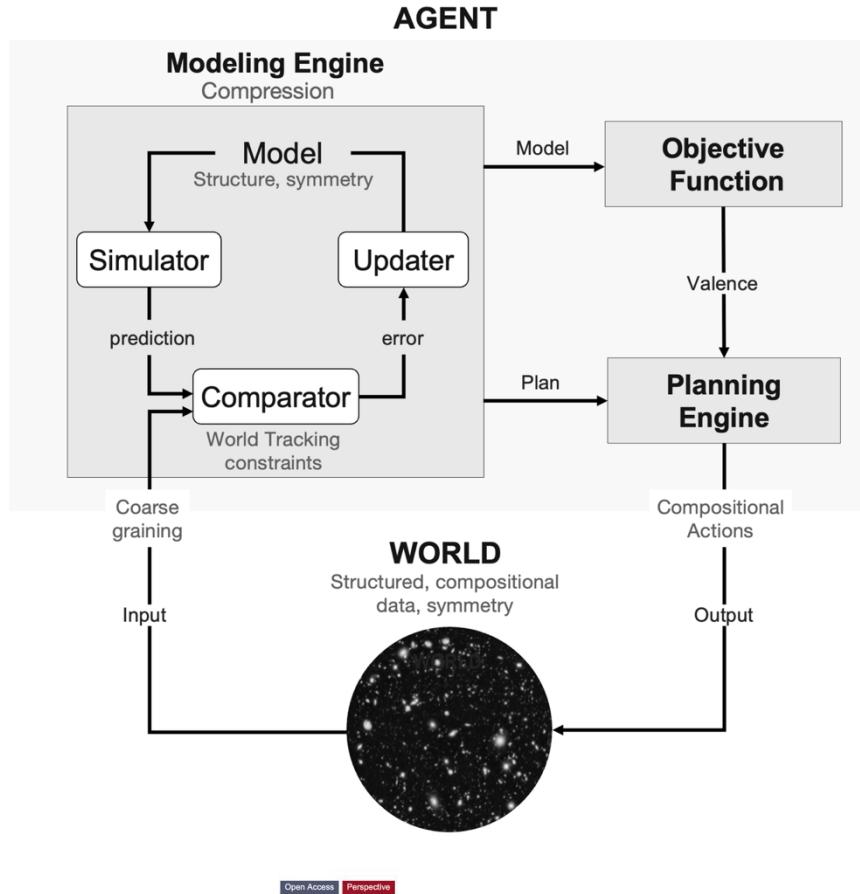
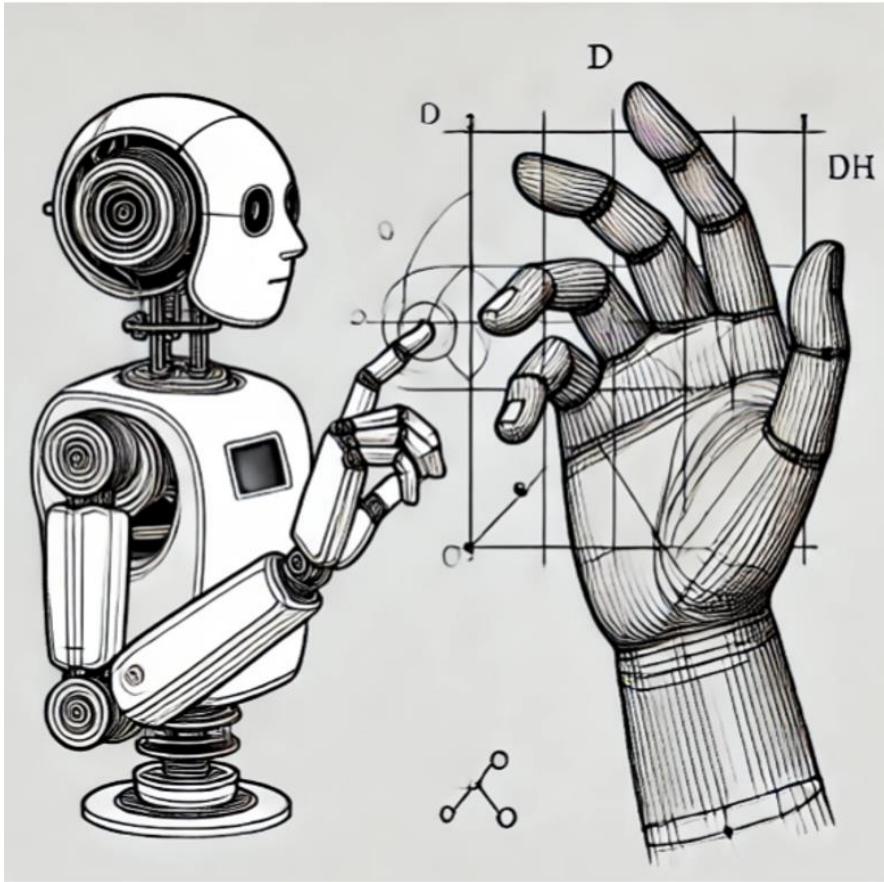
- A. Evolution gives rise to *agents* (and we are agents)
- B. Agents run *models of the world* and enjoy structured experience!
- C. Agents have *goals*. This gives origin to *valence & emotions*



## What is an algorithmic agent?

A computational system that interacts effectively with its environment by **planning** actions using **compressive predictive models** to maximize an **objective function**.

Using a model entails **computation** and **dynamics**.



## What is a *model*?

- A *program* that allows you to **compress coarse-grained** information
- A simplified but useful representation of reality
- A *mathematical object*

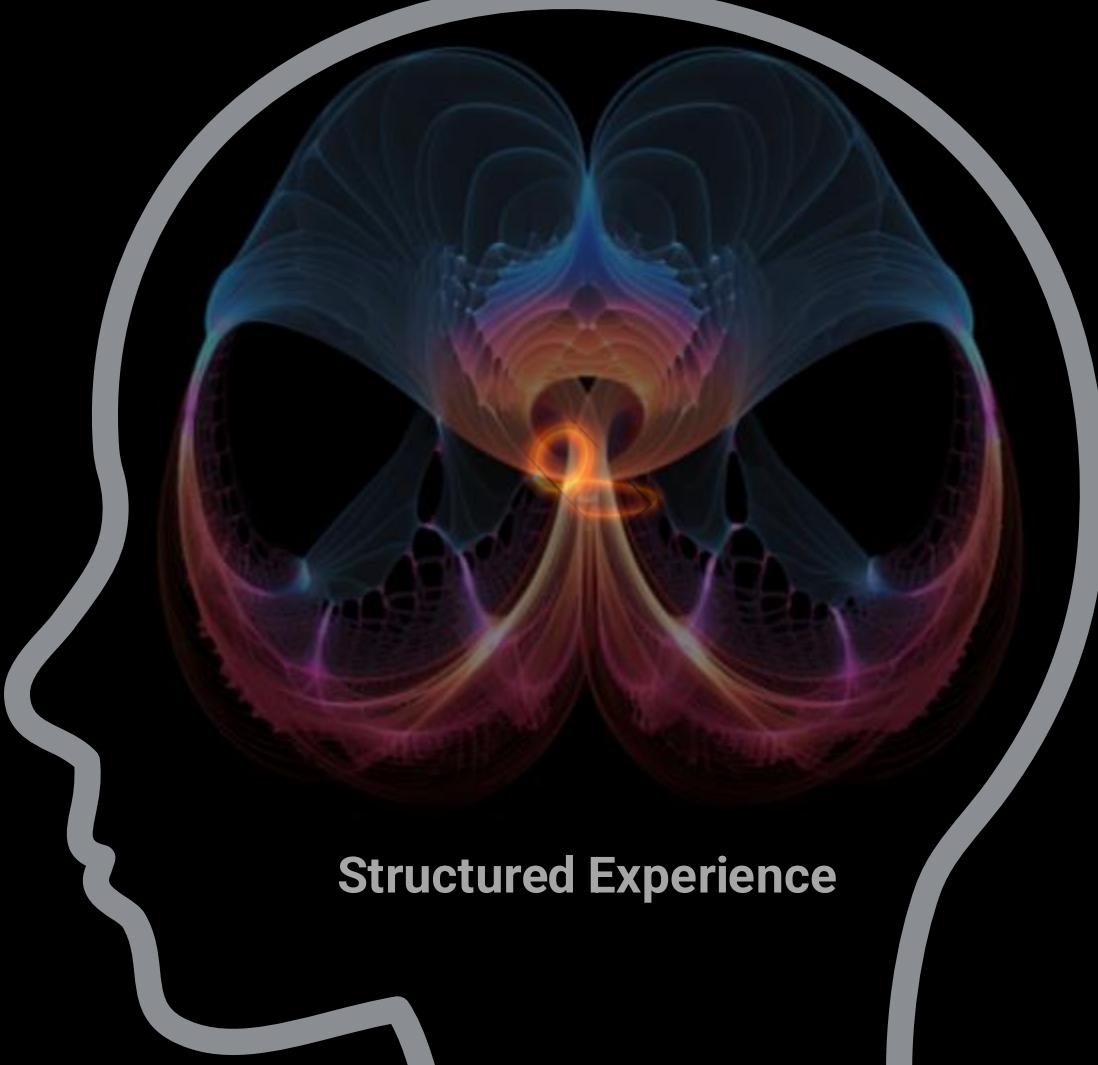
A model is *computation* and *dynamics*.

The brain computes\*, it is a dynamical system.

Dynamics is mathematics and geometry.

\* Classical or Quantum. Quantum ≠ Hypercomputation. Does not compute “new” things.





**Structured Experience**

# How do we define model structure?



Formalize *model* using **group theory**, capturing the idea of **simplicity** as **symmetry**. Then, we can show that

- 1) Tracking the world forces the agent as a dynamical system to mirror the symmetry in the data. Dynamics collapses to **reduced manifolds**.
- 2) The hierarchical nature of world data leads to **coarse-graining** and the notion of hierarchical constraints and manifolds

Open Access Article

Structured Dynamics in the Algorithmic Agent

by Giulio Ruffini 1,\* , Francesca Castaldo 1 , and Jakub Vohryzek 2,3

# The central hypothesis in KT

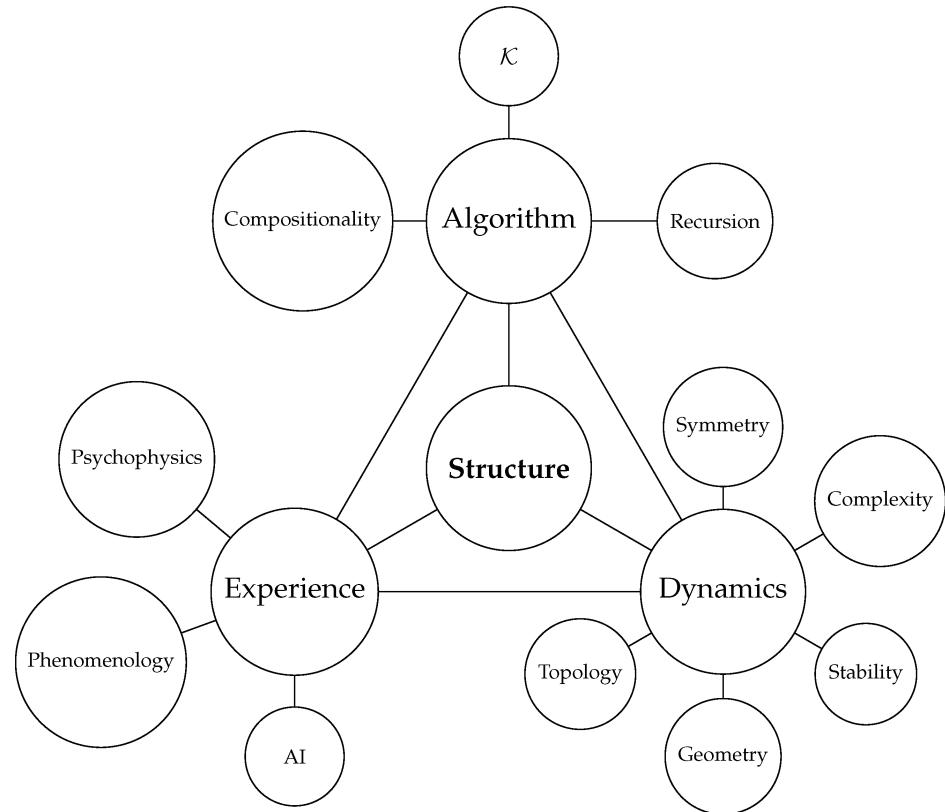
An agent has **structured experience ( $\mathcal{S}$ )** to the extent it has access to encompassing and **compressive models** to interact with the world.

More specifically, **the event of structured experience arises in the act of running models.**

**Model structure determines the structure of experience.**

Successful comparison with data leads to **wakeful presence.**

Much structured experience may be **unreported!**



# KT in practice #1

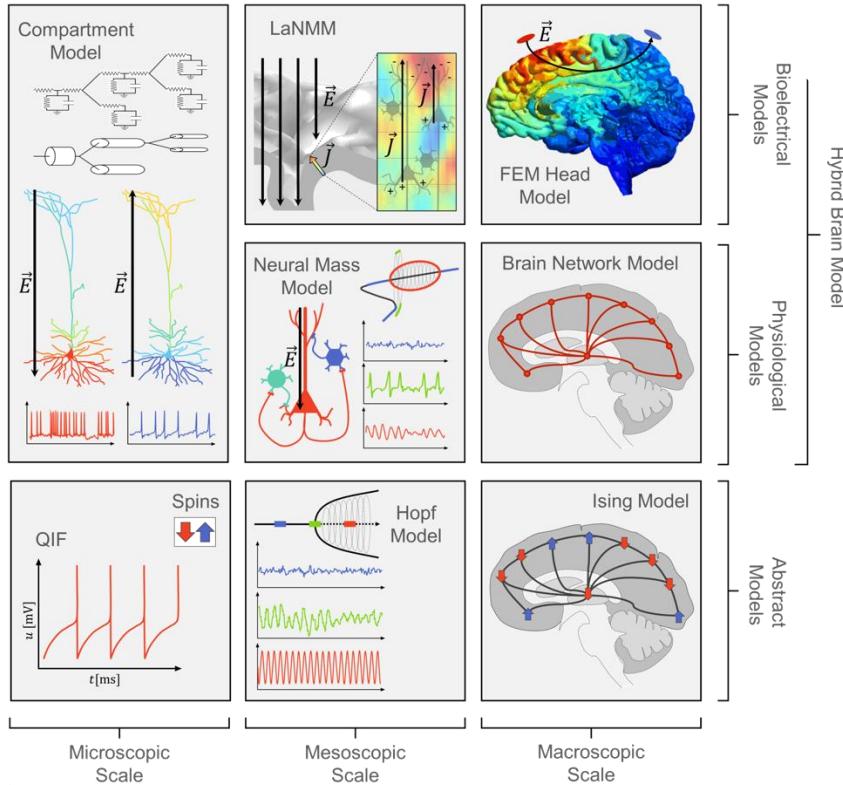
Requirements for  
structured experience

and

The Neural Correlates of  
Structured Experience



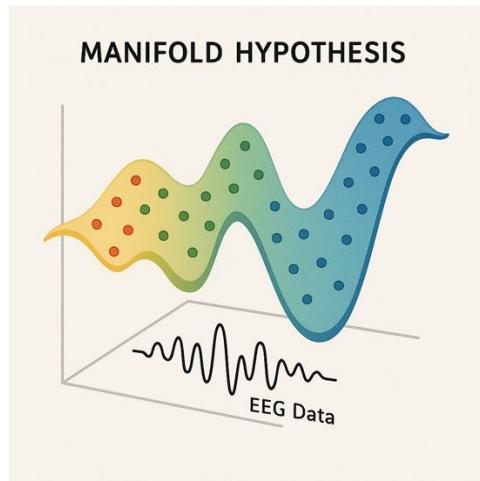
# Tool 1: Computational Modeling, Criticality



**Aim:** Mechanistic interpretation of brain data using whole-brain computational models. The *computational, critical brain* as a requirement.



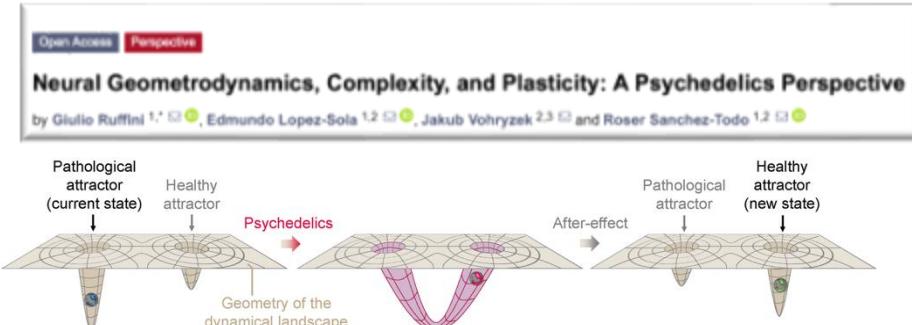
# Tool 2: Topology, Group Theory



**Open Access Perspective**

**Neural Geometrodynamics, Complexity, and Plasticity: A Psychedelics Perspective**

by Giulio Ruffini <sup>1,\*</sup>, Edmundo Lopez-Sola <sup>1,2</sup>, Jakub Vohryzek <sup>2,3</sup> and Roser Sanchez-Todo <sup>1,2</sup>



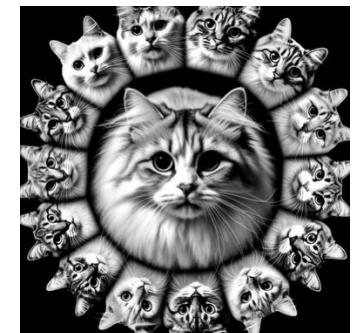
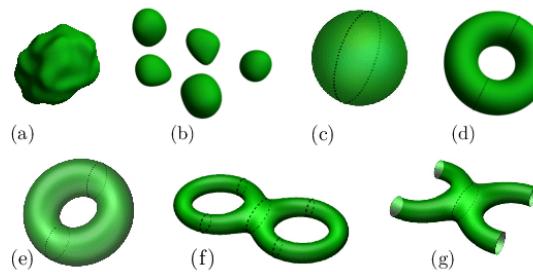
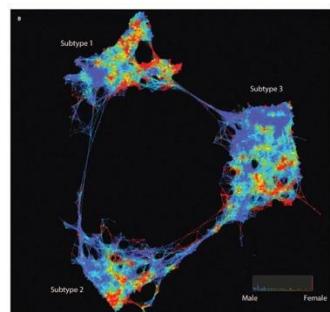
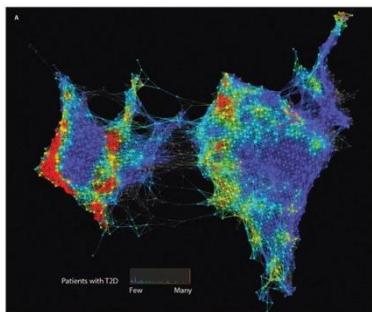
**Netw Neurosci.** 2019 Jul 1;3(3):725–743. doi: [10.1162/netn\\_a\\_00002](https://doi.org/10.1162/netn_a_00002)

**Topological exploration of artificial neuronal network dynamics**

Jean-Baptiste Bardin <sup>1</sup>, Gard Spreemann <sup>2</sup>, Kathryn Hess <sup>3,\*</sup>

**Structured Dynamics in the Algorithmic Agent**

by Giulio Ruffini <sup>1,\*</sup>, Francesca Castaldo <sup>1</sup> and Jakub Vohryzek <sup>2,3</sup>



# KT in practice #2

**Computational  
Psychiatry:**

**Where first-person and  
third-person views  
meet**

Open Access Perspective

**The Algorithmic Agent Perspective and Computational Neuropsychiatry: From Etiology to Advanced Therapy in Major Depressive Disorder**

by Giulio Ruffini 1,\* , Francesca Castaldo 1,\* , Edmundo Lopez-Sola 1,2 , Roser Sanchez-Todo 1,2  and Jakub Vohryzek 2,3 

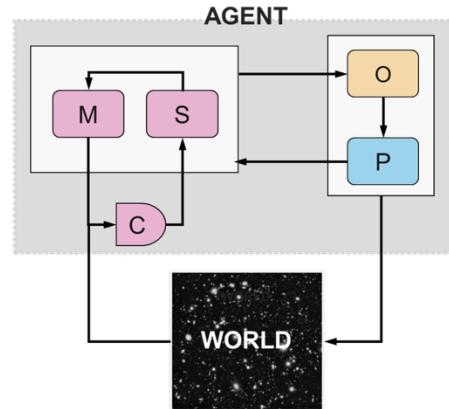


# Computational psychiatry



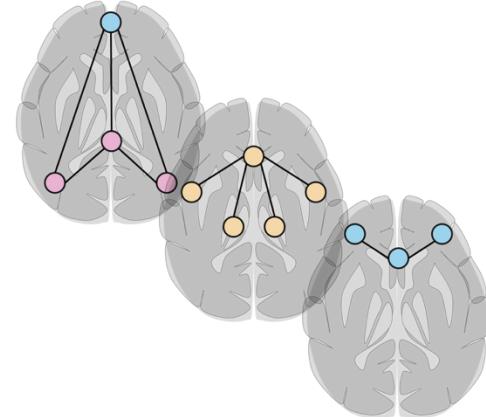
## Algorithmic Agent

Component and functions  
Structured valence  
MDD Agent Model



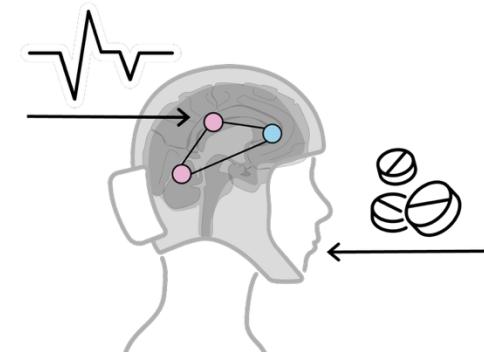
## Translational Framework

Brain circuits  
MDD biotypes  
Dynamical landscape  
Neurophenomenology



## MDD Treatment

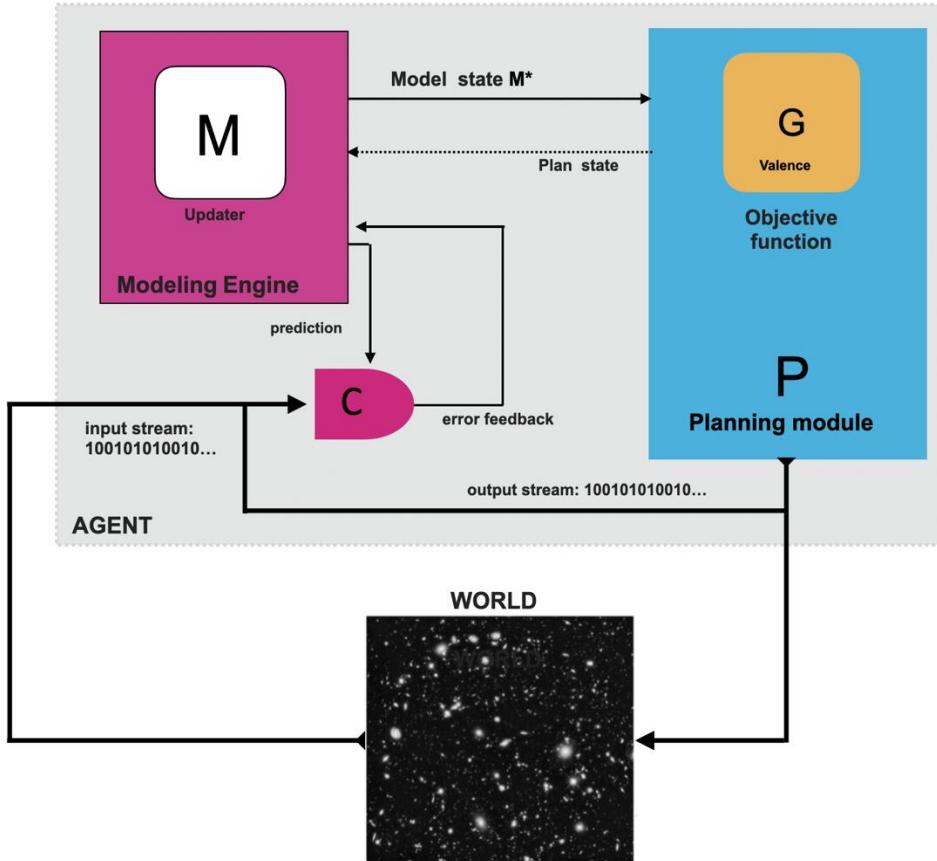
Psychedelics  
Stimulation  
Combined therapy  
Computational neuropsychiatry



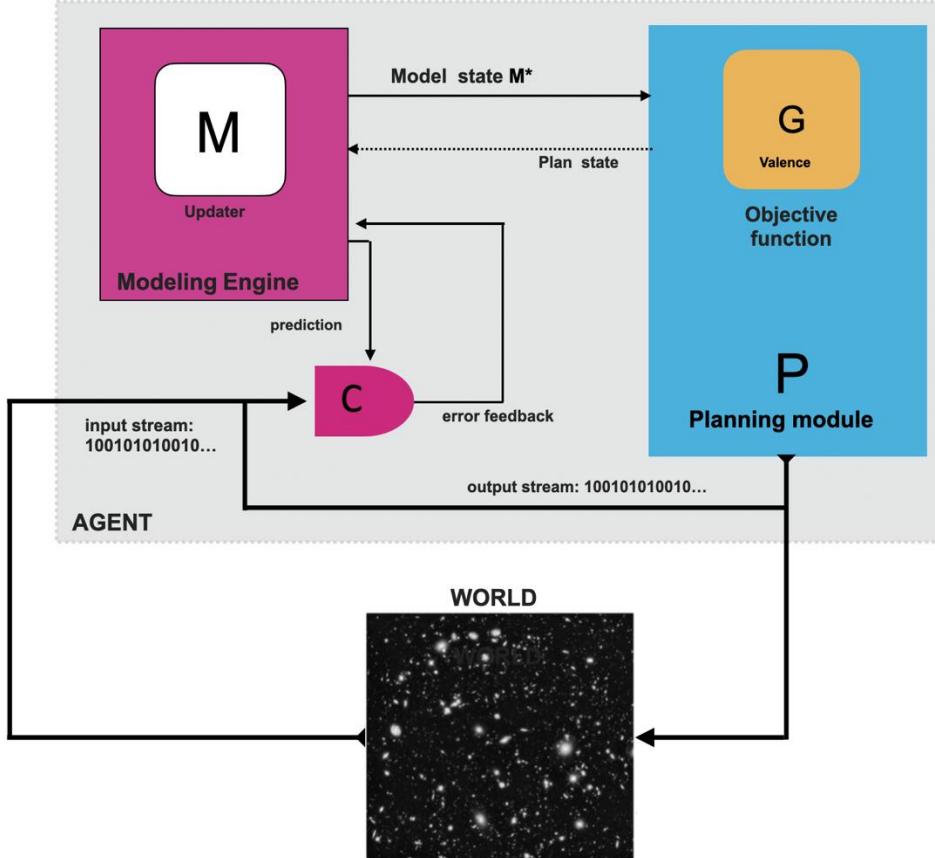


Agents have an  
**Objective Function**  
that sets their **goals**.

It quantifies how well  
or bad they are doing,  
the mathematical  
analog of **valence**  
(pleasure and pain).



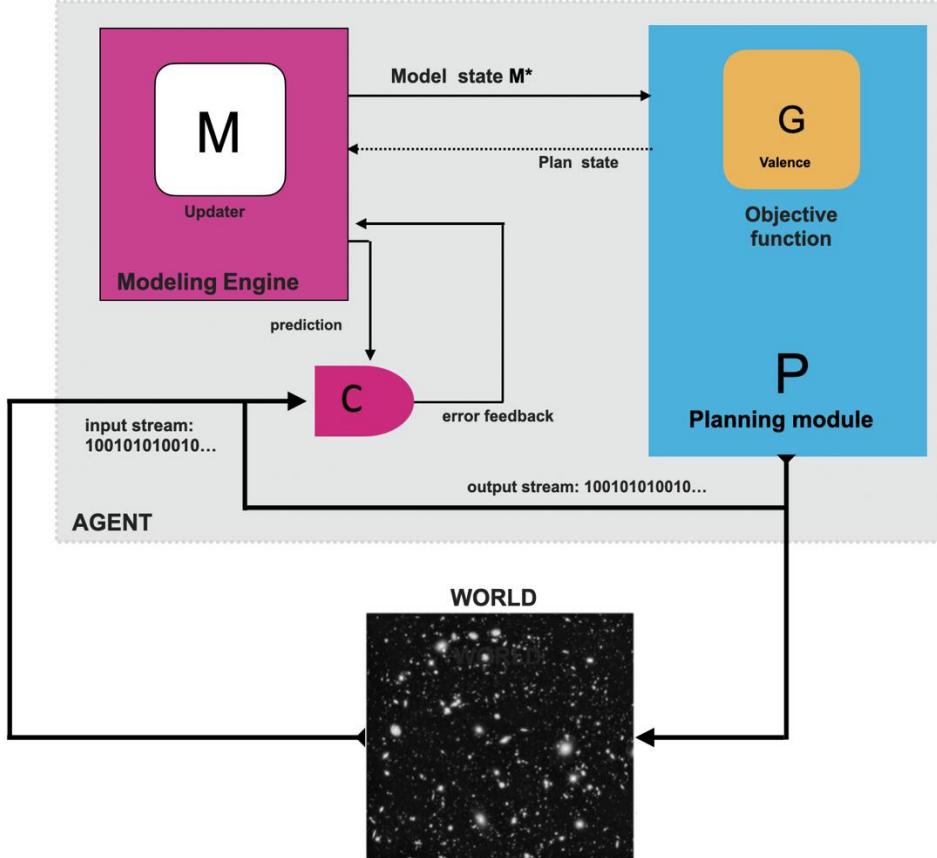
The Agent: Model +  
Goal + Planning



## The Agent: Model + Goal + Planning

We are now in the position to define *emotion*:

**Emotion = Model + Valence**

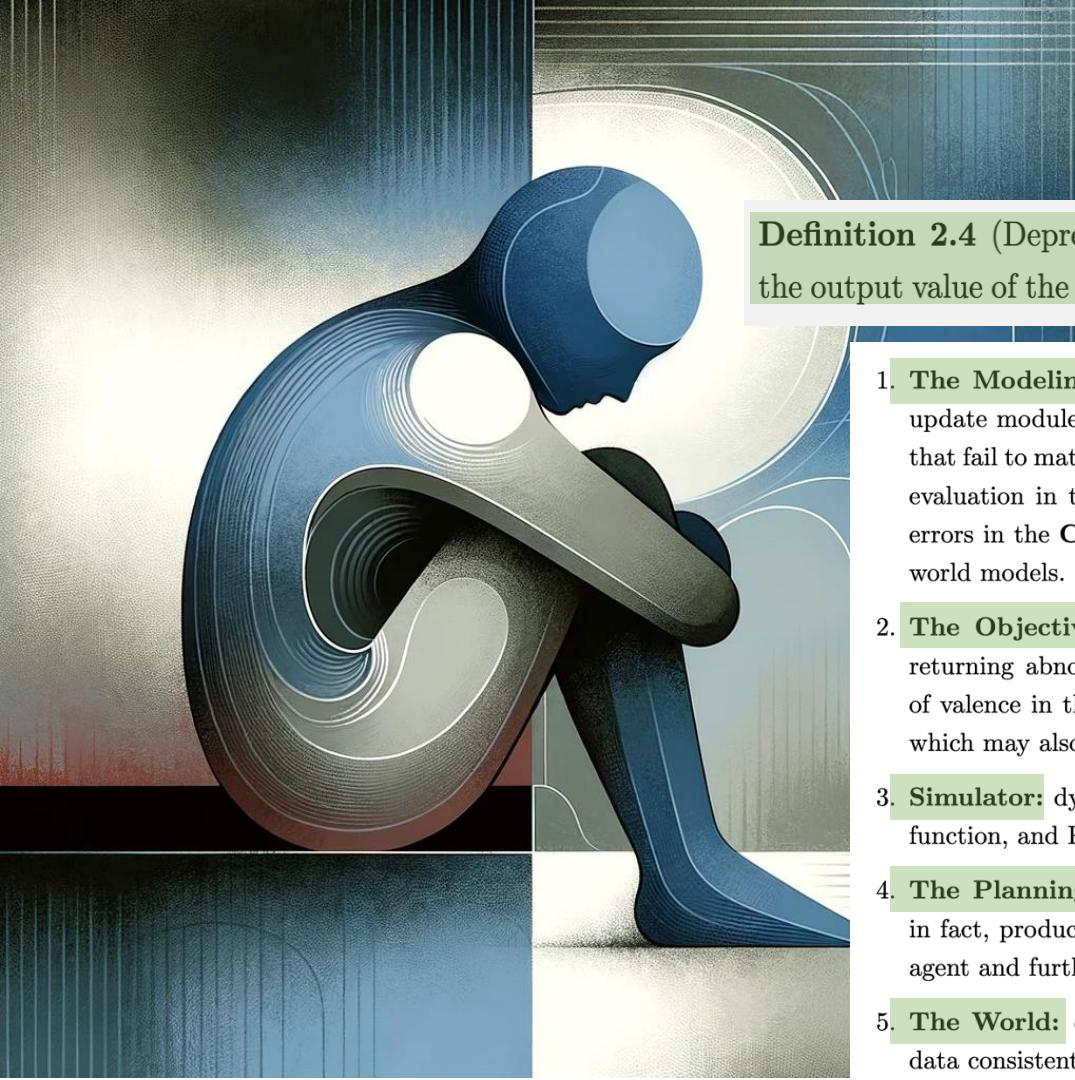


## The Agent: Model + Goal + Planning

We are now in the position to define *emotion*:

**Emotion = Model + Valence**

... and *depression*:  
A pathological state of  
persistent low **Valence**



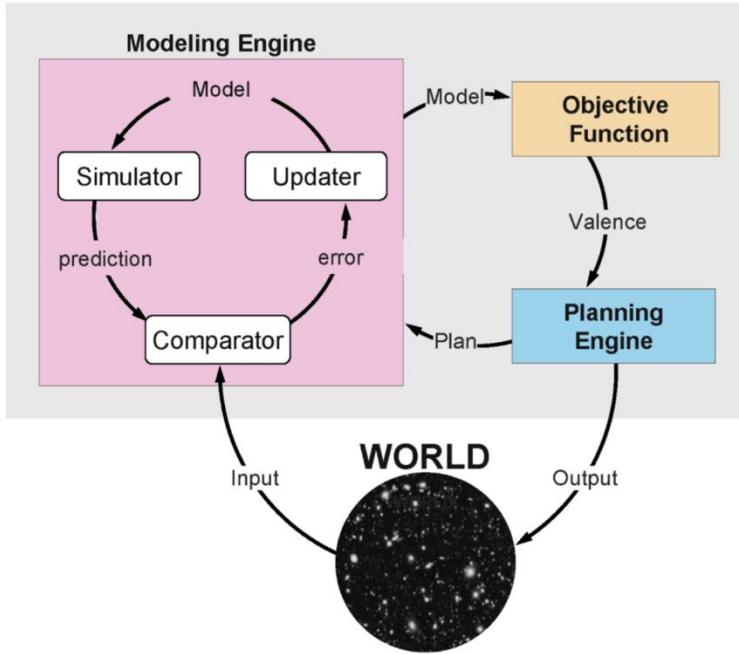
# Multiple roads to a depressed agent

**Definition 2.4** (Depressed Agent). Depression is a pathological state in which the output value of the objective function (valence) of an agent is persistently low.

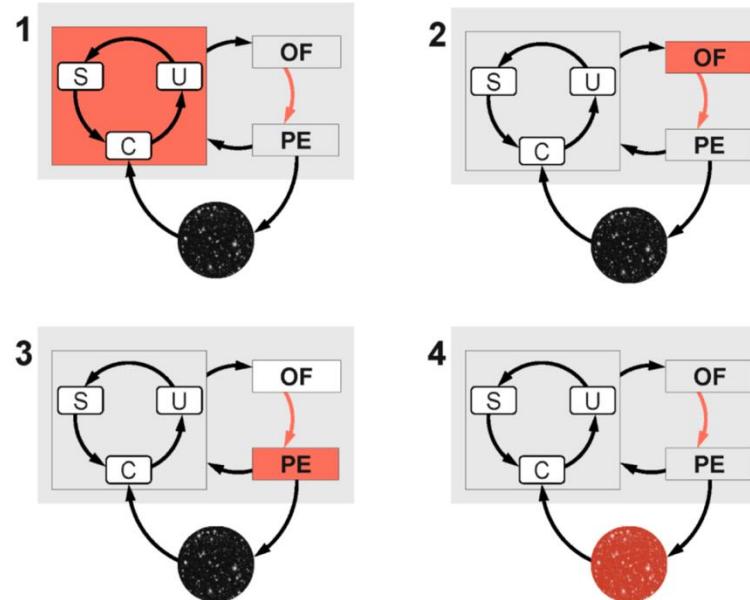
1. **The Modeling Engine:** inaccurate world models due to a dysfunction of the update module (model building errors, dysfunctional plasticity, etc.), i.e., models that fail to match input data, thus leading to high prediction errors and low valence evaluation in the Objective function. Since model updating requires evaluating errors in the **Comparator**, Comparator dysfunction may also lead to inaccurate world models.
2. **The Objective Function:** dysfunctional objective function, i.e., persistently returning abnormally low valence regardless of the input data. The evaluation of valence in the Objective function is very complex and requires the Simulator, which may also be at fault.
3. **Simulator:** dysfunction in the simulator will affect the Modeling engine, Objective function, and Planning engine.
4. **The Planning engine:** inability to find plans to increase valence. This may, in fact, produce plans that impact the World with negative consequences for the agent and further decreases of valence.
5. **The World:** objectively hostile world conditions<sup>6</sup>, i.e., the agent receives input data consistent with genuine threats to its homeostasis.

# Agent-types of depression

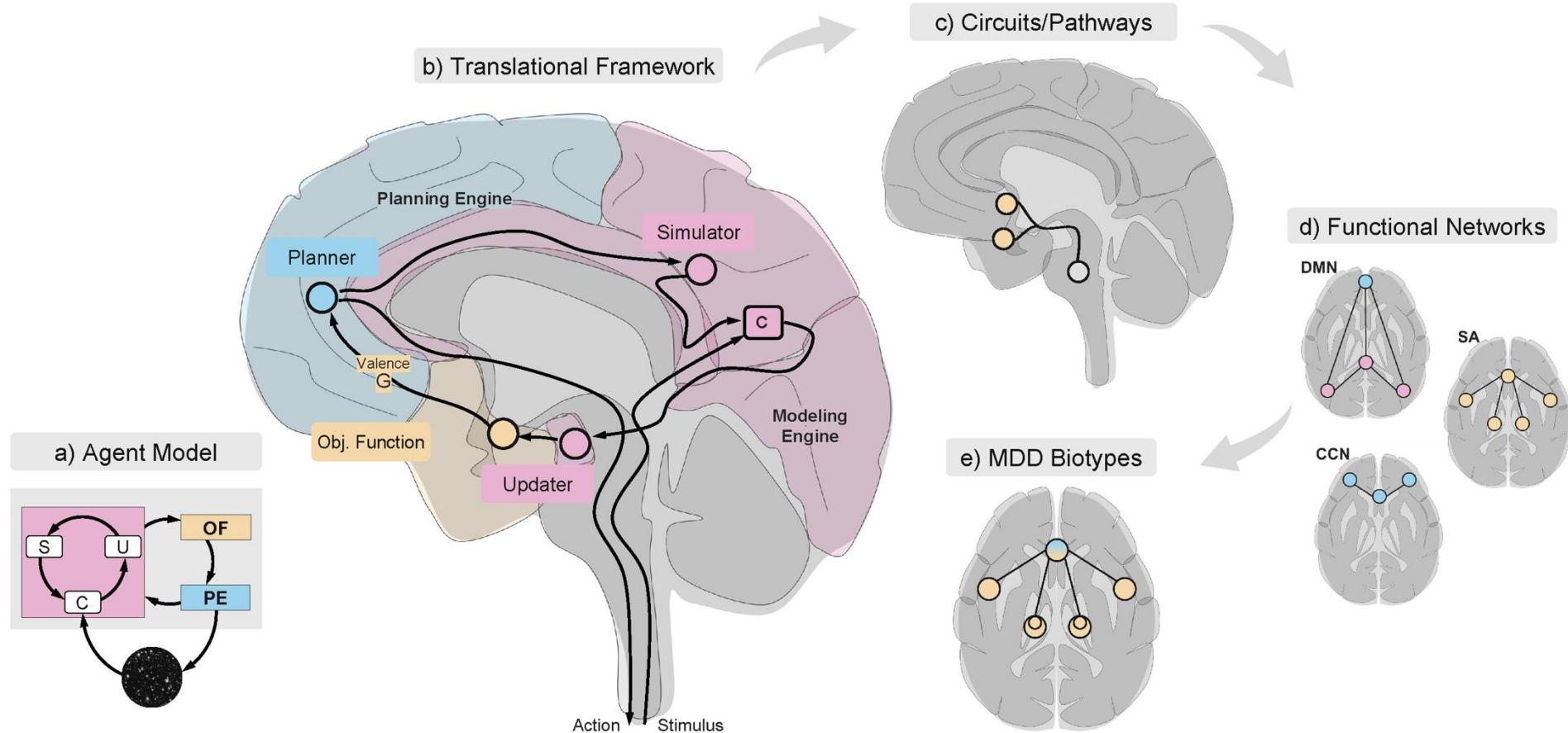
## a) AGENT



## b) MDD AGENT



# Depression: circuits and biotypes



# KT in practice #3

1. Predictive processing theory / Active Inference (Friston)
2. Alzheimer's and Psychedelics
3. How do you connect a whole-brain model?

Open Access Perspective

## Neural Geometrodynamics, Complexity, and Plasticity: A Psychedelics Perspective

by Giulio Ruffini 1,\* , Edmundo Lopez-Sola 1,2 , Jakub Vohryzek 2,3 , and Roser Sanchez-Todo 1,2 

## Cross-Frequency Coupling as a Neural Substrate for Prediction Error Evaluation: A Laminar Neural Mass Modeling Approach

 Giulio Ruffini,  Edmundo Lopez-Sola,  Raul Palma,  Roser Sanchez-Todo,  Jakub Vohryzek,  Francesca Castaldo,  Karl Friston

doi: <https://doi.org/10.1101/2025.03.19.644090>

## Fast Interneuron Dysfunction in Laminar Neural Mass Model Reproduces Alzheimer's Oscillatory Biomarkers

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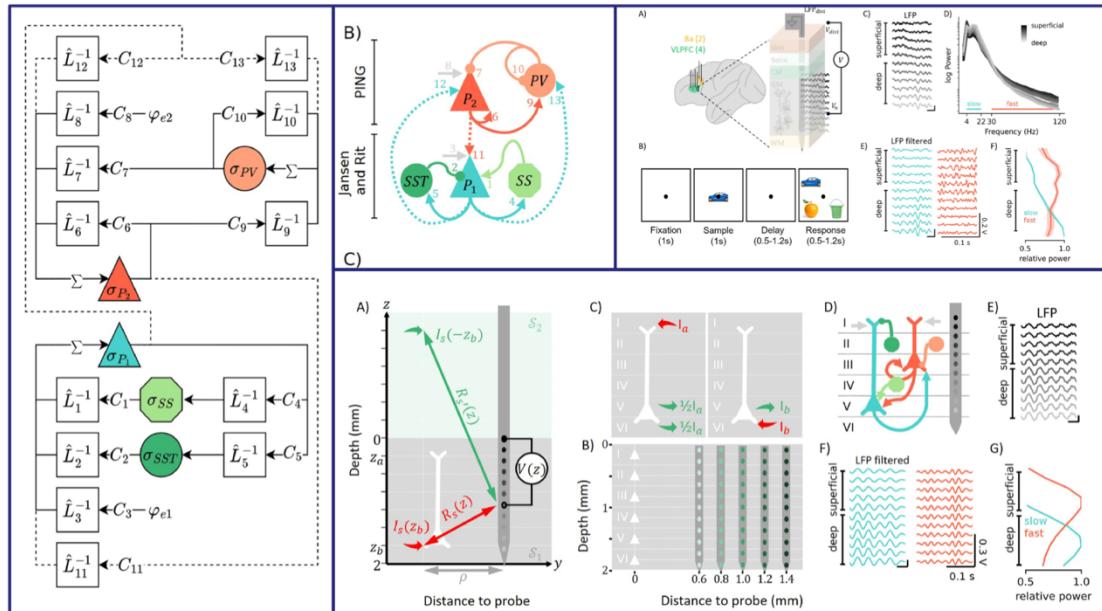
 Jan C. Gendra,  Edmundo Lopez-Sola,  Francesca Castaldo,  Élia Leal-Custey,  Roser Sanchez-Todo,  Jakub Vohryzek,  Ricardo Salvador,  Ralph G. Andrzekaj,  Giulio Ruffini, the Alzheimer's Disease Neuroimaging Initiative

doi: <https://doi.org/10.1101/2024.12.15.628565>

A physical neural mass model framework for the analysis of oscillatory generators from laminar electrophysiological recordings

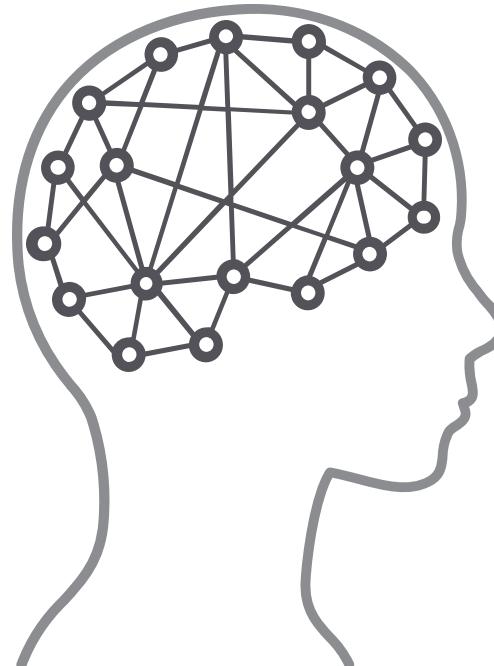
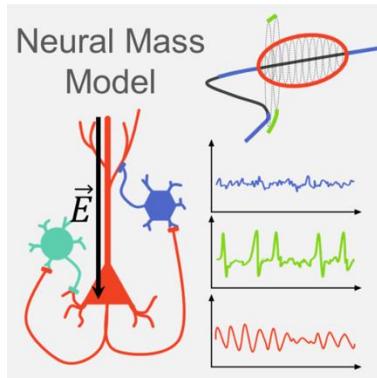
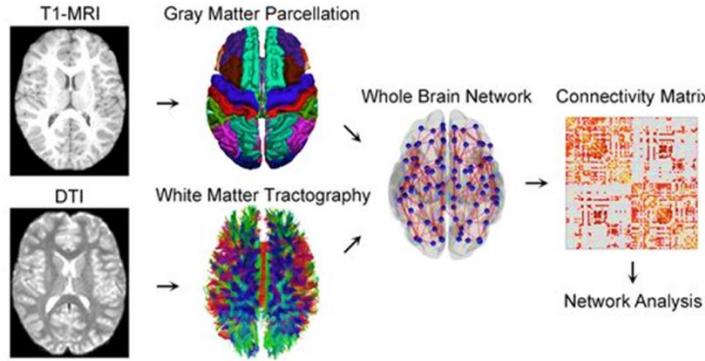
# Neurotwin Technology

- Biophysical model of a cortical column with laminar (superficial/deep) structure.
- Integrates alpha (slow) and gamma (fast) oscillatory subnetworks.
- Merges Jansen-Rit (alpha) and PING (gamma) models.
- Includes deep/superficial pyramidal cells (P1/P2), inhibitory interneurons (PV), and excitatory stellate inputs.

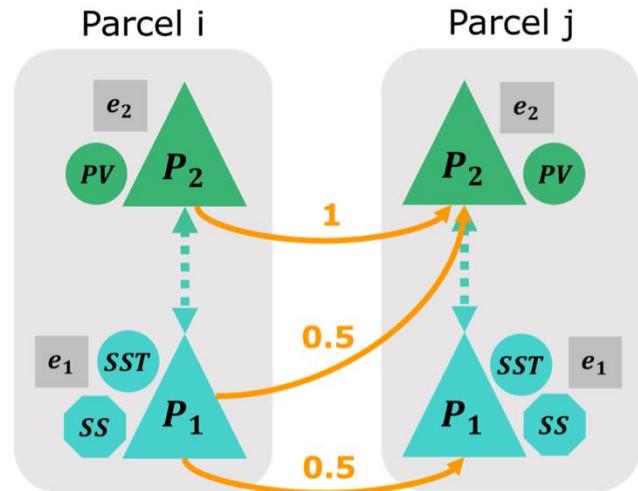
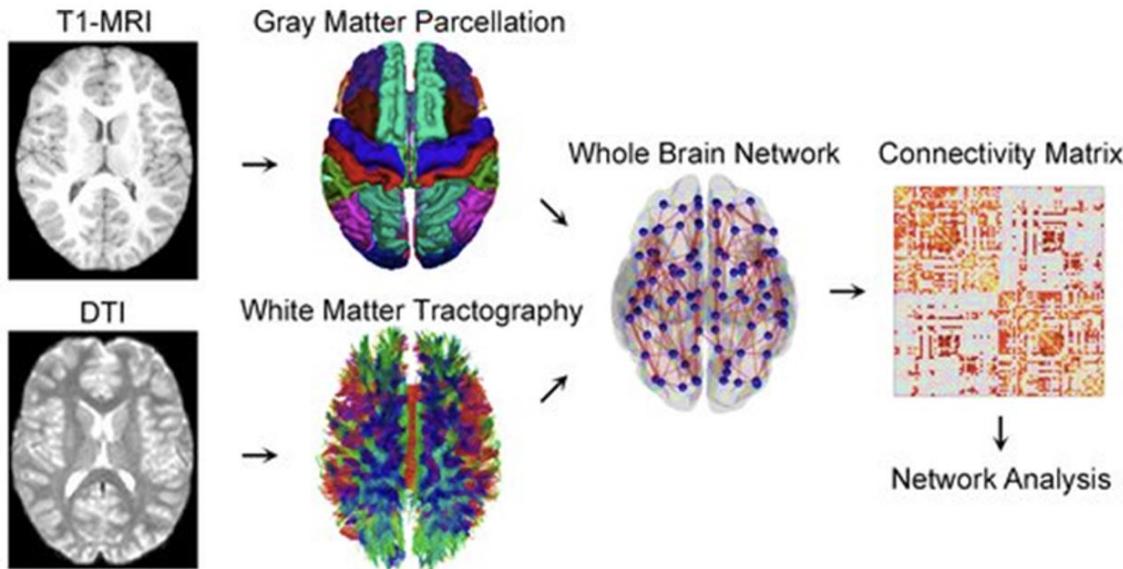


A physical neural mass model framework for the analysis of oscillatory generators from laminar electrophysiological recordings

# How do you wire a Whole-brain Model?



# Undirected links? Where, precisely?



Gendra et al 2024

# How do you connect the computational brain?

## Comparator Mechanism (Concept)

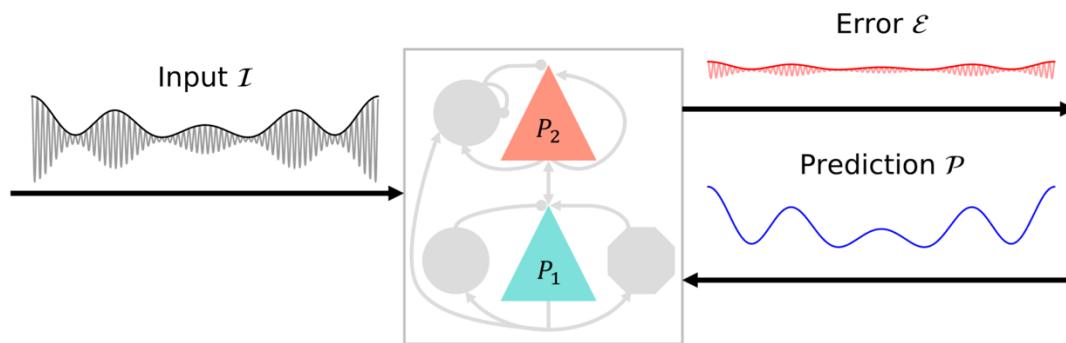
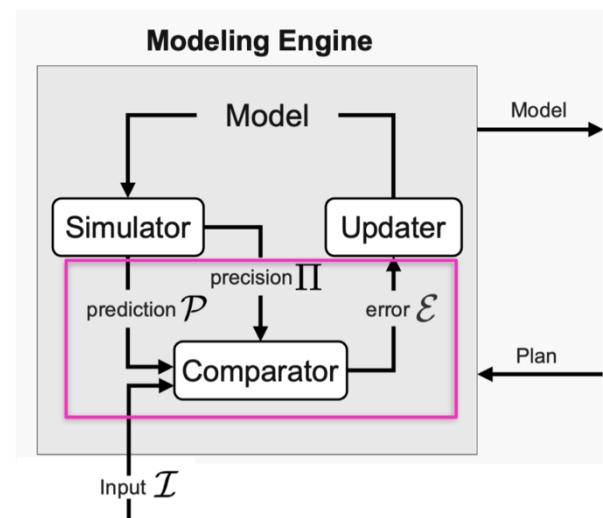


Figure: Conceptual diagram of the Comparator, illustrating how an input  $I(t)$  (fast signal + envelope) and a prediction  $P(t)$  (slow signal) combine to produce an error signal  $E(t)$ , with precision signals as envelopes controlling gain

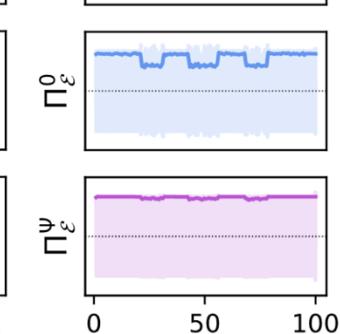
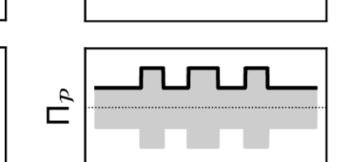
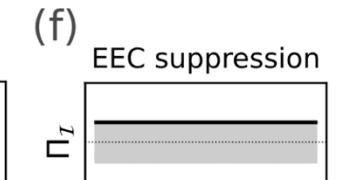
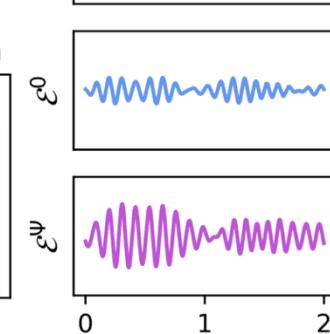
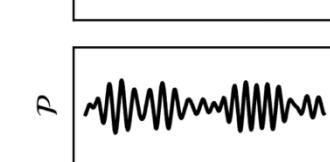
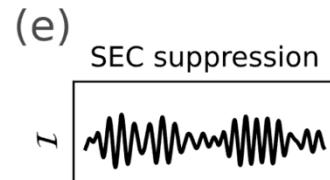
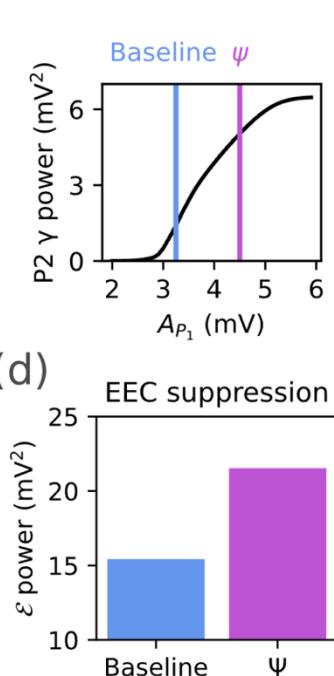
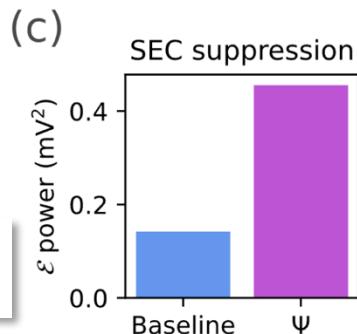
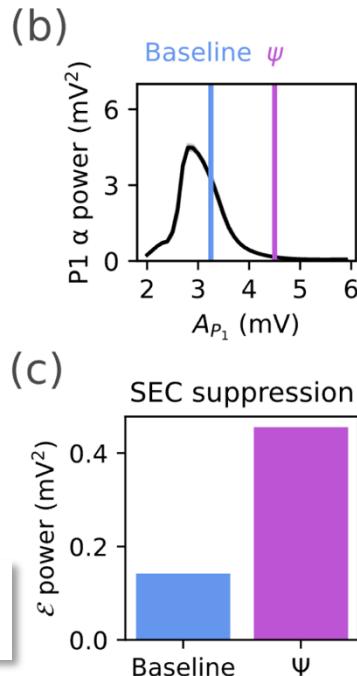
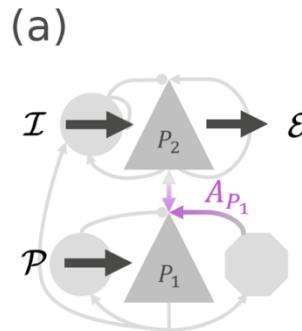


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# Effects of Psychedelics



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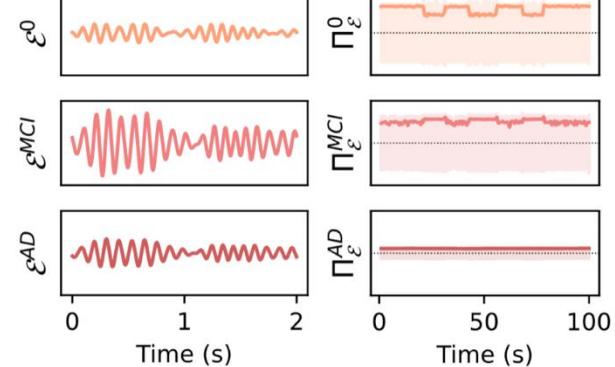
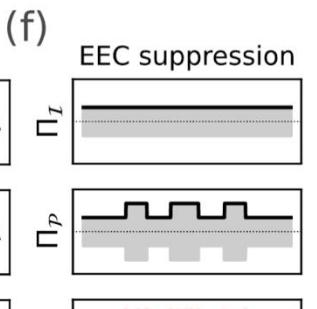
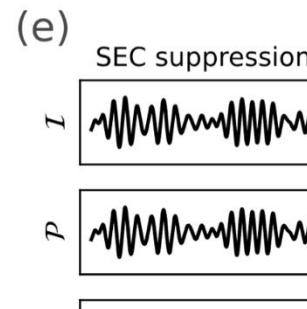
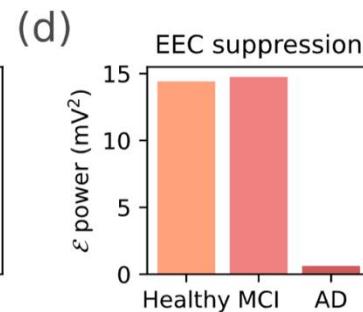
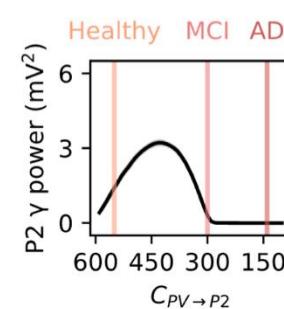
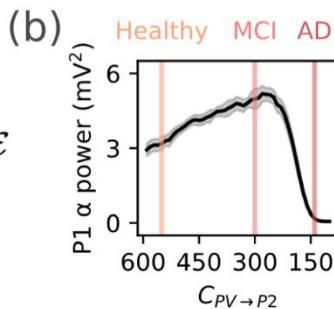
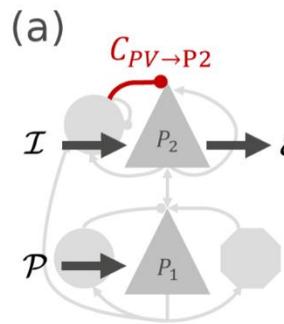
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# The comparator on psychedelics



- **Result:** deep-layer  $\alpha$  power was markedly reduced, and superficial  $\gamma$  power was elevated (disinhibition of fast activity).
- Even with a matching prediction, the error signal remained abnormally high – the model failed to attenuate prediction errors under this hyper-excitable condition.
- **Interpretation:** Weakened top-down constraints (reduced precision of priors) lead to unfiltered bottom-up signals and excessive prediction errors. This aligns with the REBUS model of psychedelics: **relaxed priors → an “anarchic” increase in error signals.**

# Comparator under PV dysfunctions perturbations (AD and others)



Fast Interneuron Dysfunction in Laminar Neural Mass Model Reproduces Alzheimer's Oscillatory Biomarkers

Roser Sanchez-Todo, Borja Mercadal, Edmundo Lopez-Sola, Maria Guasch-Morgades, Gustavo Deco, Giulio Ruffini  
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# Perturbation: PV interneuron dysfunction AD model)



- **Moderate PV loss (early stage):** gamma power increases and prediction error signals are amplified (hyper-excitable cortex with excessive surprise signals).
- **Severe PV loss (late stage):** gamma oscillations collapse into slow-wave dominance (hypoactive cortex), and error signals are greatly attenuated or absent.
- **Interpretation:** Early interneuron dysfunction causes exaggerated prediction errors (**overestimating surprise**), whereas advanced dysfunction leads to a breakdown of error signaling (**failure to propagate errors**).

# Conclusions and Future Directions



'Agent' emerges

$K$

```

 $N^N$  BB(N)
 $N^2-N^3$  if A'(N) >
A(N) then
A'=M(A)
yB N M
B_k O_2N B
a\B M(C)
BB(A) C
if B'(N) >
B(N) 2^
then
B'=M
a_j (B)
yC M
C(N) n
D(N) D
xJ (C)
yD M
n
D(N) D

```

PROVING DARWIN  
Making Biology  
Mathematical

GREGORY CHAITIN



# The Algorithmic Weltanschauung

- There is **Spirit/Experience** and **Mathematics**
- Mathematics gives rise to an **"algorithmic soup"** of possibilities
- There are **persistent patterns** in the soup. Some we call Agents, driven by telehomeostasis.
- Each is the **Observer**
- Agents **coarse-grain** information to create **compressive models** (**Emergence**).
- This leads to subjective **Valenced Structured Experience**
- This is **Observer's Reality**

# The Algorithmic Weltanschauung: Key Concepts



- Pure vs structured experience
- Mathematics (science of structure)
- Algorithms/computation
- Algorithmic Soup
- Kolmogorov Complexity and Mutual Algorithmic Information
- Persistent algorithmic patterns: Agents and telehomeostasis (*life*)
- Coarse-graining for Emergence (useful compression)
- Modeling, compression. Simplicity.
- Goals, Model structure + Valence => Emotion
- Reported vs. unreported experience => a crucial conceptual element

*What people normally call consciousness is here “reported (to self or others) structured experience”*

# Future



Demonstrate how to **computationally evolve agents**.

KT conjecture: *Under the right conditions, persistent patterns are unavoidable in a computational soup if we wait long enough.*

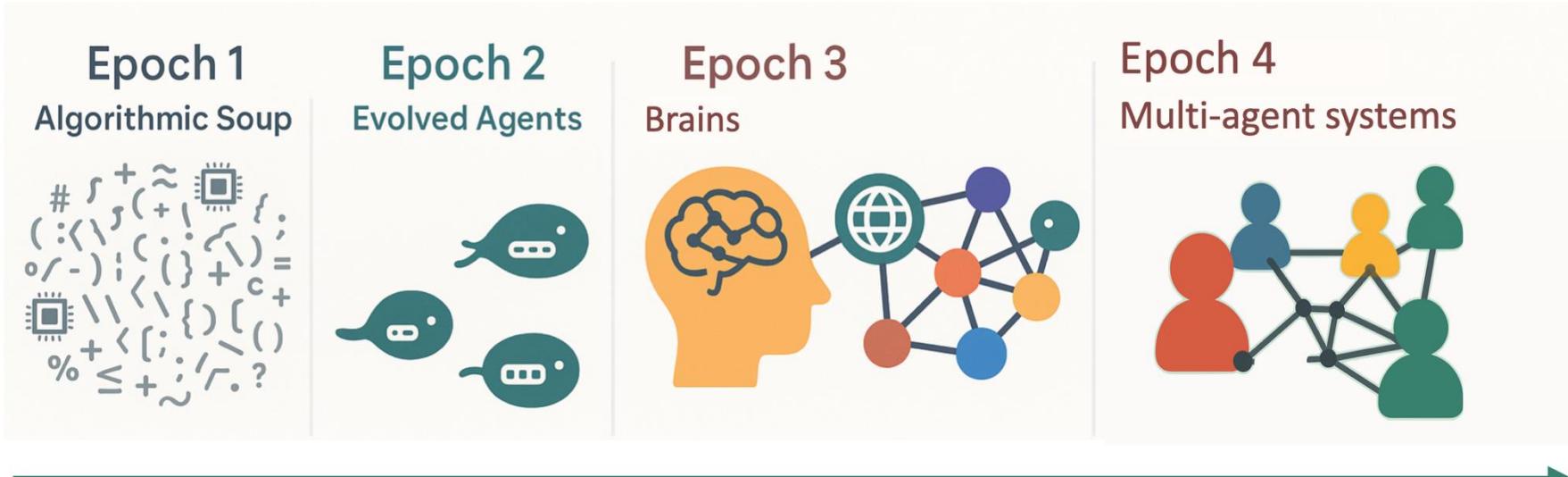
Are there persistent patterns other than **agents**?

Devise methods to **detect** an **agent** through its behavior, inner dynamics or structure

Associate the structure of dynamical reduced manifolds with 1P and 3P data

Map the neurobiology of agenthood

# The Algorithmic Weltanschauung



Iterations

# Summary

- 1) We focused on the requirements for *structured experience*
- 2) Reality is a model, KT is well aligned with Idealism
- 3) Tracking the world requires computation to run models
- 4) This constrains brain structure and also collapses dynamics to reduced manifolds, the characteristics of which are good candidates for “neural correlates of structured experience (NCSE)”
- 5) Emotion is defined by combining structured experience (model structure) and Valence (Objective function)
- 6) This framework can guide computational neuroscience, bringing together 3P and 1P perspectives in neuropsychiatry

Thanks to my collaborators and the Neuroelectrics team, and to my EU funders (HIVE, Luminous, Neurotwin, Galvani, Luminous projects).  
Special thanks to the EU FET program.

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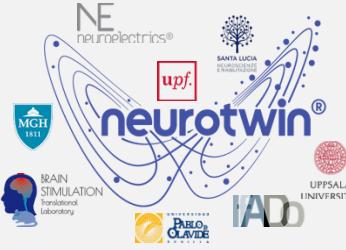
galvani  
LTSI  
UNIVERSITÉ DE  
RENNES 1

- Whole-brain Personalization Methods
- Whole-brain Optimization methods
- Clinical study design and analysis

The project is investigating the impact **weak electric fields** have on the physiology of neurons and neural networks. The key objective is to understand if these electric pulses can improve the patient-specific **epileptogenic network**.



Funded by  
the European Union



- Laminar Neural Mass Model
- Whole-brain Model
- Analysis Clinical Studies

The **aim** is to develop **advanced brain models** that characterize individual pathology and predict the physiological effects of **tES** and use them to design optimal **brain stimulation protocols** in Alzheimer's disease.



Funded by  
the European Union



# Special Issue

## The Mathematics of Structured Experience: Exploring Dynamics, Topology, and Complexity in the Brain



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### Guest Editors

Dr. Giulio Ruffini

Dr. Johannes Kleiner

Dr. Ryota Kanai

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### Deadline

20 March 2026

A yellow circular badge containing the text "IMPACT FACTOR 2.0".

A white circular badge with the text "Indexed in: PubMed".

A white circular badge with the text "CITESCORE 5.2".

# Thank You

Dr. Giulio Ruffini  
Co-founder & CTO  
Starlab /Neuroelectrics

Barcelona, July 7, 2025  
[giulio.ruffini@neuroelectrics.com](mailto:giulio.ruffini@neuroelectrics.com)



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