Dynamic functional connectivity organized by critical roaming correlates with cognitive resilience across the adult lifespan

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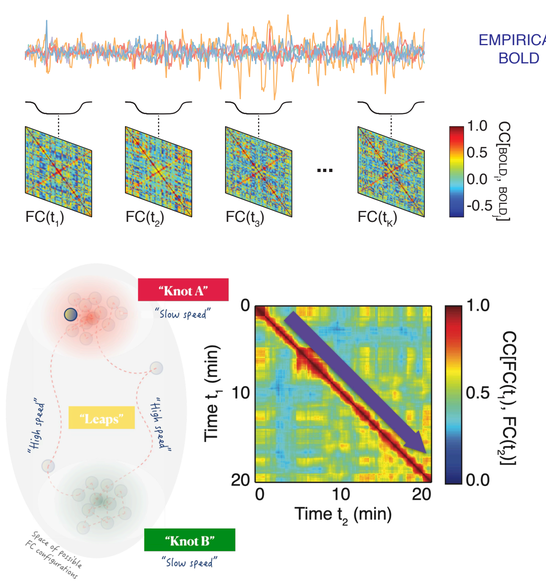
Key messages

- ***Functional connectivity*** *of the resting state* ***evolves in time in a spatio- temporally organized manner*** *different from generic variability*
- *Maintainance of f****luid and richly structured dynamic Functional Connectivity*** *predicts* ***maintainance of cognitive performance*** *despite decline due to aging, possibly contributing to* ***cognitive reserve***.
- ***Whole-brain computational models*** *of resting-state activity explain the organization of dynamic functional connectivity, suggesting that* ***the brain operates near critical "ignition" and "flaring" transitions****, while* ***fluctuations in arousal*** *drive the system to roam across these critical boundaries.*
- ***Aging and cognitive reserve*** *affect relation to* ***critical landscape***.

Quantitative description of dFC spatiotemporal organization

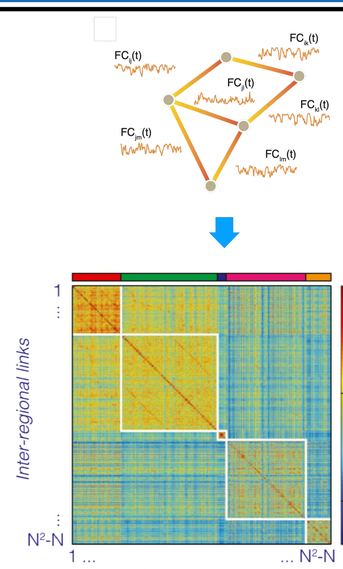


- Measuring correlation distance between FC networks at different times we can quantify **"fluidity" χ** , capturing overall level of variability...
- ... and **"speed" ν** capturing specific sequential variability along the flow of network reconfiguration

$$\chi(t_1,t_2) = 1 - \mathrm{corr}\left(FC(t_1), FC(t_2)\right)$$
$$\nu(t) = 1 - \mathrm{corr}\left(FC(t), FC(t+\tau_W)\right)$$

- We also study the varying **degree λ of similarity between SC and FC**

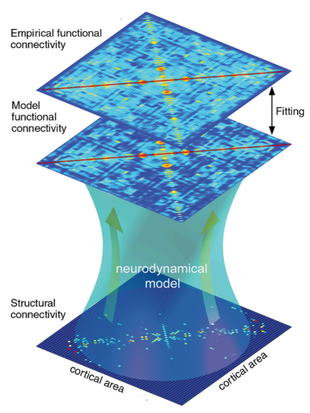
$$\lambda(t) = \mathrm{corr}\left(FC(t), SC\right)$$

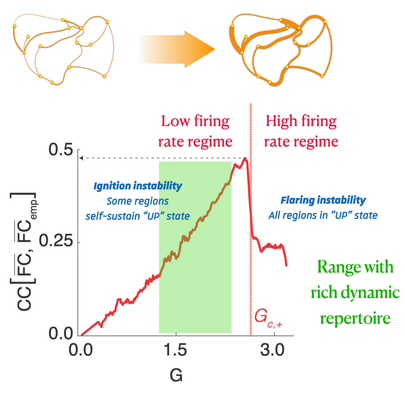


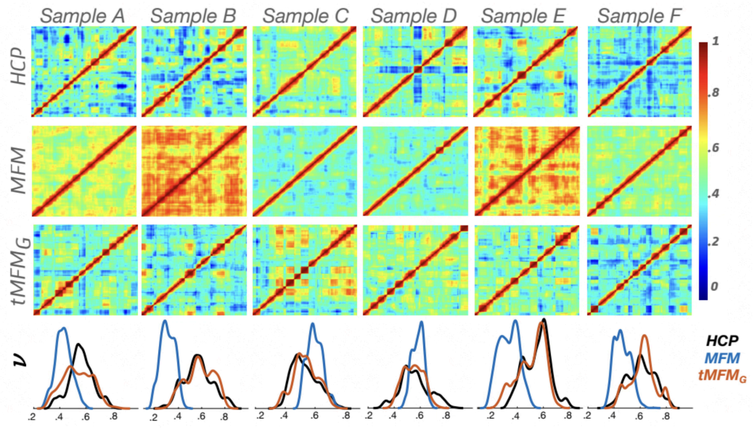
$$m_{ij,kl} = \mathrm{corr}\left(FC_{ij}(t), FC_{kl}(t)\right)$$
$$\rho_{i,j} = \mathrm{corr}\left(x_i(t), x_{jl}(t)\right)$$

- Beyond **classical FC** whose entries **ρ** capture internode synchronization we evaluate **Meta-Connectivity *m*** whose entries capture inter-link synchronization, i.e. the higher-order interdependencies shaping dFC fluctuations in space and time.

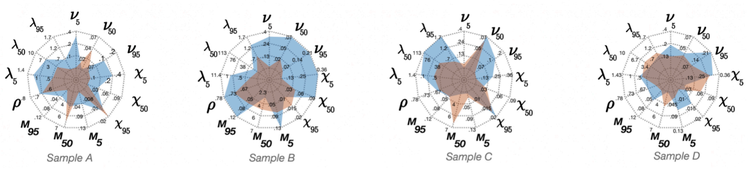
Mechanistic explanation of dFC organization: the Critical roaming hypothesis





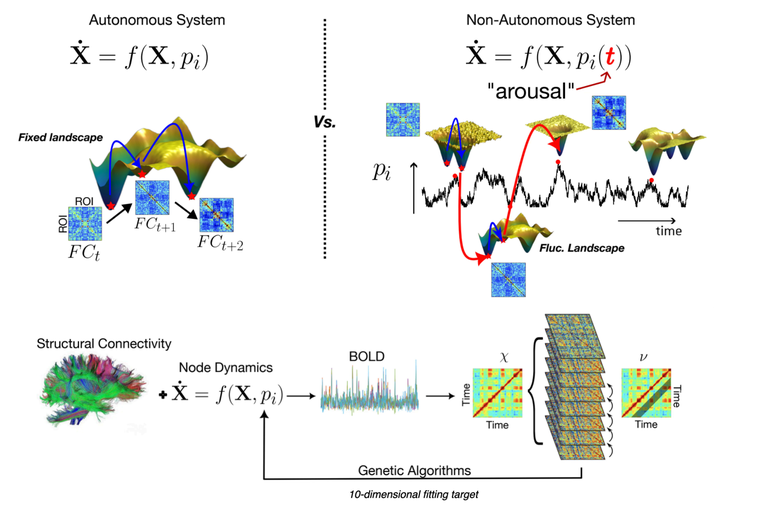


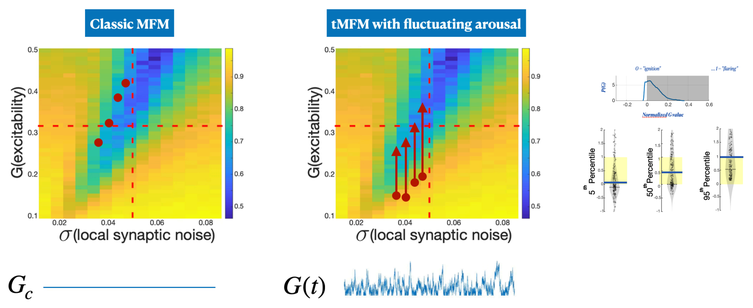
- **Connectome-based models** reproduce at best resting state functional connectivity when tuned in **proximity of a critical instability** point ("flaring" instability)
- Slightly subcritically to this point some **qualitative traits of dynamic Functional Connectivity** are reproduced as well (Hansen et al., 2015) but there is **no proper matching with precise quantitative descriptors** of dFC.



Classical Mean Field Models (MFMs) don't capture e.g. dFC speed distributions with sufficient precision to claim a status of personalized digital twins
Next-generation models (tMFMs) do much better !

(see here example HCP subjects)

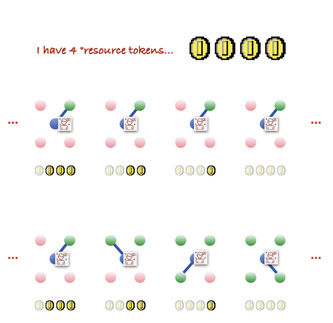




- In **next-generation models**, the **dynamic working point** of the system is made to **fluctuate in time**, emulating fluctuations of **arousal** (combined phenomenological effect of variations in neuromodulatory tonus, etc.)
- We **fit parameter stochastic variation** (not only mean) against **distribution quantiles** (not only means) of **dFC fluidity χ** and **speed ν**. Rendering of additional dFC metrics (ρ, λ, m) used as **off-target validation**.
- dFC properties as median and tails of **speed distribution** here shown **depend on model global parameters** in a way **organized by critical lines**
- Classical model fitting infers static slight subcriticality, but non autonomous model fitting suggests that **dFC properties are better explained by roaming of the dynamic working point** between the ignition and flaring lines.

Pathak & Battaglia, PLoS Biology (2026, in press)

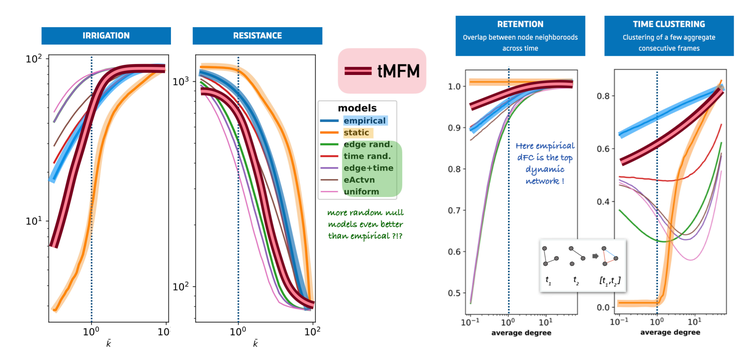
Dynamic of strong links suggests optimal integration/segregation tradeoff



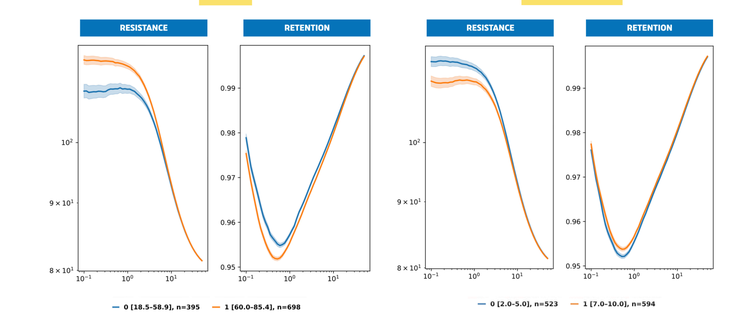
- *FCis a* ***proxy for the communication capacity*** *between any two regions in a* ***toy model of information dispatch****...*

How efficient is the observed dFC in:
- *dispatch information to many targets* ***("irrigation")****; do it in shorter or faster time* ***("resistance")****; maintain info in a local neighborood* ***("retention")***

If ***creating and keeping active a link has a COST****, how do we better spend our budget: create* ***fewer longer lasting links****? Or a* ***larger number of more volatile links****?*

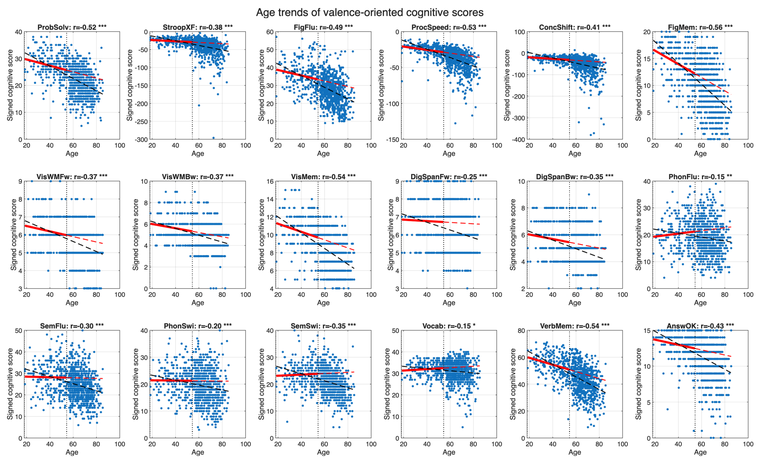


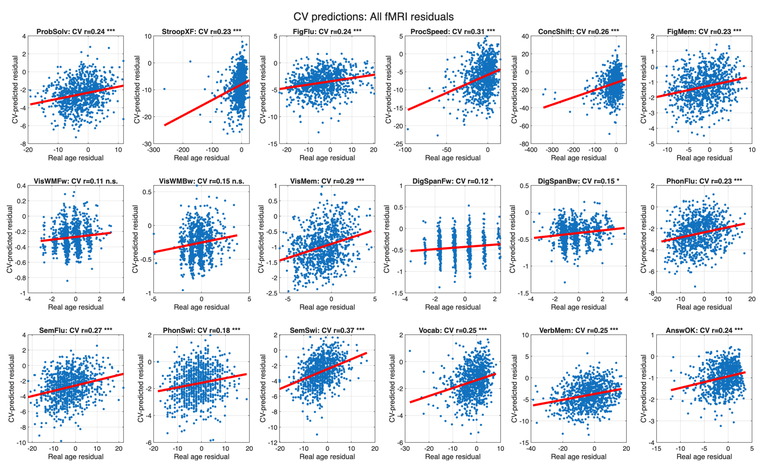
- *We apply* ***thresholding*** *to temporal networks from empirical dFC, various null models and tMFM simulations to extract toy binary information dispatch networks.* ***Lower budget corresponds to higher thresholds*** *and more diluted networks. We compare* ***tnet dispatch performance at equal cost****.*
- ***Empirical dFC tnet have higher irrigation and lower resistance*** *than equal cost static networks, especially when link cost is large and budget low. However, other* ***null models could irrigate even better*** *than empirical dFC...*
- *... however* ***empirical dFC has better retention and segregative properties*** *than other dynamic models, achieving* ***simultaneously superior integration and segregation*** *in information dispatch in a frugal way.*
- *t****MFM naturally reproduce empirical dFC*** *like integrative and segregative dispatch profile.*



- ***Age and education affect integrative and segregative properties*** *in a way suggesting that they may be contributing to cognitive reserve mechanisms.*

dFC properties predict deviations from age trend in cognitive performance





- We analyze the **age and education dependence of cognitive performance** based on the **1000 BRAINS DATASET** (Caspers, S et al. Front Aging Neurosci, 2014)
- **Performance declines with age** but **higher education confer higher performance at equal age**. Residuals around trend tend to become larger at elderly age.
- We try **predicting deviations from trend** (better or worse performance than expected according to normative age trend) in terms of **mulinear models based on dFC** properties (deviations from age-related expected slowing).
- Linear prediction based on **dFC residuals** achieve significant crossvalidated prediction of **cognitive performance residuals**.

- Fitting MFMs to measured dFC properties suggest **modulation of working point by age and education**
- Example: higher cortical gain *G* as a function of higher education?