Whole-brain models fitting and applications

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Why using models?

- Proposing new **causal mechanisms.**
- Recover **latent information.**
- Create a **test bench** for biomedical interventions.
- **Guide** the development of useful experiments and **inspire** new technologies.

Building a model

eNeuro

Research Article: Methods/New Tools | Novel Tools and Methods

A how-to-model guide for Neuroscience

https://doi.org/10.1523/ENEURO.0352-19.2019

A how-to-model guide for Neuroscience

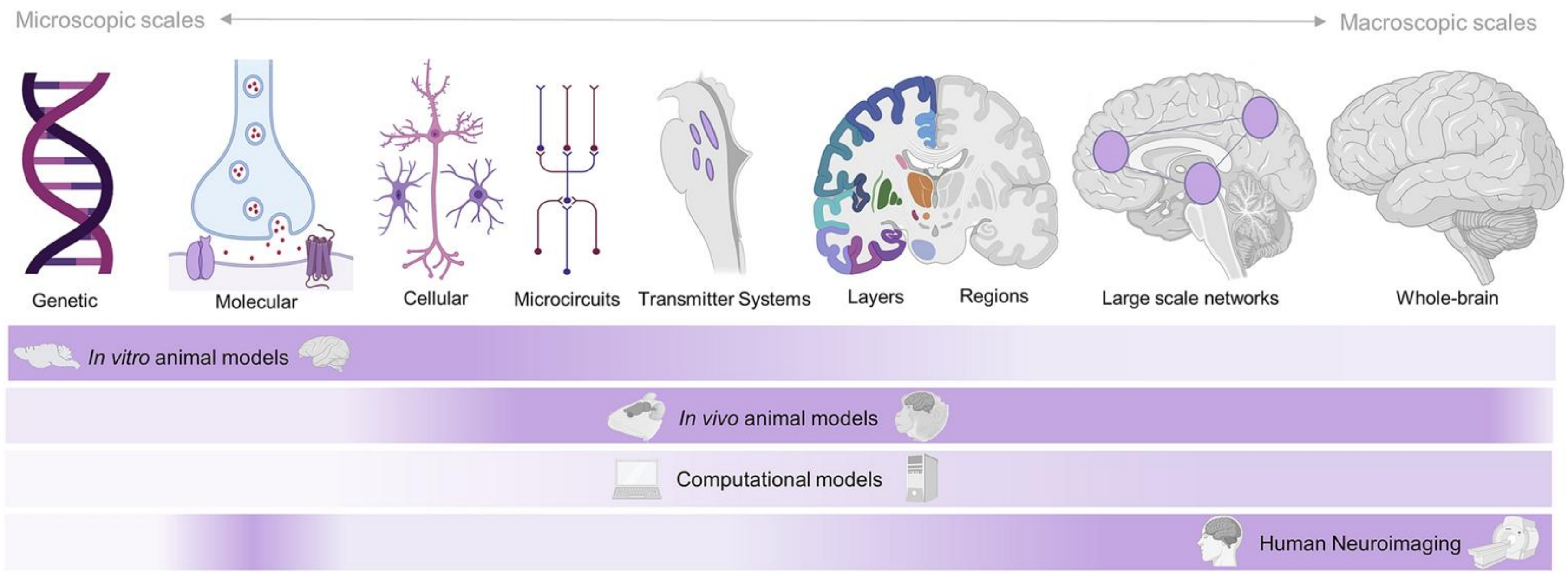
G. Blohm[1], K.P. Kording[2], P.R. Schrater[3]

Building a model

A good model should answer these three questions:

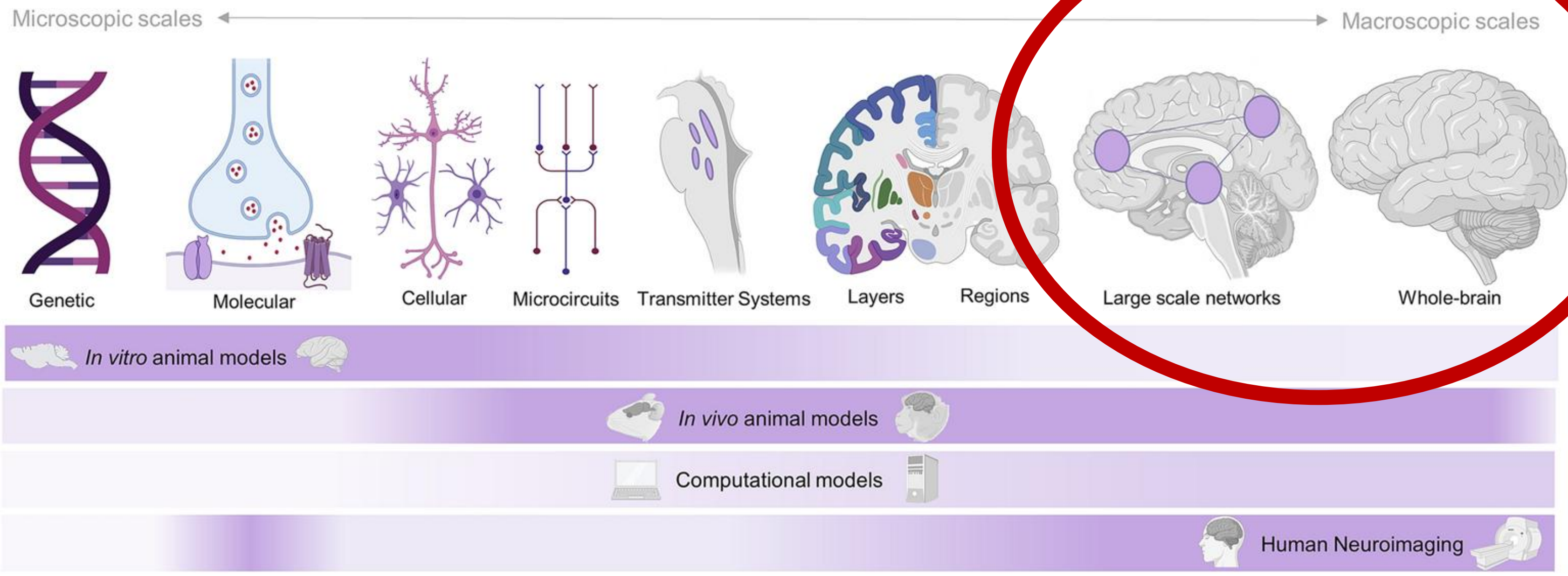
- **The what?:** The model must describe the experimental result.
- **The how?:** related to the mechanisms of the model that reproduce the data.
- **The why?:** explain what is the motivation of the "entity" (e.g., the brain) to function based on the proposed mechanisms.

Modeling Scales



Luppi et al. (2021)

Modeling Scales



Luppi et al. (2021)

Whole-brain models

Basic elements of whole-brain models:

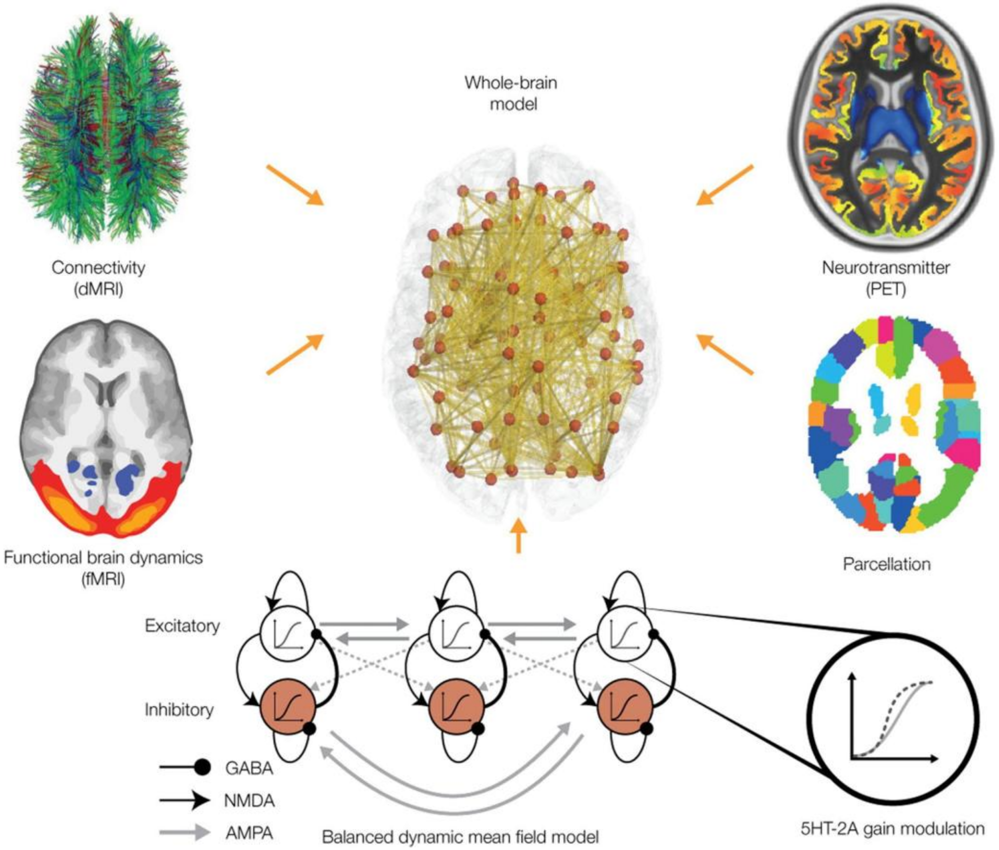
Dynamic model: A system of differential equations that describes the dynamics of a brain region.

Structural connectivity: A topology used to connect network elements.

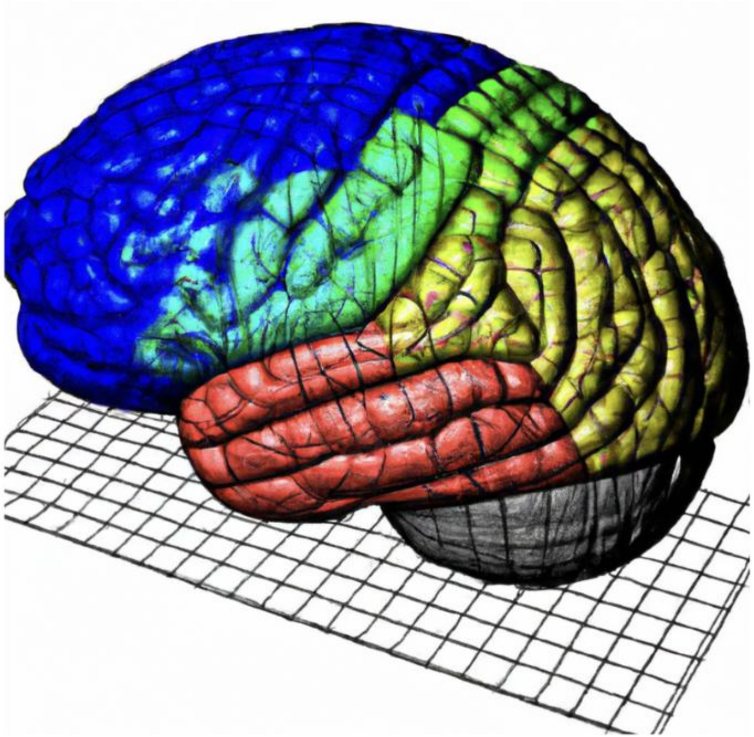
Heterogeneities of the model: depending on the research question to be answered, the model may include distance matrices, receptor density, and asymmetries in the assignment of parameters, among others.

Whole-brain models

Deco et al. (2018, Current Biology)

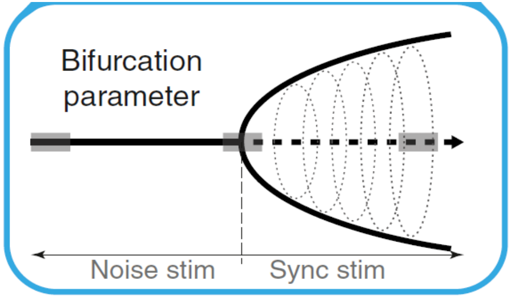


What models?



Phenomenological models

Hopf Model



Hopf: Local dynamics

Deco et al. (2019)

$$\frac{dx_i(t)}{dt} = \boxed{a_i} x_i(t) - \left[x_i^2(t) - y_i^2(t)\right] x_i(t) - \boxed{w_i} y_i(t) + \boxed{\beta \eta_i(t)}$$

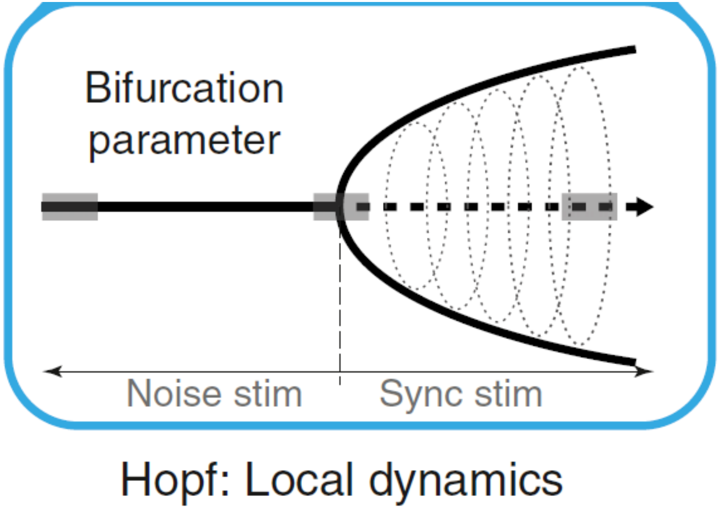
$$\frac{dy_i(t)}{dt} = \boxed{a_i} y_i(t) - \left[x_i^2(t) - y_i^2(t)\right] y_i(t) - \boxed{w_i} x_i(t) + \boxed{\beta \eta_i(t)}$$

Oscillatory frequency ***Background noise***

Bifurcation parameter

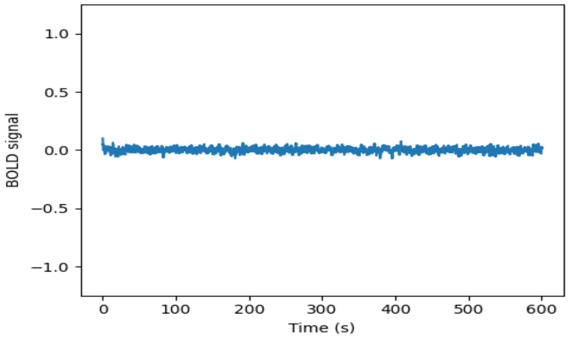
Phenomenological models

Hopf Model

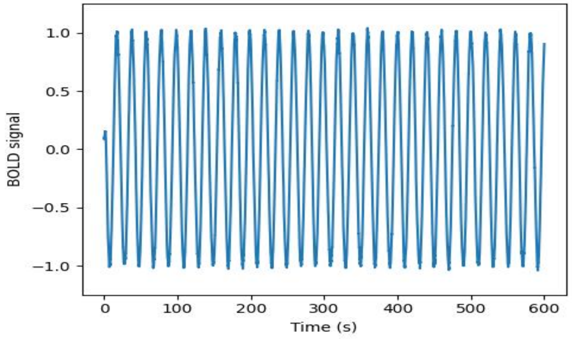


Deco et al. (2019)

a = -1 (noisy signals)



a = 1 (Sustained oscillations)



Phenomenological models

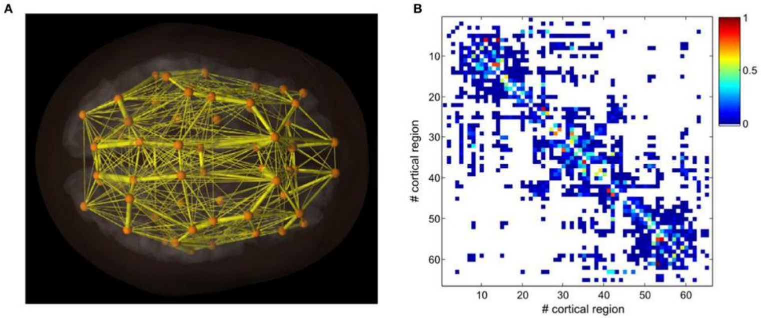
Hopf Model

Structural connectivity connections (M_{ij})
Scaled by a global coupling parameter

$$\frac{dx_i(t)}{dt} = a_i x_i(t) - \left[x_i^2(t) - y_i^2(t)\right] x_i(t) - w_i y_i(t) + \boxed{G \sum_{j=1}^{n} M_{ij} \left(x_j(t) - x_i(t)\right)} + \beta \eta_i(t)$$

$$\frac{dy_i(t)}{dt} = a_i y_i(t) - \left[x_i^2(t) - y_i^2(t)\right] y_i(t) - w_i x_i(t) + \boxed{G \sum_{j=1}^{n} M_{ij} \left(y_j(t) - y_i(t)\right)} + \beta \eta_i(t)$$

Deco et al. (2012)



Phenomenological models

Hopf Model

$$\frac{dx_i(t)}{dt} = a_i x_i(t) - \left[x_i^2(t) - y_i^2(t)\right] x_i(t) - w_i y_i(t) + G\sum_{j=1}^{n} M_{ij}\left(x_j(t) - x_i(t)\right)$$
$$\boxed{+ F_i(t)\cos(w_i t)} + \beta\eta_i(t)$$

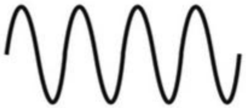
$$\frac{dy_i(t)}{dt} = a_i y_i(t) - \left[x_i^2(t) - y_i^2(t)\right] y_i(t) - w_i x_i(t) + G\sum_{j=1}^{n} M_{ij}\left(y_j(t) - y_i(t)\right)$$
$$\boxed{+ F_i(t)\sin(w_i t)} + \beta\eta_i(t)$$

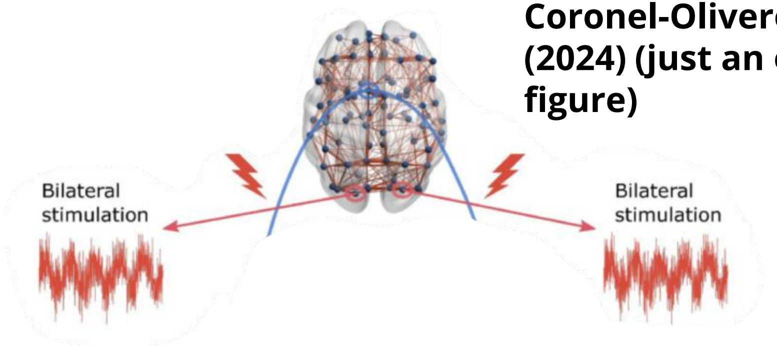
External stimulation (perturbations)

Coronel-Oliveros et al. (2024) (just an example figure)

Wave stimulation

$+F_0 cos(\omega_0 t)$ +

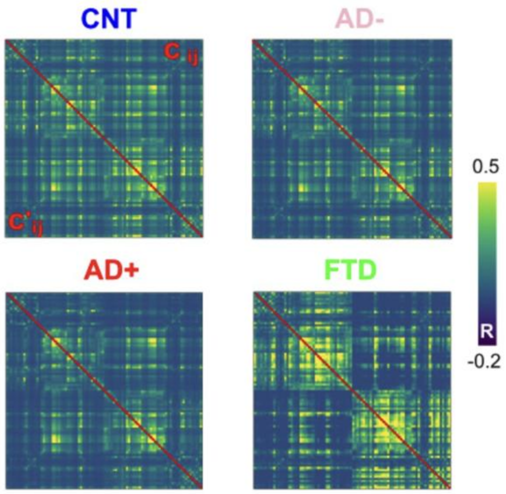




Phenomenological models

Sanz Perl et al. (2023)

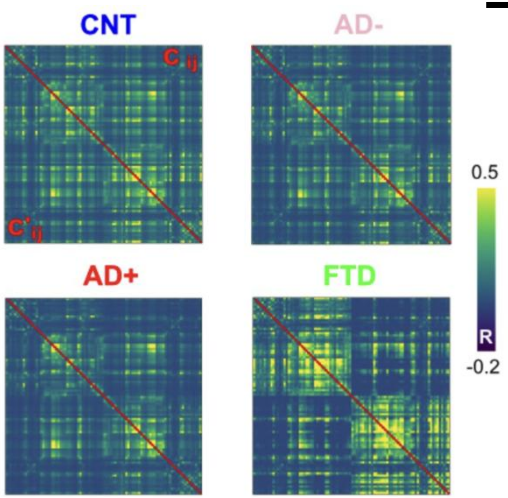
Simulated functional connectivity

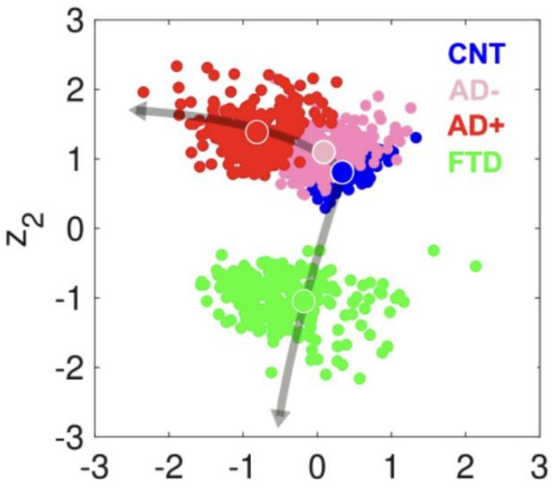


Phenomenological models

Sanz Perl et al. (2023)

Simulated functional connectivity → **Dimensionality reduction**

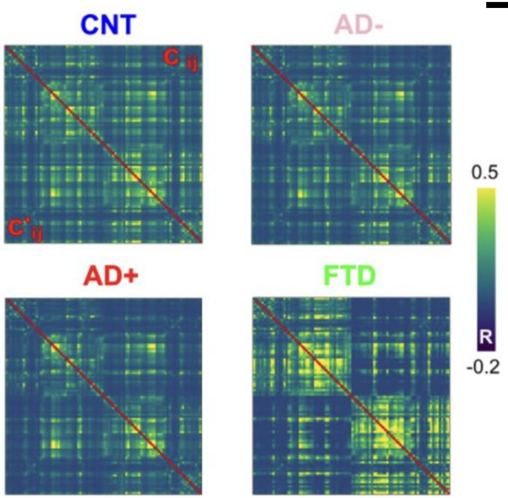




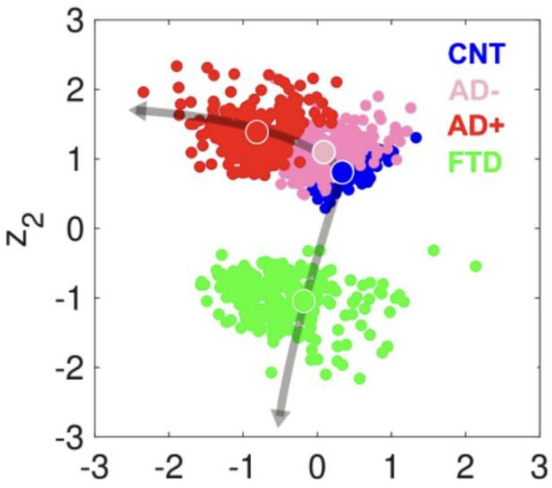
Phenomenological models

**Sanz Perl et al.
(2023)**

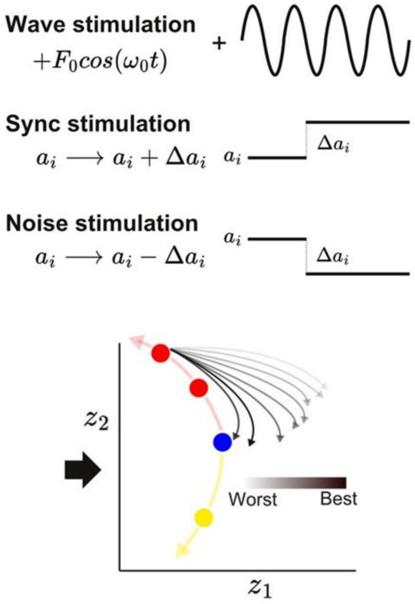
Simulated functional connectivity



Dimensionality reduction



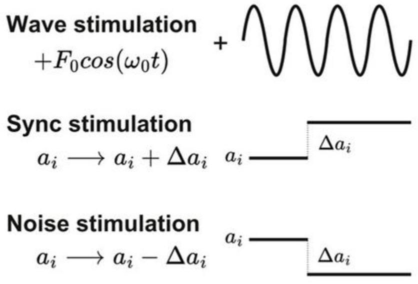
Stimulation

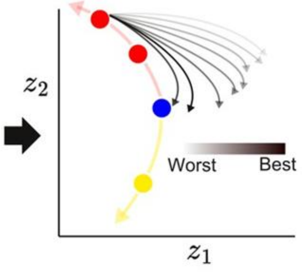


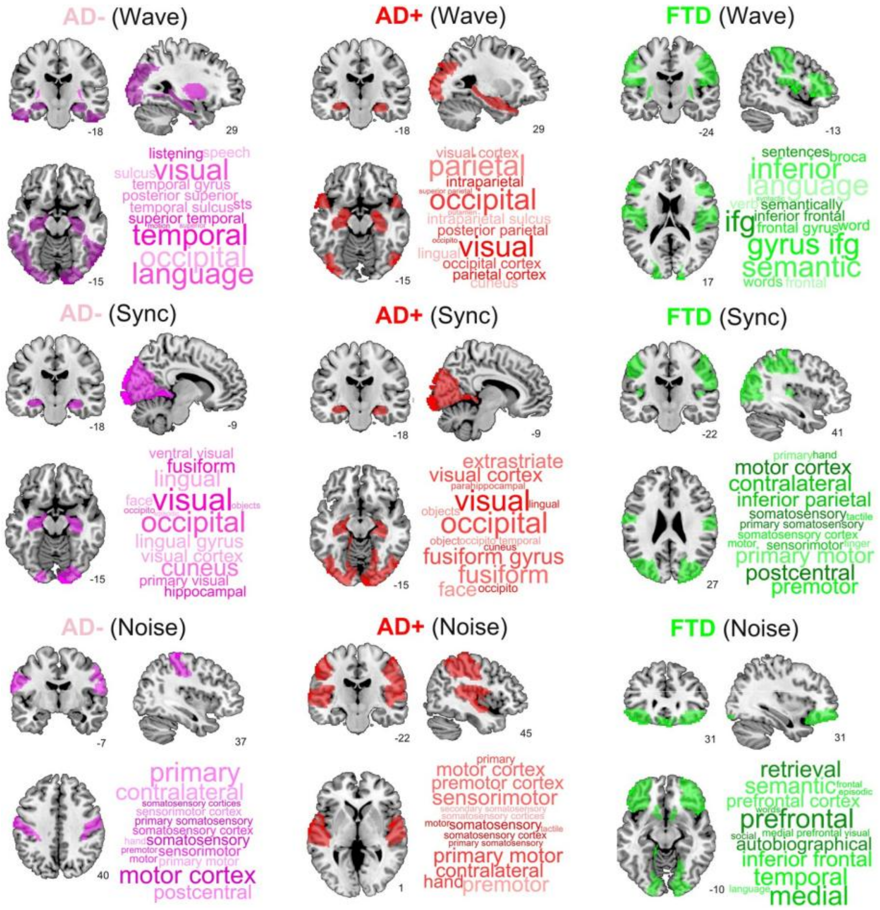
Phenomenological models

Best stimulation targets

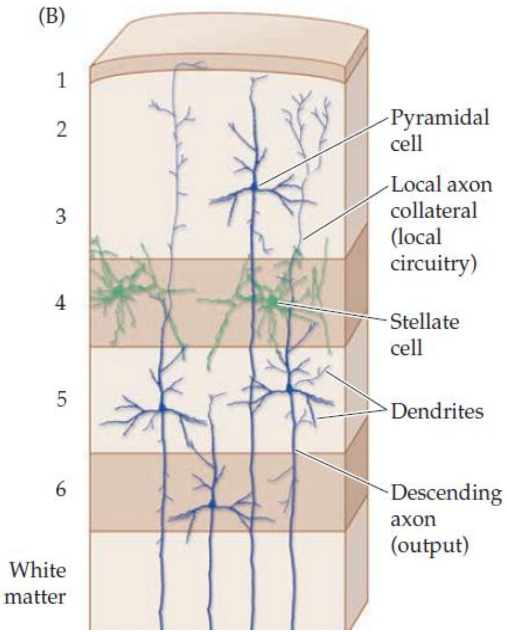
Sanz Perl et al. (2023)

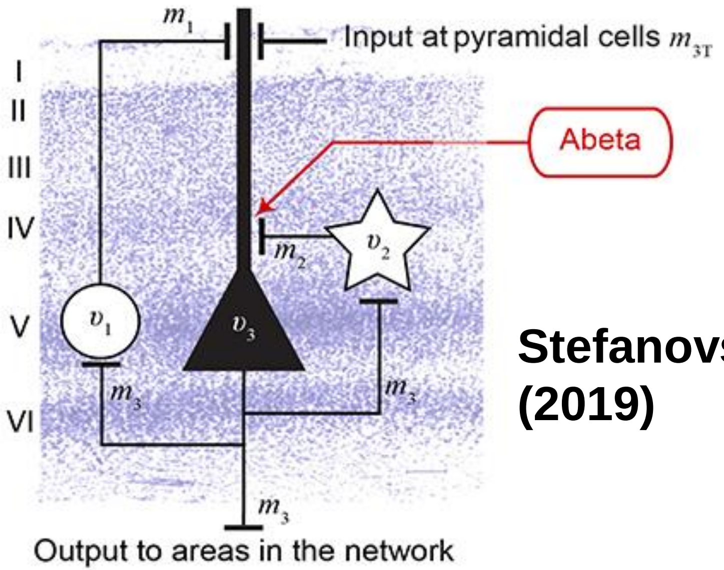






Neural mass models: Jansen & Rit



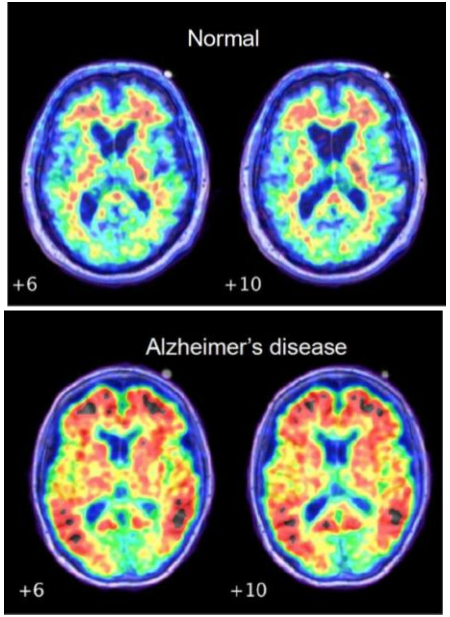


Stefanovski et al. (2019)

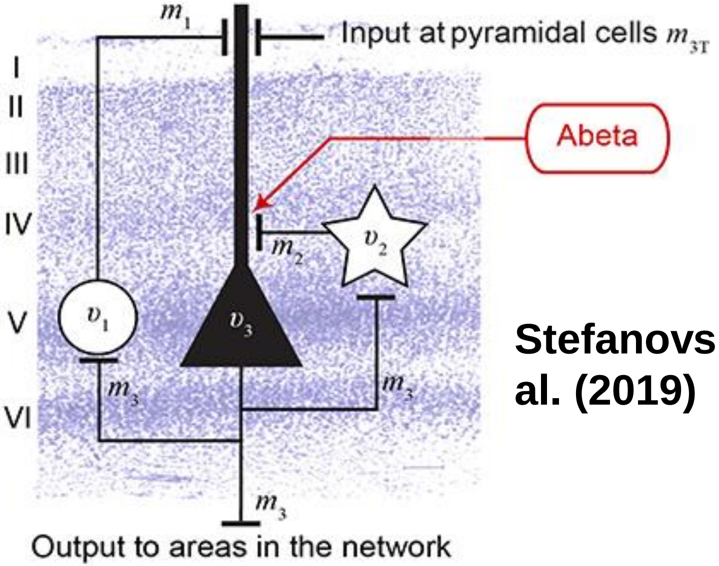
v_1: Excitatory interneurons.
v_2: inhibitory interneurons.
v_3: pyramidal neurons.

Neural mass models: Jansen & Rit

Amyloid beta aggregation (PET) in AD dementia



Chapleau et al. (2022)



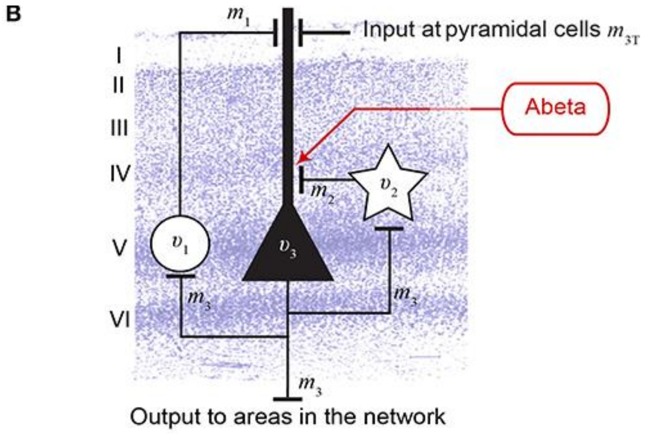
Stefanovski et al. (2019)

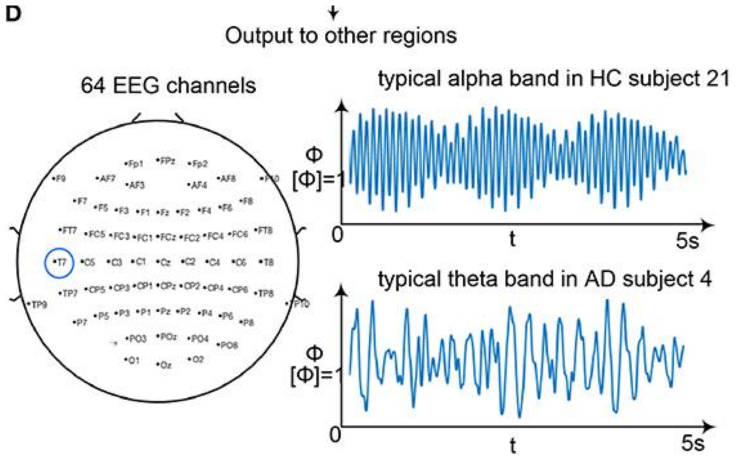
v_1: Excitatory interneurons.
v_2: inhibitory interneurons.
v_3: pyramidal neurons.

Neural mass models: Jansen & Rit

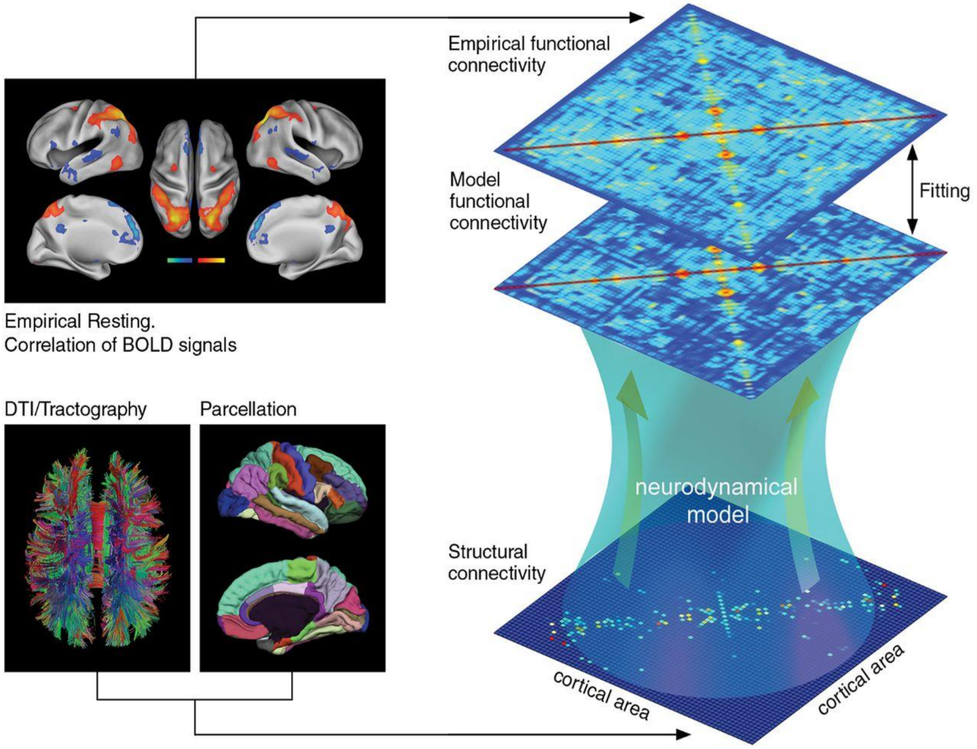
Stefanovski et al. (2019) can reproduce changes in brain activity in Alzheimer's patients.

Stefanovski et al. (2019)





Model fitting



Deco et al. (2013)

Target Function

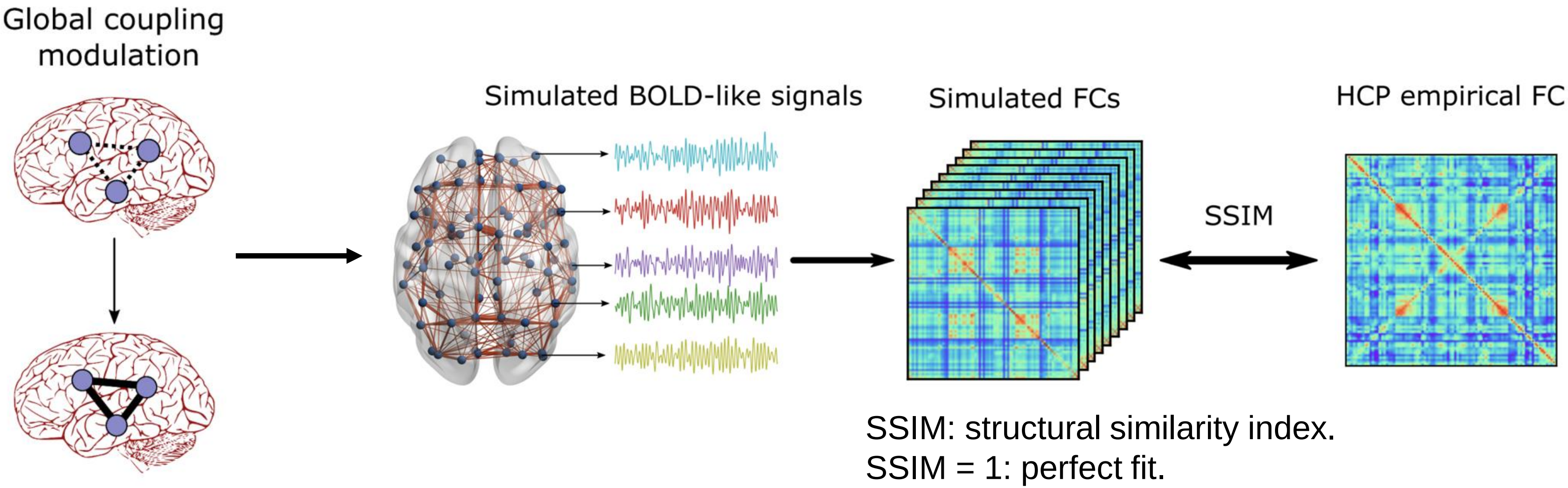
The **target function** corresponds to the function that you want to optimize (minimize or maximize) during model tuning.

Some **output of the model** that has a direct correlation with the experimental data is used.

If experimental data are not available, a value taken from the literature can be used as a **reference** (e.g., firing rates, postsynaptic potential amplitude, among others).

Target Function

Fitting functional connectivity (FC)

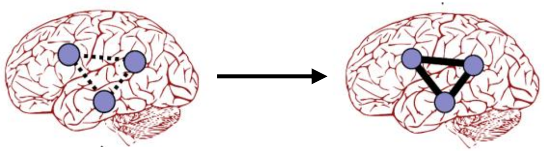


SSIM: structural similarity index.
SSIM = 1: perfect fit.
SSIM = 0: poor fit.

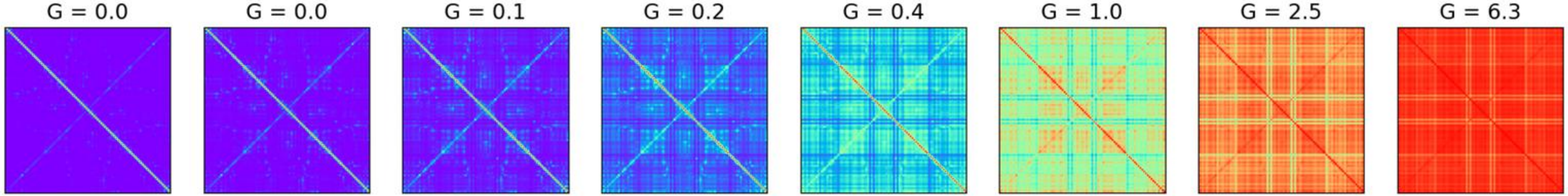
Target Function

Fitting functional connectivity (FC)

Global coupling modulation



Increasing connectivity strength in the model



0.03 0.05 0.11 0.27 0.47 0.44 0.31 0.18

SSIM

Simulated FC matrices using the Hopf model

SSIM: structural similarity index.
SSIM = 1: perfect fit.
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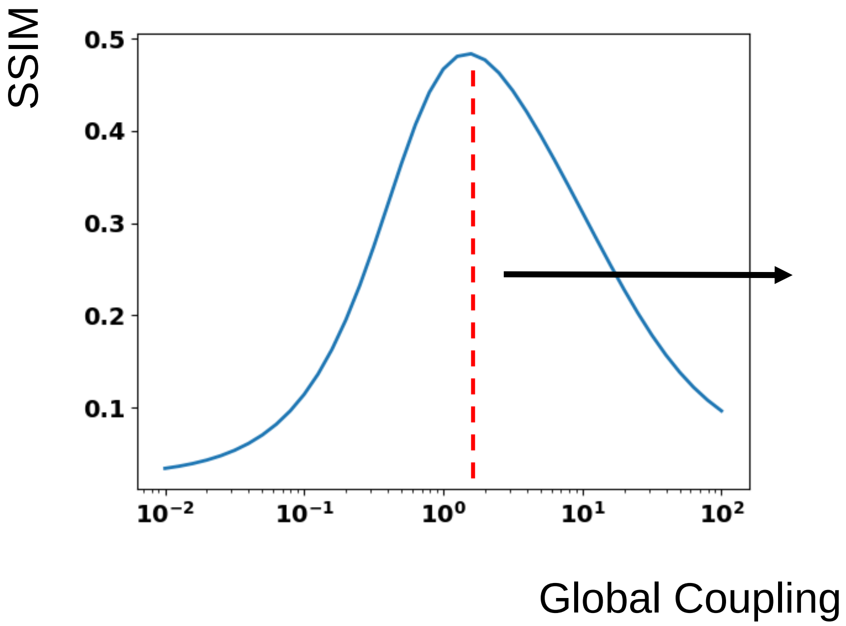
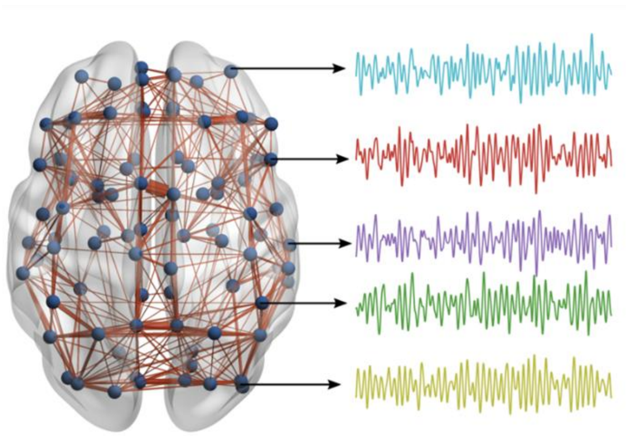
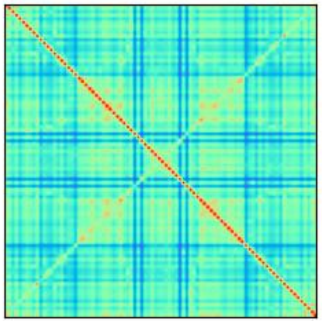
Target Function

Fitting functional connectivity (FC)

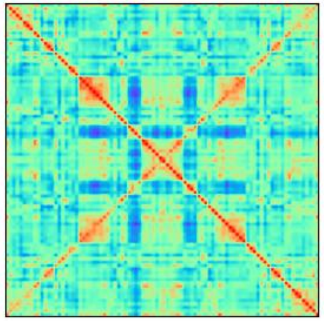




Simulated FC



Empirical FC



Brain clocks and biophysical modeling using EEG

How can we measure “brain health”?

Blood pressure: You can use just a single pair of numbers

>120/80 mm: hypertension.

<90/60 mm: hypotension.

How can we measure “brain health”?

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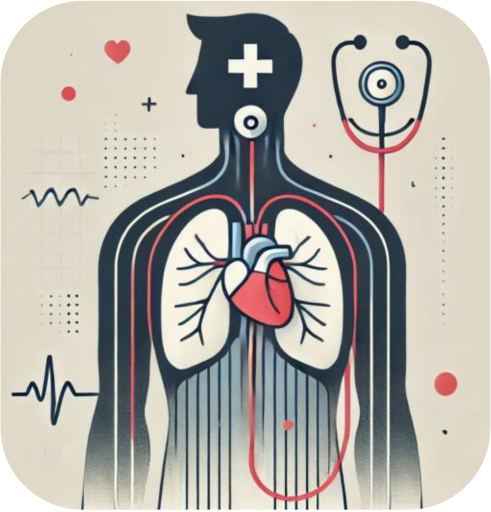

Overall health:
Frailty index:

- Physical health.
- Cognitive function.
- Psychological health.
- Social factors.

How can we measure “brain health”?

Blood pressure: You can use just a single pair of numbers

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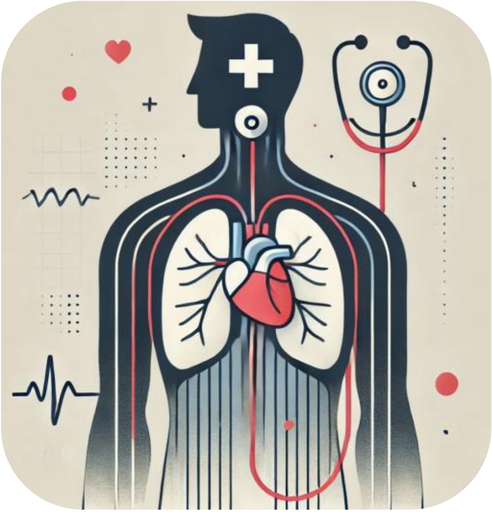


Overall health:
Frailty index:
- Physical health.
- Cognitive function.
- Psychological health.
- Social factors.

Brain health:

How can we measure “brain health”?

Brain health:

Neuroimaging:

PET: Positron Emission Tomography

MRI: Magnetic Resonance Imaging

fMRI: Functional Magnetic Resonance Imaging

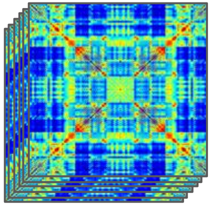
Electrophysiology:

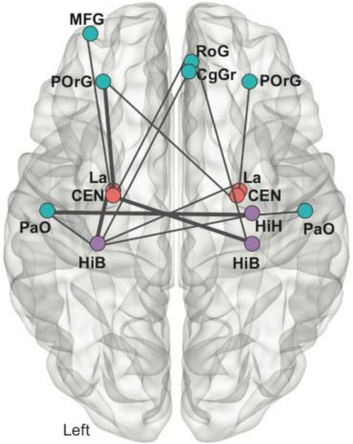
EEG: Electroencephalography

MEG: Magnetoencephalography

Dataset and brain clock model

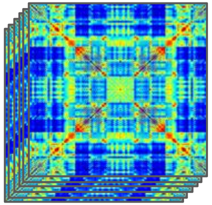
EEG Functional connectivity





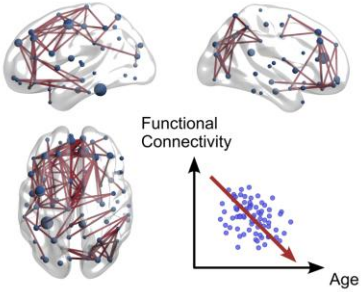
Dataset and brain clock model

EEG Functional connectivity



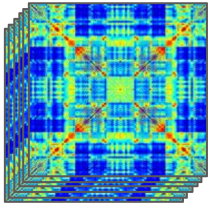
Feature extraction

(most relevant connections)



Dataset and brain clock model

EEG Functional connectivity



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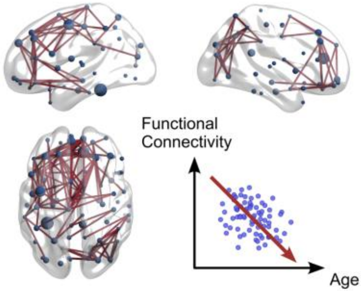
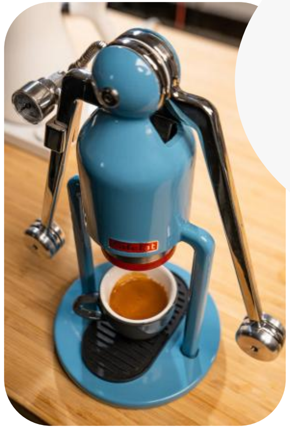


Support Vector Machine Regression

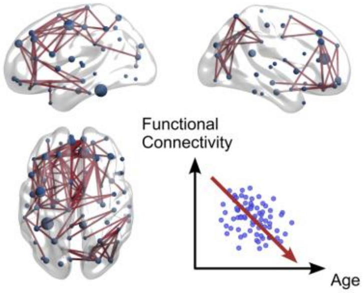
(Machine learning)



Dataset and brain clock model

Feature extraction

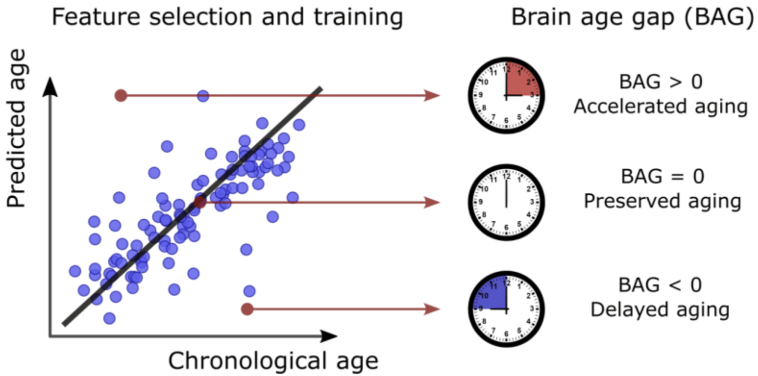
(most relevant connections)



Support Vector Machine Regression

(Machine learning)

Predictions



Brain clocks using EEG

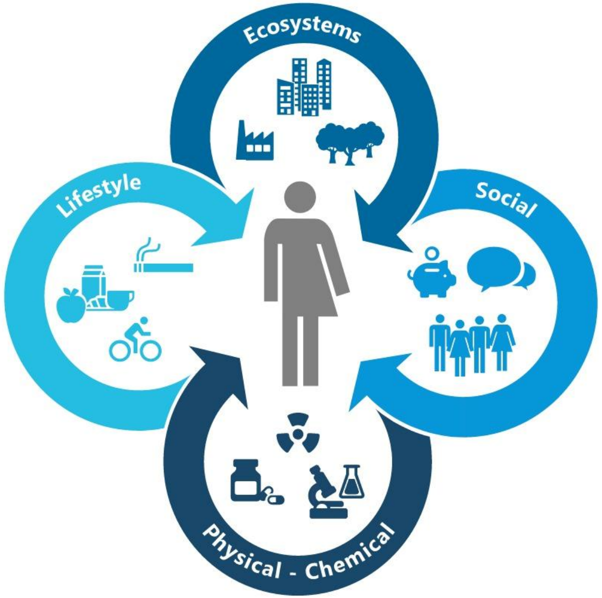
Brain age gap (BAG)

BAG > 0
Accelerated aging

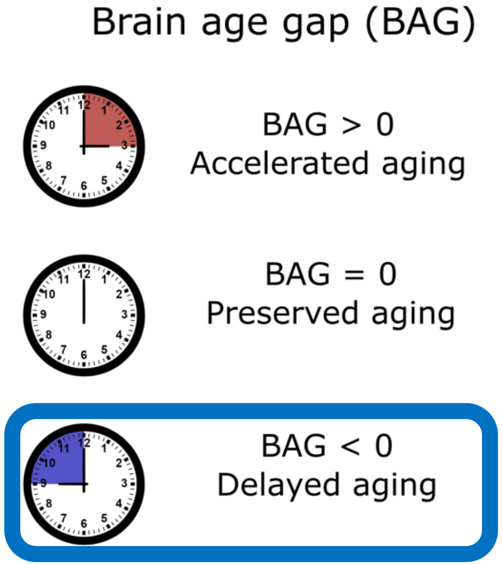
BAG = 0
Preserved aging

BAG < 0
Delayed aging

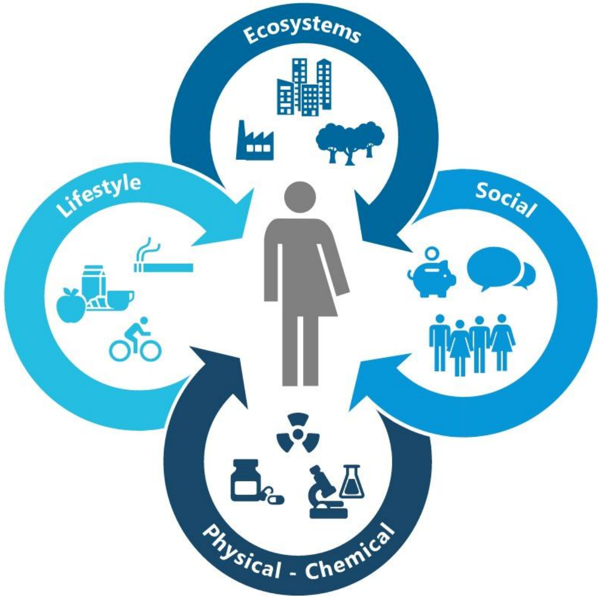
Social exposome



Brain clocks using EEG

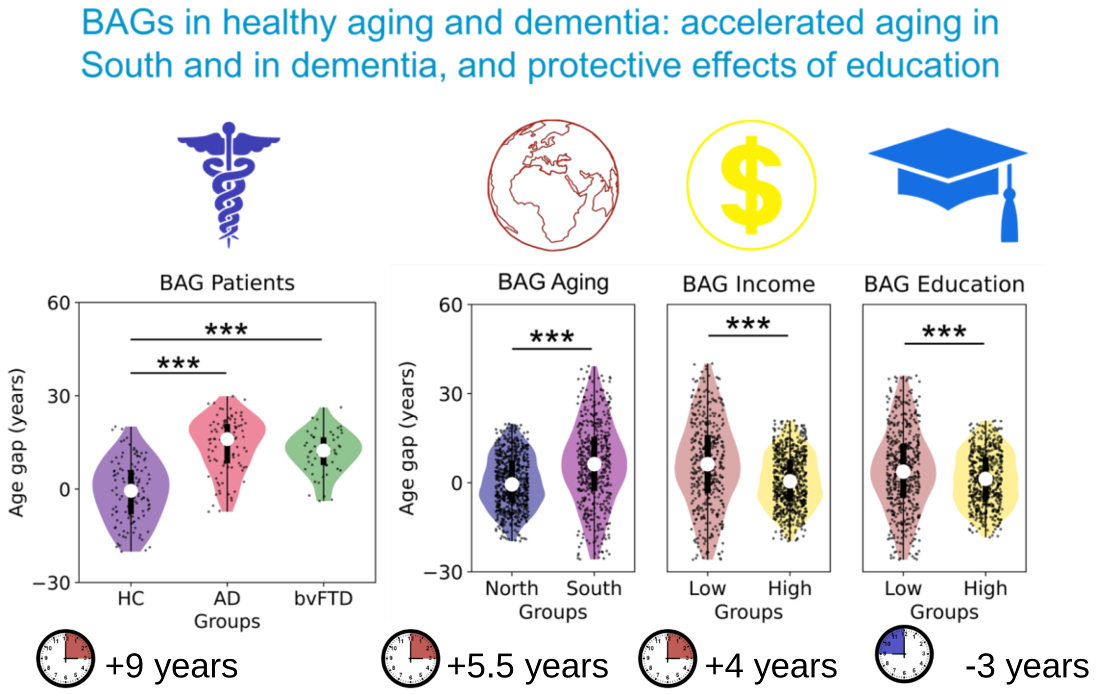


Social exposome



BAGs in aging and dementia

Normative models of healthy aging can be used to predict the brain age gaps (BAGs) in health and disease.



Comparisons:

- Patients and matched healthy controls.
- South vs North.
- Income: GDP per capita.
- Education: years education

Coronel-Oliveros et al. 2025a (Not rejected… yet)

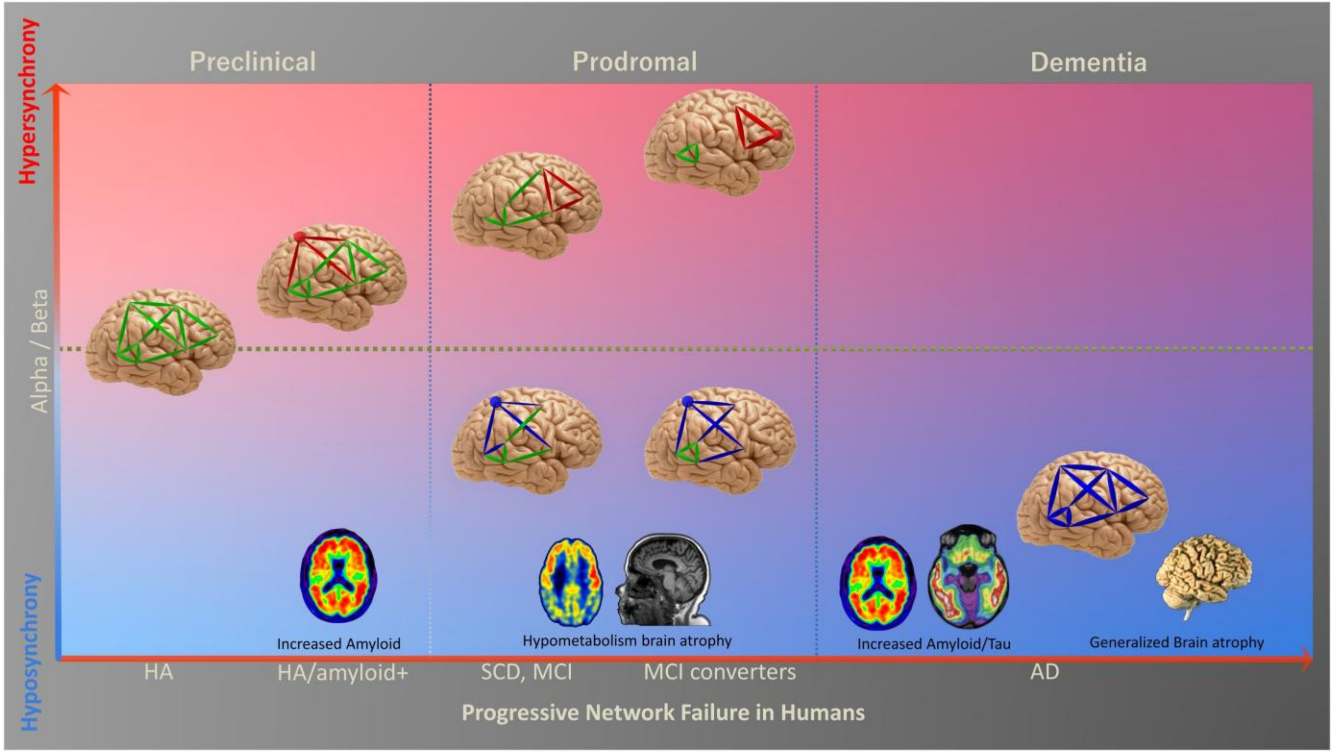
Mechanisms in aging and dementia

Ageing Research Reviews
Volume 69, August 2021, 101372

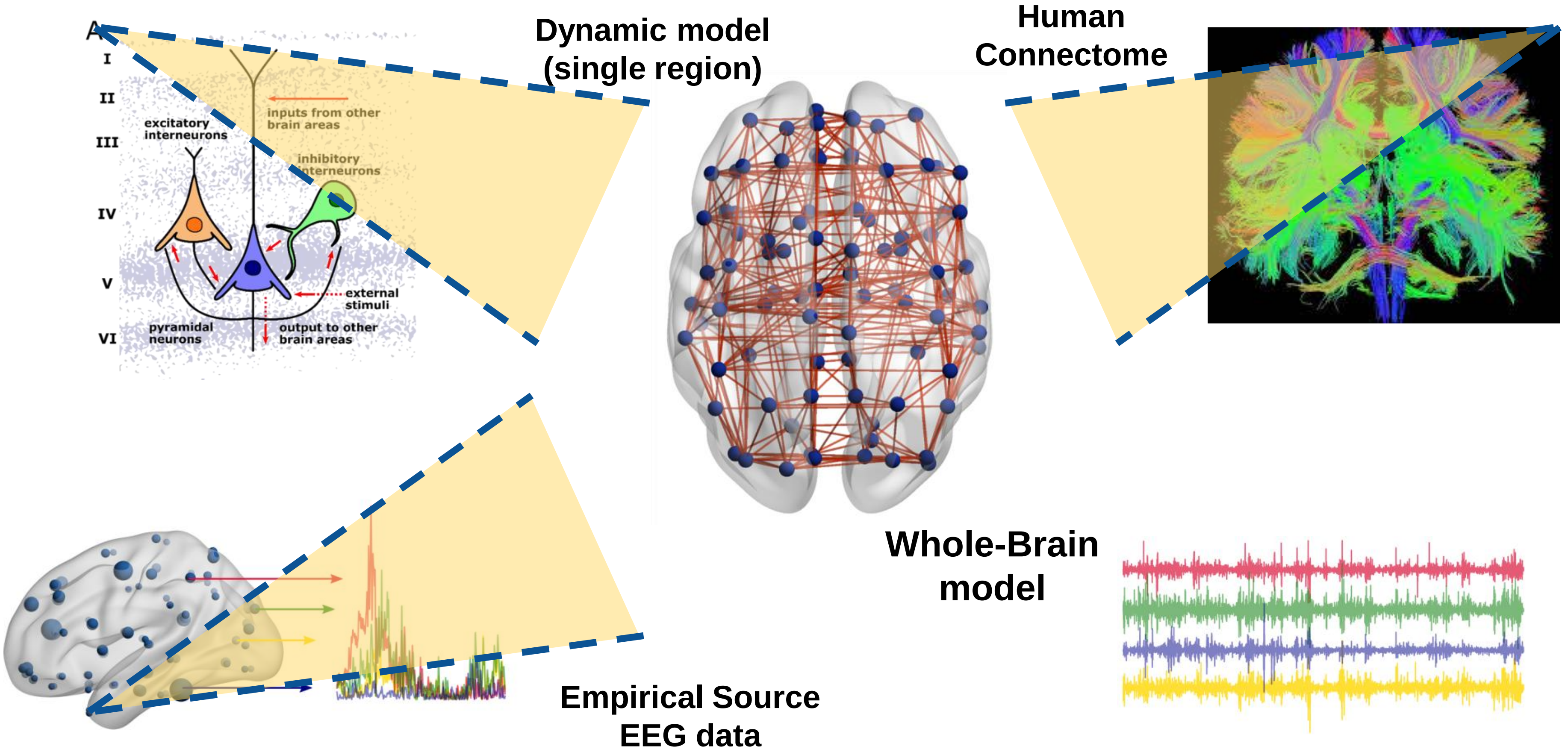
Review

Neuronal excitation/inhibition imbalance: core element of a translational perspective on Alzheimer pathophysiology

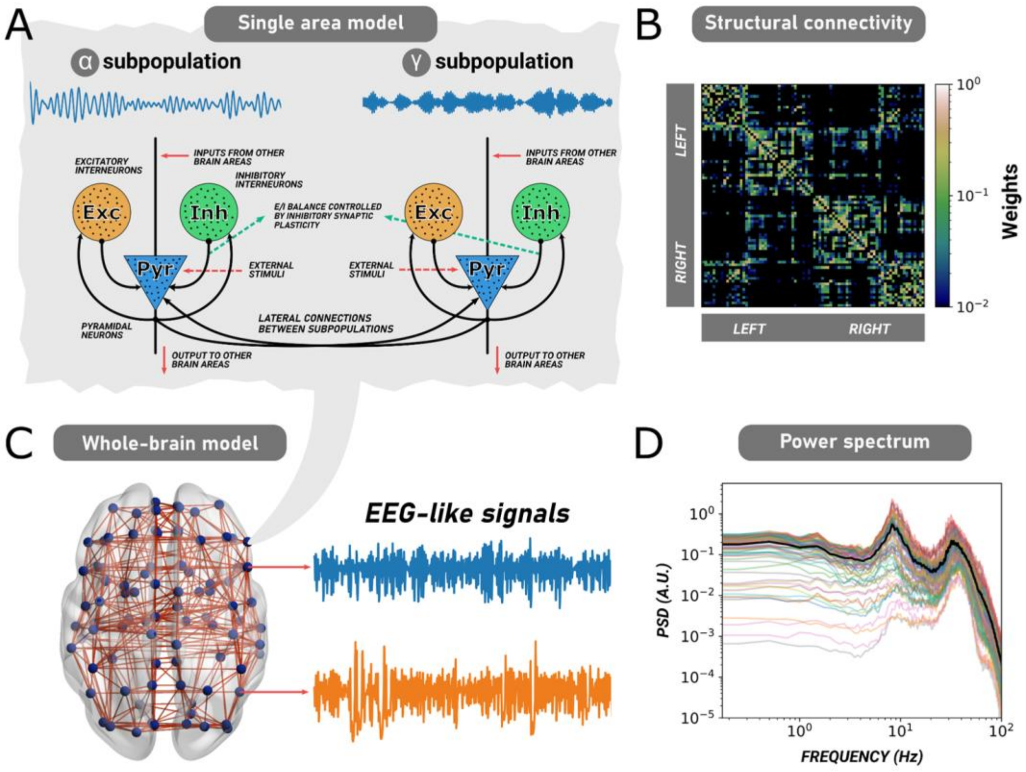
Fernando Maestú [a b c], Willem de Haan [d], Marc Aurel Busche [e], Javier DeFelipe [f g h]



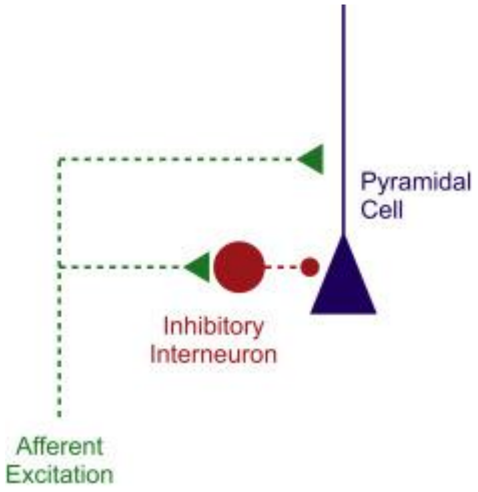
Biophysical modeling



Neural mass model (Jansen-Rit)



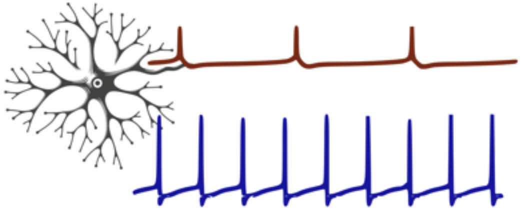
Modified Jansen & Rit model with **Inhibitory synaptic plasticity**



Coronel-Oliveros et al., 2024 (Alzheimer's & Dementia)

Mechanisms in aging and dementia

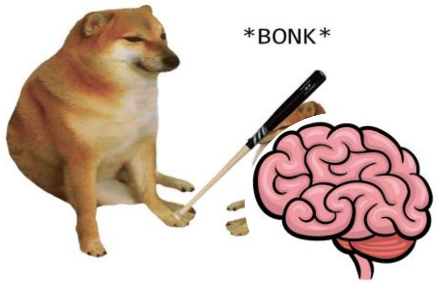
Local E/I balance estimation

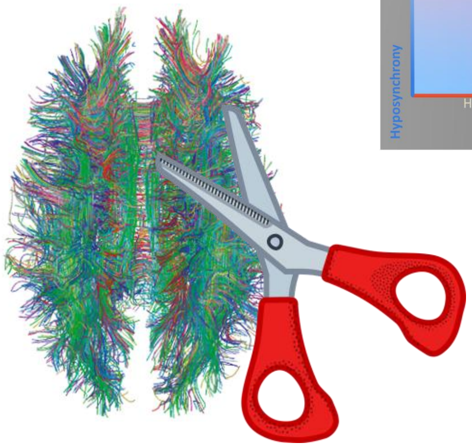


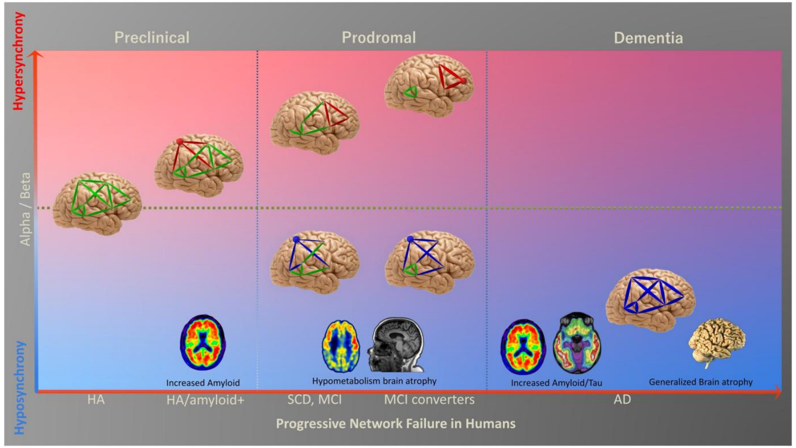
Low excitation

High excitation

Connectome “disintegration”

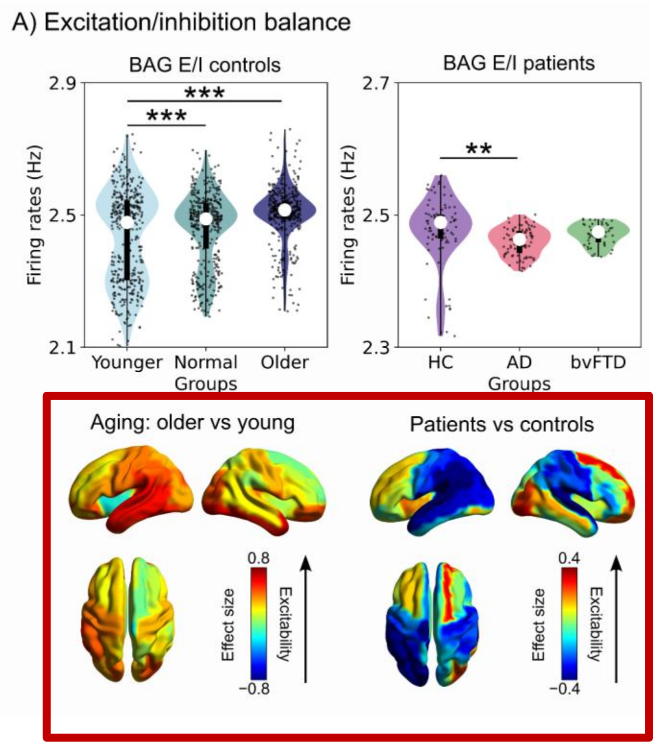






Maestú et al., 2021

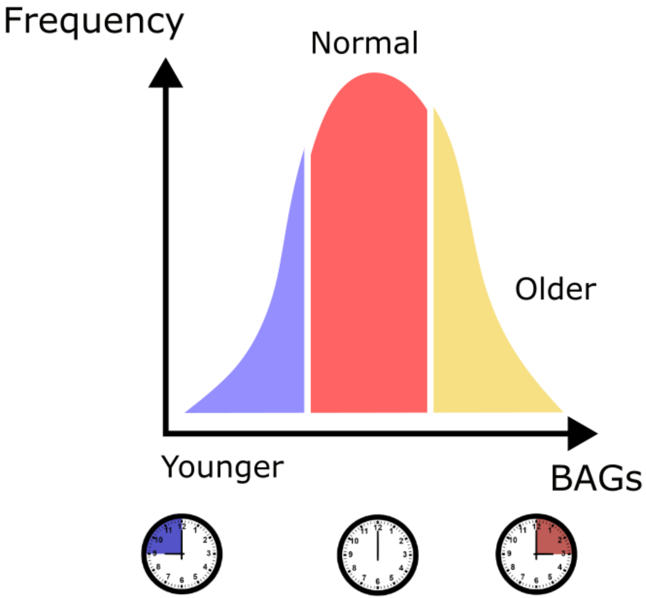
BAGs in modeling



Hyperexcitation in accelerated aging.

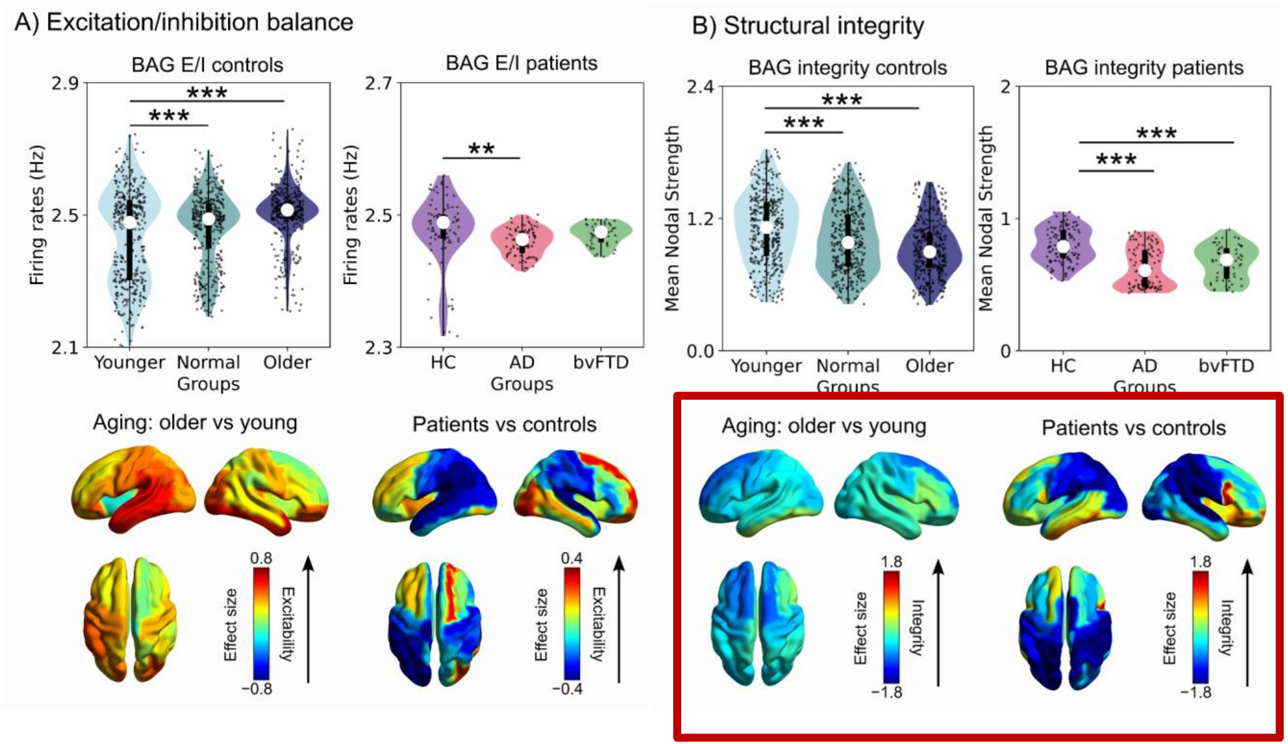
Hypoexcitation in dementia.

Specific E/I balance cortical patterns in aging and dementia.



Coronel-Oliveros et al. 2025a (Not rejected… yet)

BAGs in modeling



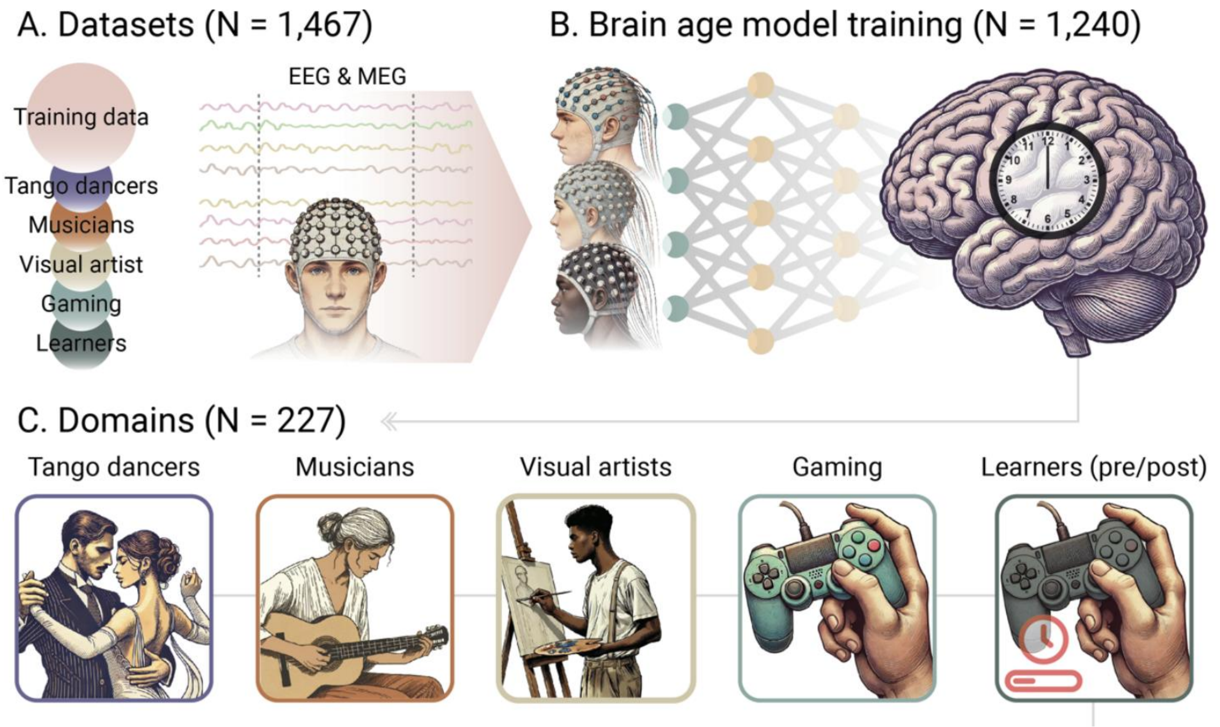
Reduced structural connectivity in aging and dementia

Specific connectivity differences in aging and dementia.

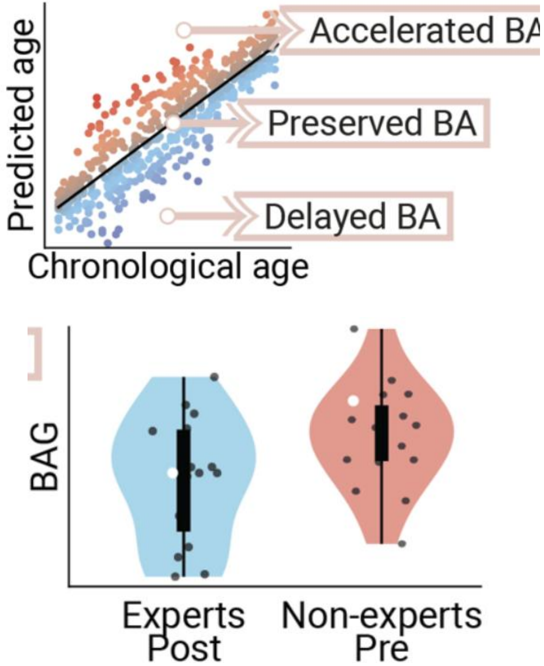
Coronel-Oliveros et al. 2025a (Not rejected… yet)

Aging Gracefully: How Our Brains Bend but Don't Break

Expertise and neural plasticity



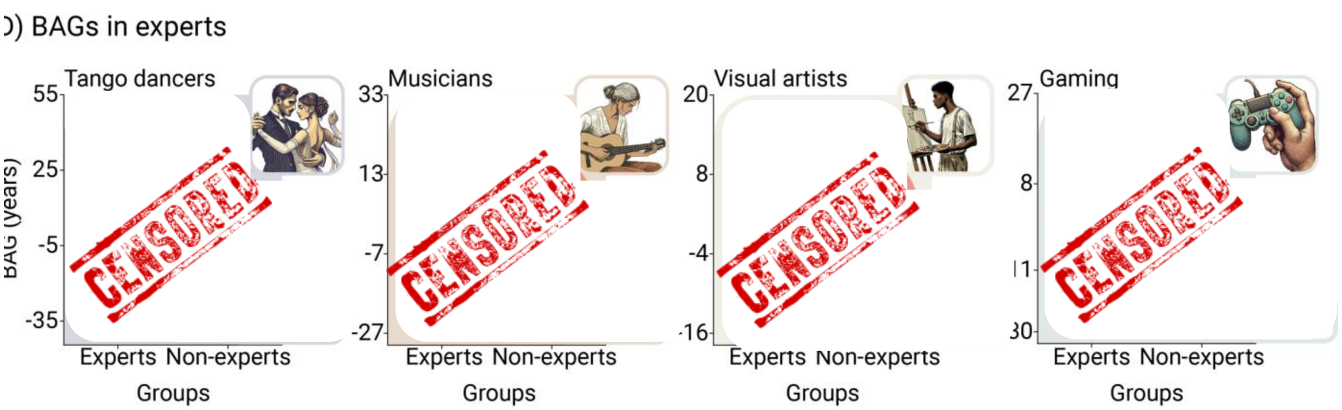
Compared BAGs in different creative domains



Coronel-Oliveros et al. 2025b (Not rejected… yet)

Expertise and neural plasticity

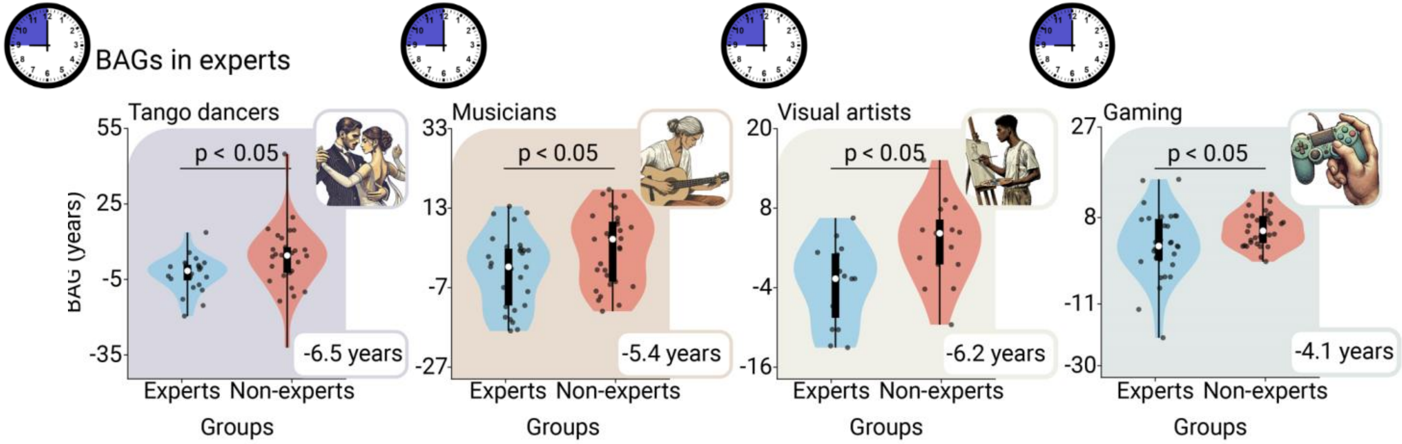
Lower BAGs across creativity domains (**expertise**)



Coronel-Oliveros et al. 2025b (Not rejected… yet)

Expertise and neural plasticity

Lower BAGs across creativity domains (**expertise**)



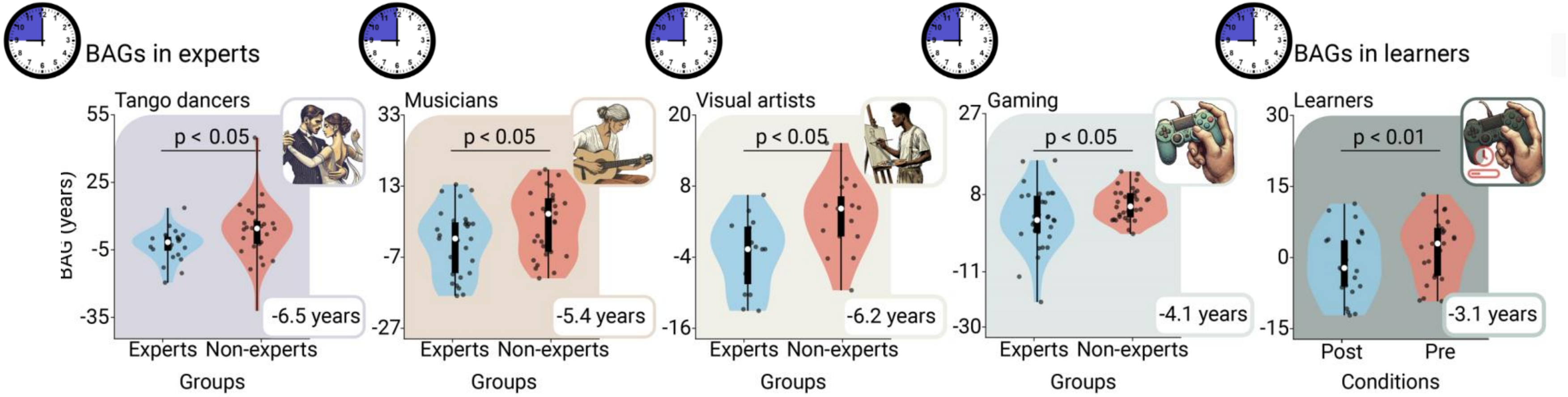
Coronel-Oliveros et al. 2025b (Not rejected… yet)

Personal disclaimer: this is not a recommendation about what you should do to improve your brain health. I'm not recommending anyone, for example, playing videogames for hours and hours (without doing anything else) as a healthy habit. The same applies to music and drawing or whatever. Do exercise and sleep well ☺

Expertise and neural plasticity

Lower BAGs across creativity domains (**expertise**)

Scalable effects: stronger effect in experts than learners.



Coronel-Oliveros et al. 2025b (Not rejected… yet)

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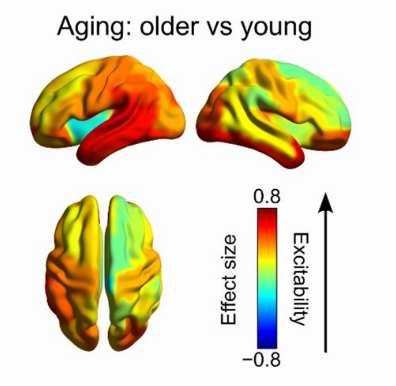
Expertise and neural plasticity

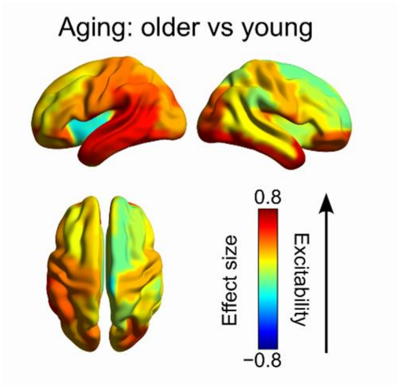
From part II: accelerated aging is characterized by hyperexcitability

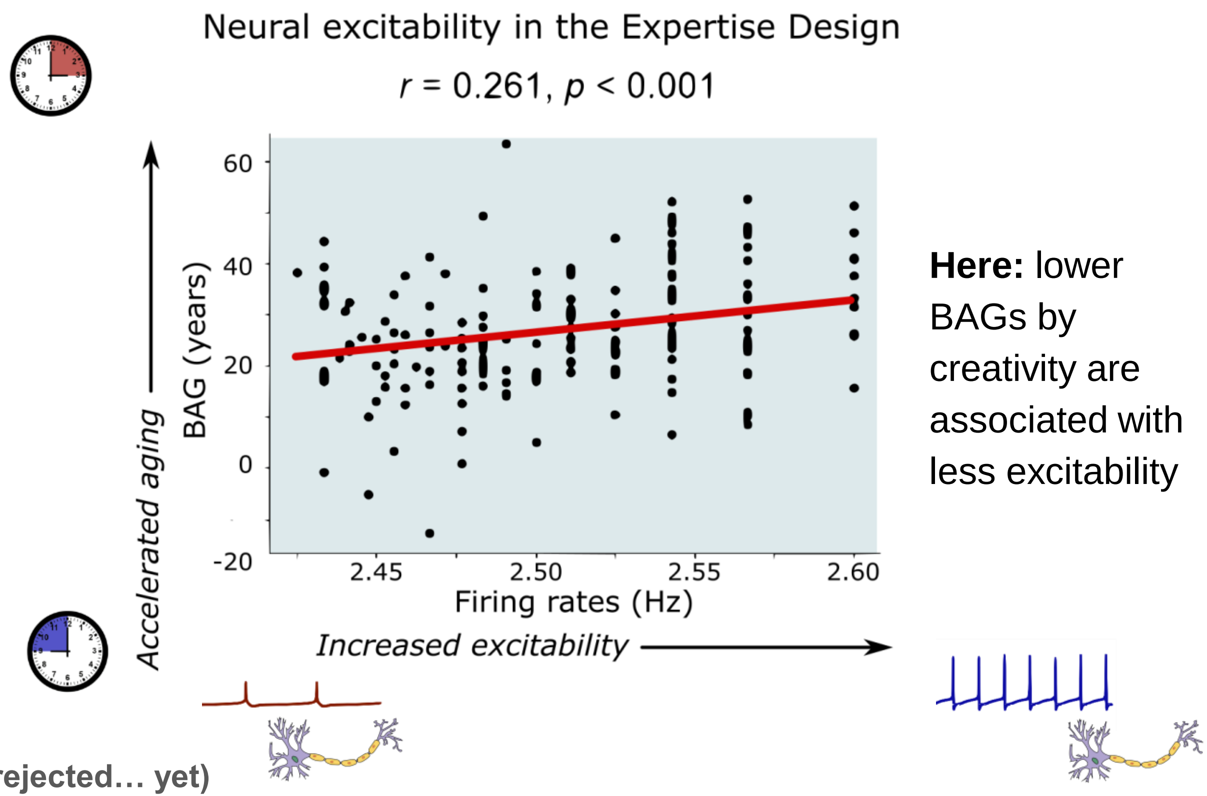


Coronel-Oliveros et al. 2025b (Not rejected… yet)

Expertise and neural plasticity

From part II: accelerated aging is characterized by hyperexcitability

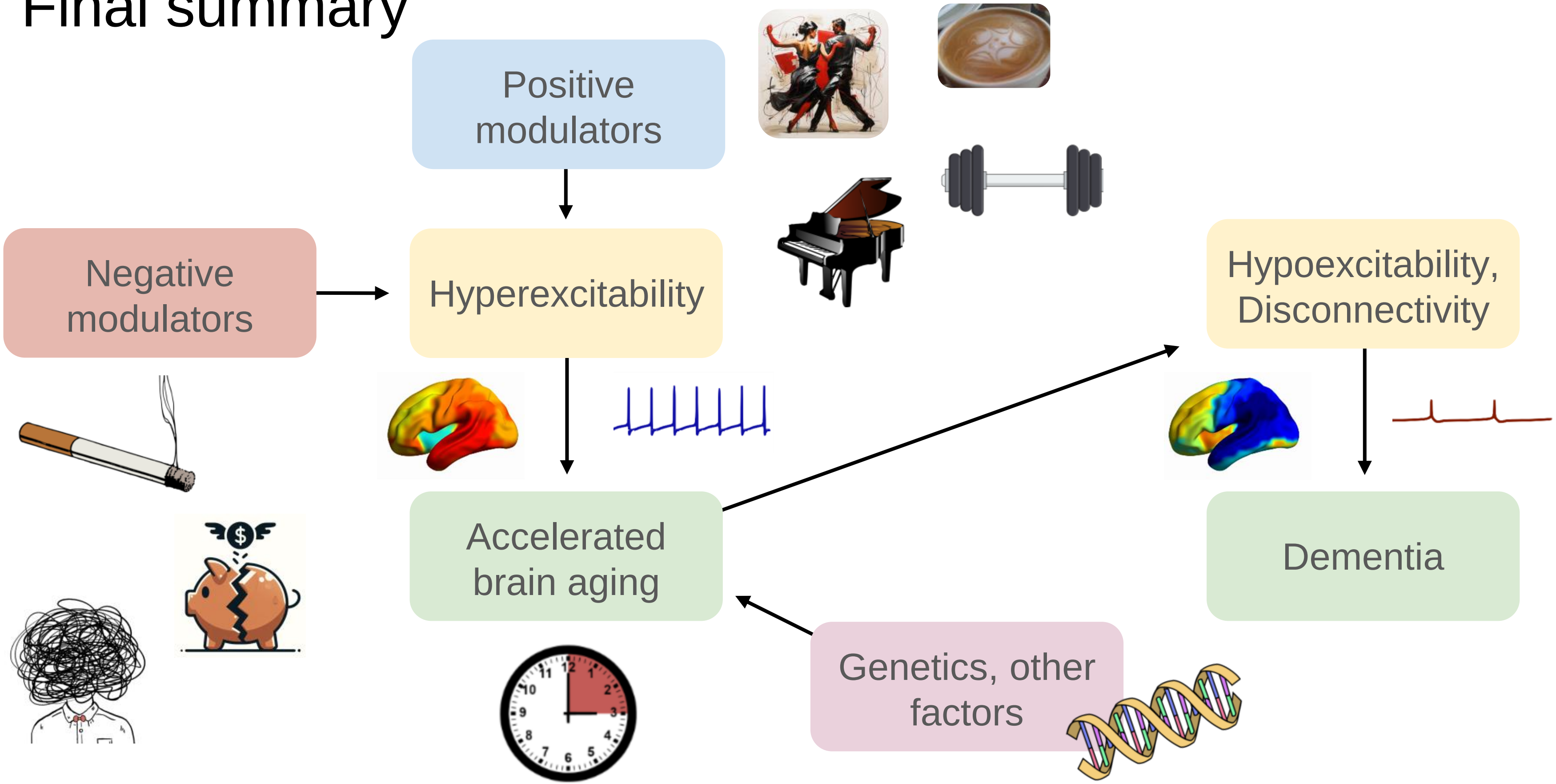




Here: lower BAGs by creativity are associated with less excitability

Coronel-Oliveros et al. 2025b (Not rejected… yet)

Final summary



Whole-brain models fitting and applications

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May, 2025