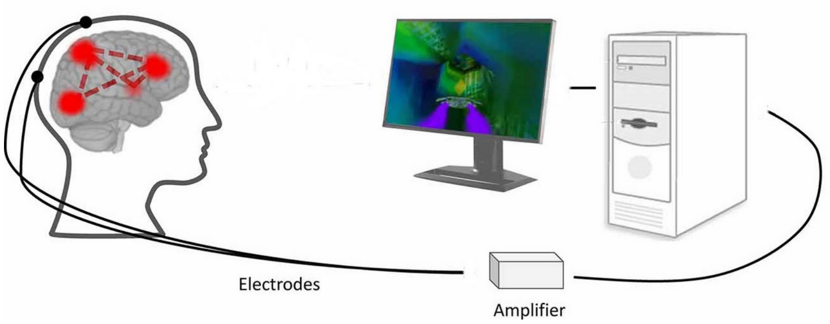
Michele Allegra
Brain Controllability: mirage or reality?

Towards brain control

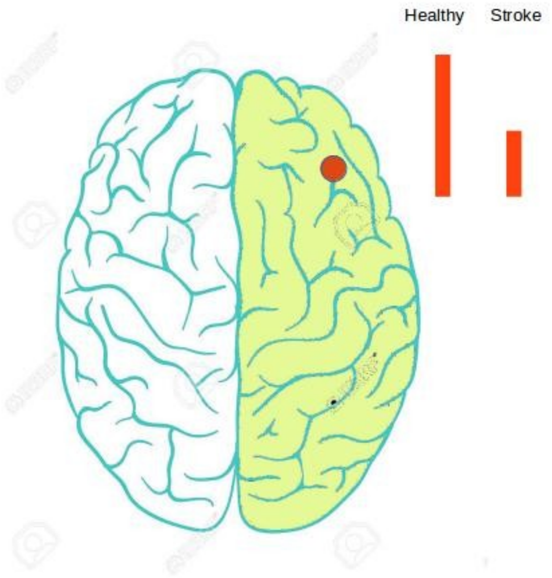
- Remote control of thoughts?

- Manipulating brain activity through controlled external interventions (e.g. electric stimuli)

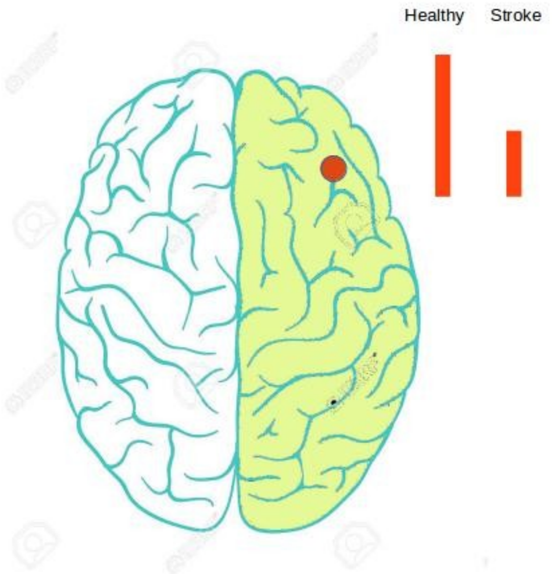


- Design effective intervention paradigms using control theory

Towards brain control



Towards brain control



Towards brain control

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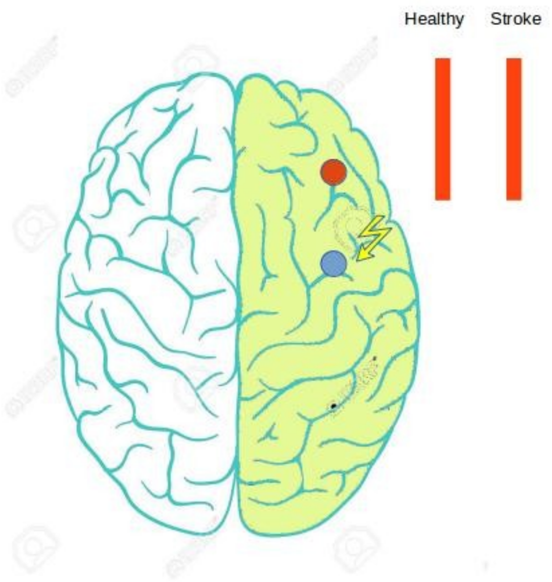

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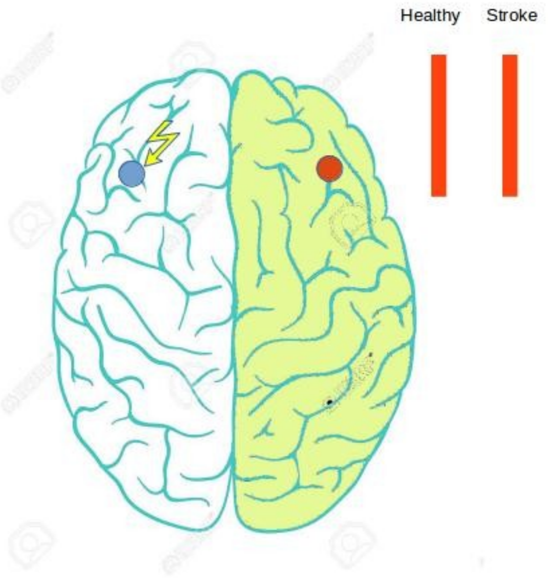
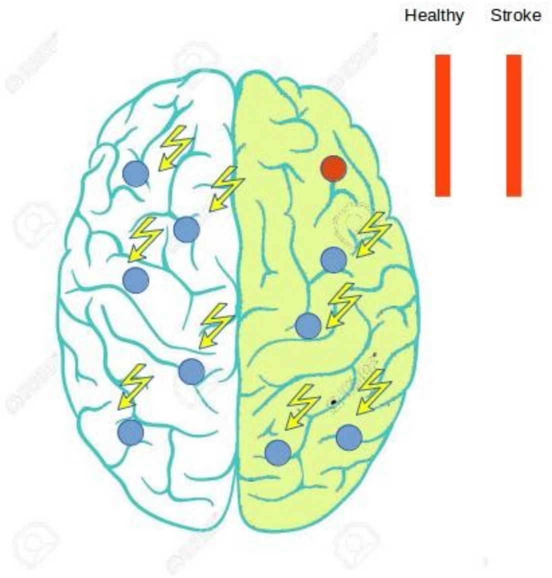


Towards brain control



Towards brain control

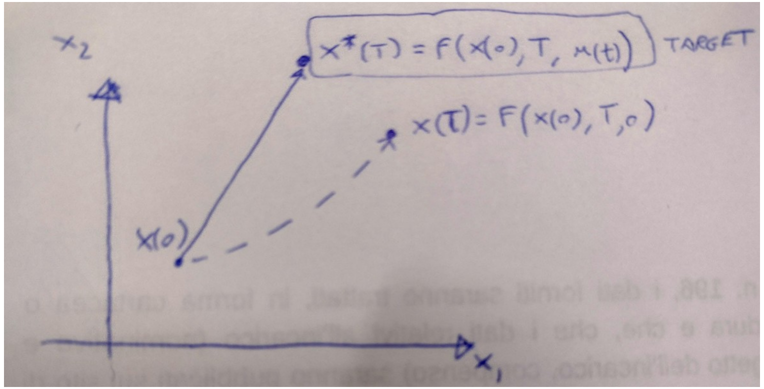
Transcranial magnetic stimulation

Transcranial direct current stimulation

Control theory in engineering

- *Design external perturbations to control a system*
- **x**(t) *state* of the system at time t [vector]
- **u**(t) external *input* [vector]
- F: system *dynamics*, **x**(T) = F(**x**(0),T,**u**(t))
- Invert relation to find **u**(t) = G(**x**(0),**x***(T),T) to achieve *target state* **x***(t)
- Theory predicts when this can be done

By smartly harnessing the system's intrinsic dynamics, we may control the whole system by acting only on (small) subsystem



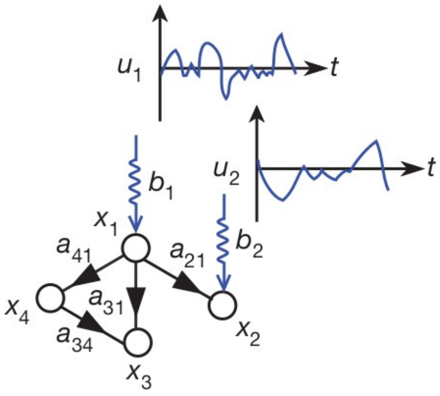
Linear Controllability

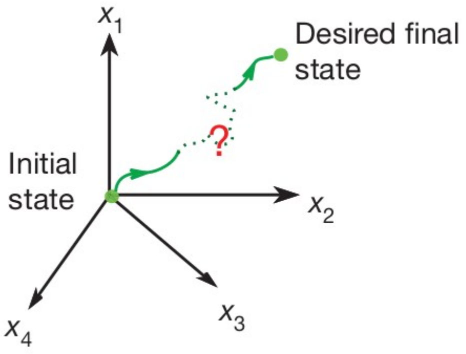
- **x**(t) - state vector for N "network nodes" at time t
- Dynamics is given by Linear Time Invariant(LTI) system:

$$\frac{d\mathbf{x}(t)}{dt} = A\mathbf{x}(t) + B\mathbf{u}(t)$$

- *A* - (N,N) connectivity matrix
- *B* - (N, r) input matrix with "r" being number of control nodes required to control the system.

$$A = \begin{pmatrix} 0 & 0 & 0 & 0 \\ a_{21} & 0 & 0 & 0 \\ a_{31} & 0 & 0 & a_{34} \\ a_{41} & 0 & 0 & 0 \end{pmatrix}; B = \begin{pmatrix} b_1 & 0 \\ 0 & b_2 \\ 0 & 0 \\ 0 & 0 \end{pmatrix};$$





Linear Controllability

$W = \int_0^{\infty}$ … τ

- Can we drive the system towards any desired final state with a suitable choice of input signal vector **u**(t)?

- *Given A,B,* **algebraic condition** on *controllability Gramian:* W>0

$$W = \int_0^{\infty} d\tau e^{A\tau} B B^T e^{A^T \tau}$$

- The minimum *control energy* to steer the system to target state is

$$E = \int_0^{\infty} d\tau ||u(t)||^2 = x^T W^{-1} x^T$$

- In the worst case, energy is the minimum inverse eigenvalue of W

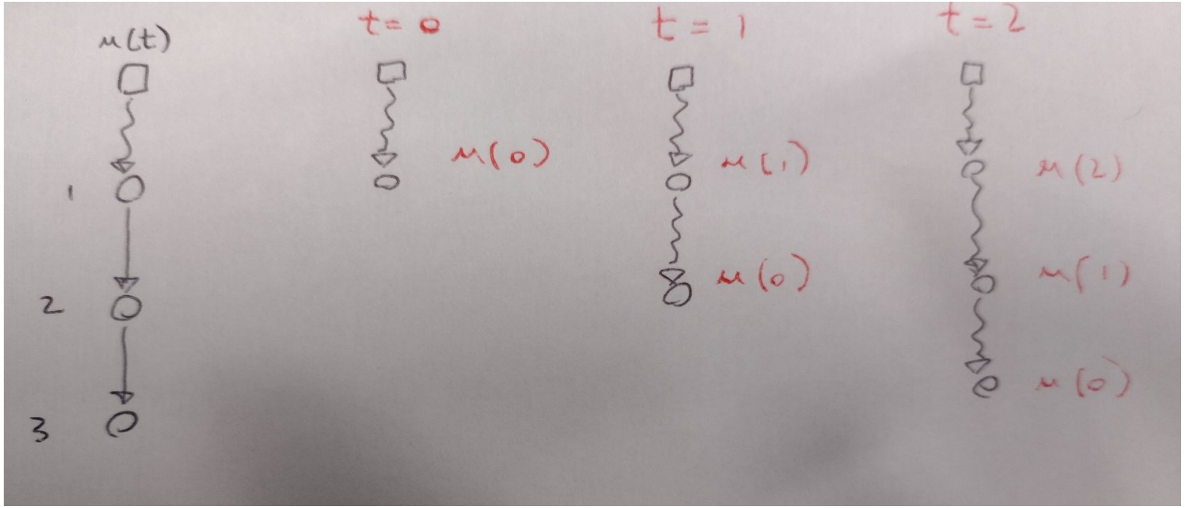
$$E_{max} = 1/\lambda_{min}(W)$$

- On average

$$E = Tr[W^{-1}]$$

Linear Controllability

- *Given A,* how should we select B (control nodes) such that the system is controllable?



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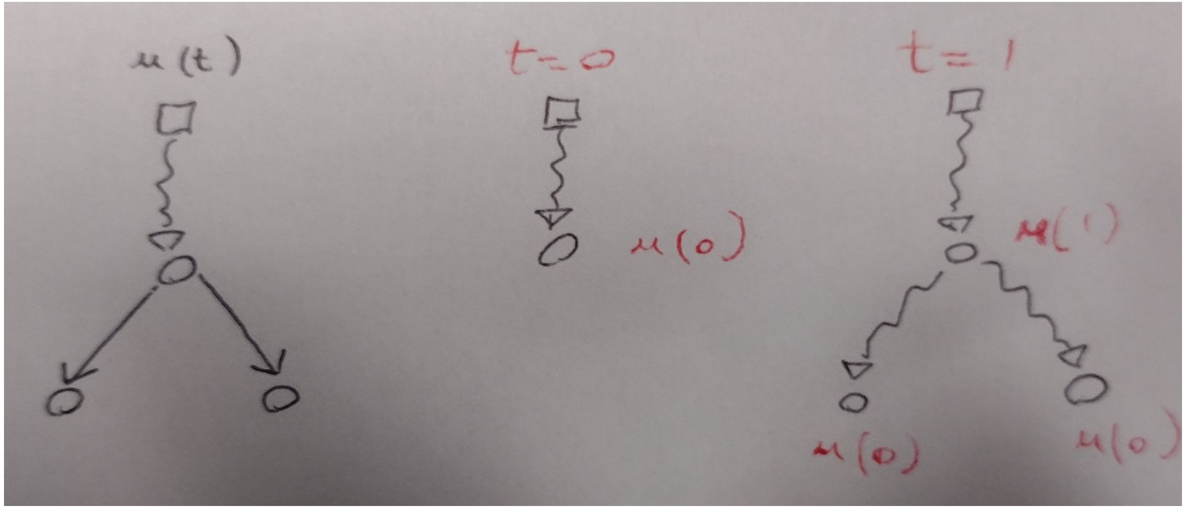

Linear Controllability

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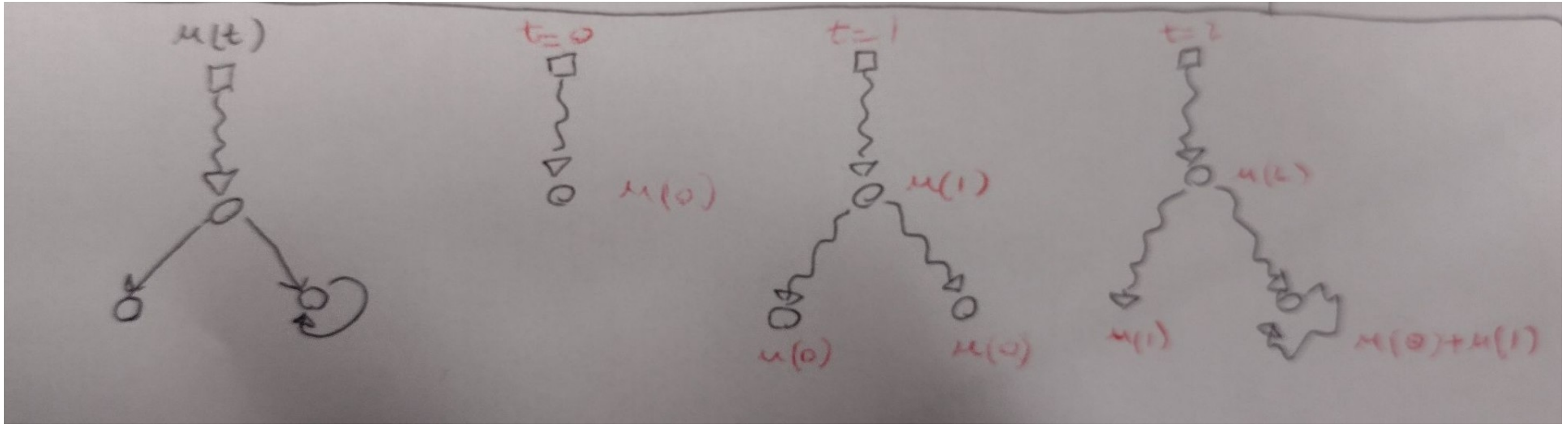
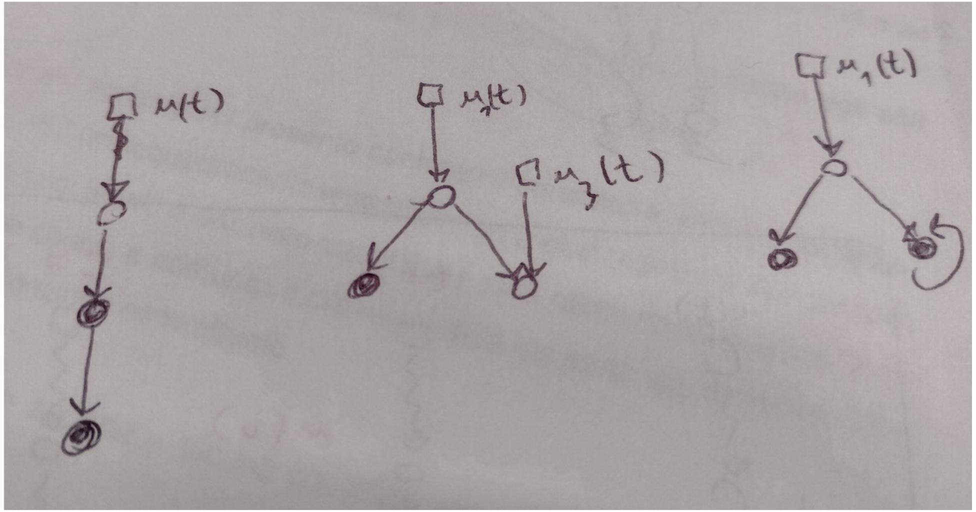


Linear Controllability

- *Given A,* how should we select B (control nodes) such that the system is controllable?
- **Graph-theoretical criterion**: control *unmatched nodes*
- maximum matching: set of links with no common starting/ending points



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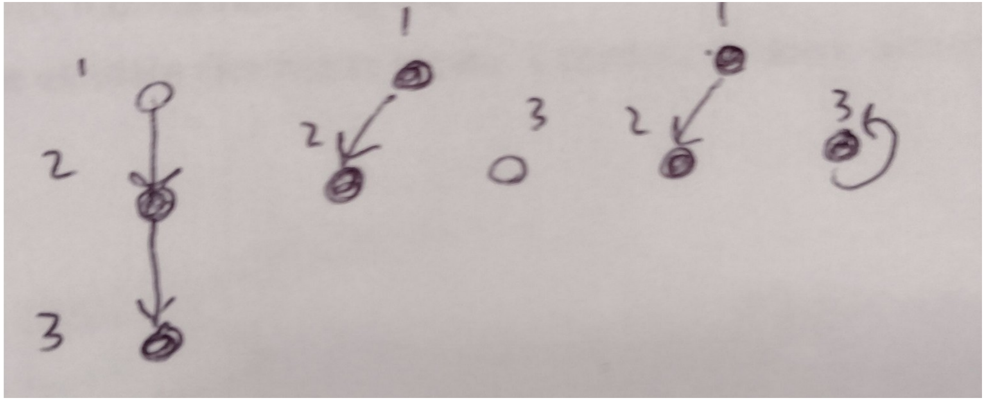


Controlling the brain with a single node?

Open Access | Published: 01 October 2015

Controllability of structural brain networks

Shi Gu, Fabio Pasqualetti, Matthew Cieslak, Qawi K. Telesford, Alfred B. Yu, Ari E. Kahn, John D. Medaglia, Jean M. Vettel, Michael B. Miller, Scott T. Grafton & Danielle S. Bassett

- Resting-state fMRI recordings
- N=243 'nodes' (regions of Lausanne atlas)
- **x**(t) activity vector (region time series from fMRI)
- *A* structural connectivity matrix (from dTI)
- *B* single-node input matrix
- Repeat the procedure over each and every node

$$\frac{d\mathbf{x}(t)}{dt} = A\mathbf{x}(t) + \mathbf{B}\mathbf{u}(t)$$

Controlling the brain with a single node?

- **W**>0: brain networks are '**theoretically controllable**' from a single node

- they are **practically uncontrollable**: the control energy $||u^2|| > 10^{22}$

- ...it is hard to drive the system towards an arbitrary desired target states

- Look at '*average controllability*' inverse of average energy required for control (average over target states)

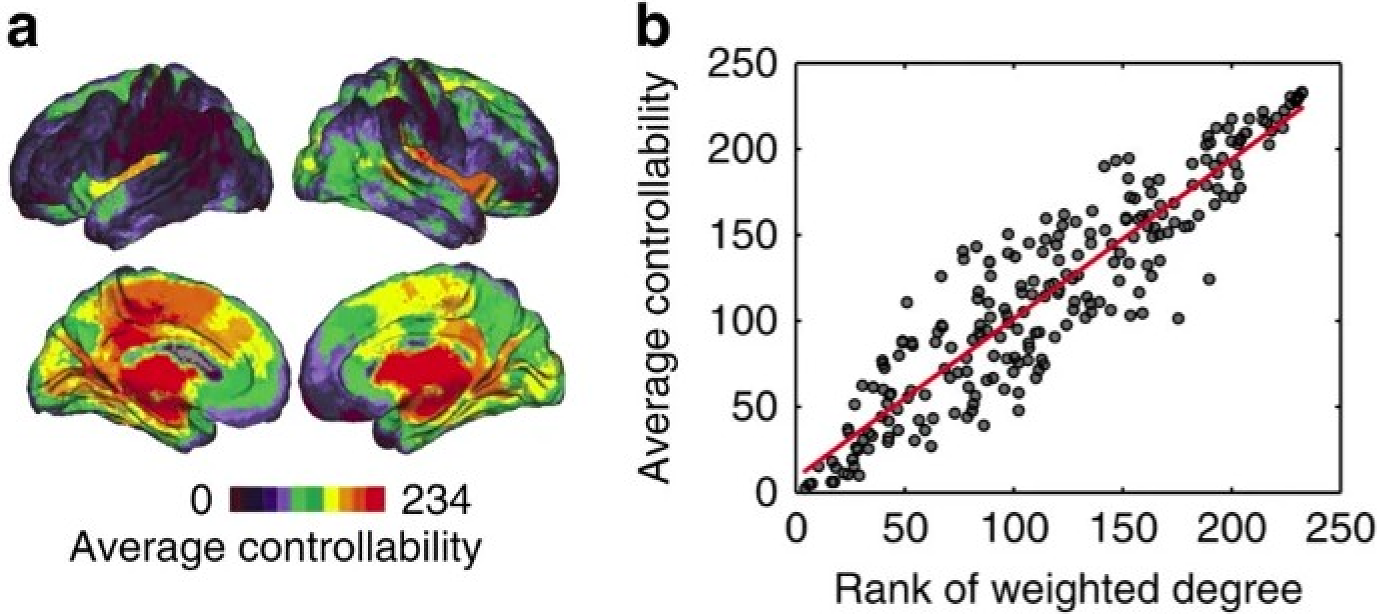
$$a_i = Tr[W] \leq \frac{1}{Tr[W^{-1}]} = E$$

- Look at '*modal controllability*' ease of controlling slow modes of A

$$m_i = \sum_j (1 - \mu_j)^2 V_{ij} \qquad A = V \mathrm{diag}(\boldsymbol{\mu}) V^T$$

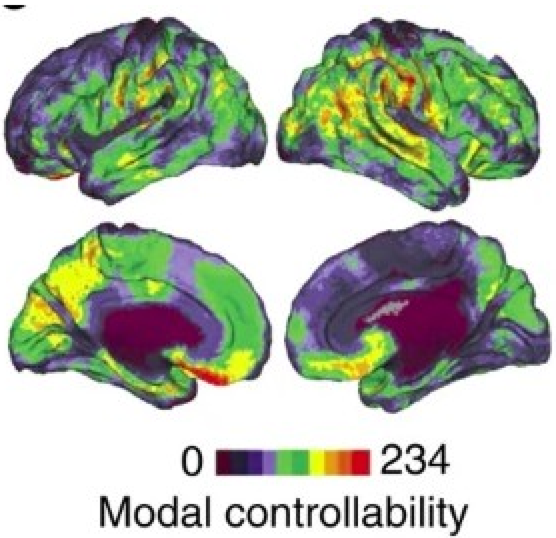
Controlling the brain with a single node?

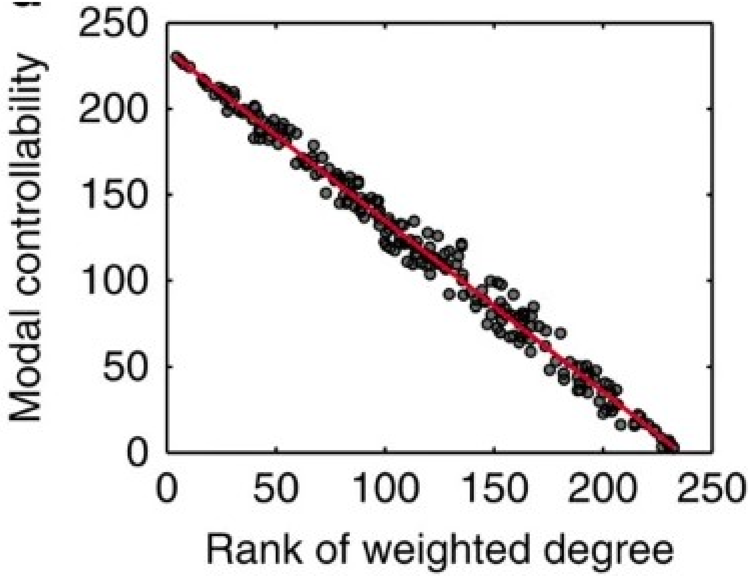
Average controllability is larger when controlling hubs



Controlling the brain with a single node?

Average controllability is larger when controlling peripheral nodes





… Limitations with the framework

Warnings and caveats in brain controllability

Chengyi Tu [a, f], Rodrigo P. Rocha [a, f], Maurizio Corbetta [b, c, f], Sandro Zampieri [d, f], Marco Zorzi [e, f, g], S. Suweis [a, f]

- **Limitation (1): choice of dynamic model**
- ***A = S*** ***structural connectivity matrix***
- This model is unstable and far from the actual dynamics!
- the proper model requires a *diagonal decay term* …

$$A = -\frac{1}{\tau}\mathbb{I} + cS$$

- Other limitations: noiseless dynamics, linear dynamics

… Limitations with the framework

Limitation (2): the energy is extremely large

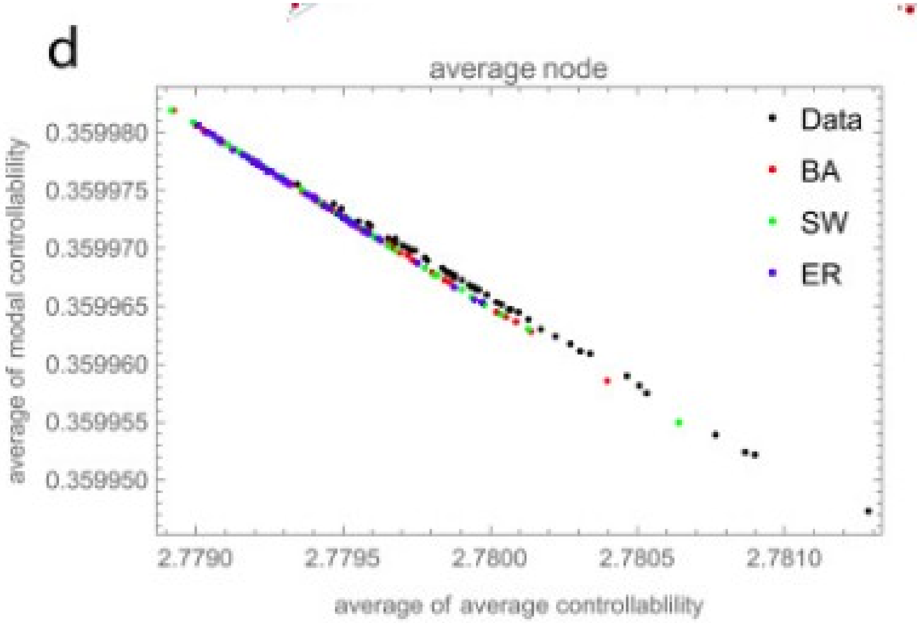
To have $E_{min} < 10^{10}$ you need to control >45% of nodes …

Table 1. The minimum number of nodes (and fraction with respect the size of the network) that are needed to control the system spending a minimum energy not greater than $\varepsilon_{min} = 10^{10}$.

	Data		BA		SW		ER	
Centrality measure	Low	High	Low	High	Low	High	Low	High
Degree centrality	51/0.46	49/0.45	44.64/0.41	42/0.38	45/0.41	43.5/0.40	44.64/0.41	42/0.3

… Limitations with the framework

- **Limitation (3): the controllability/topology relation is not specific of brain networks**



Using a 'good' dynamics

K. Kabbur, ..., S. Suweis, A. Bertoldo, M. Allegra, in prep.

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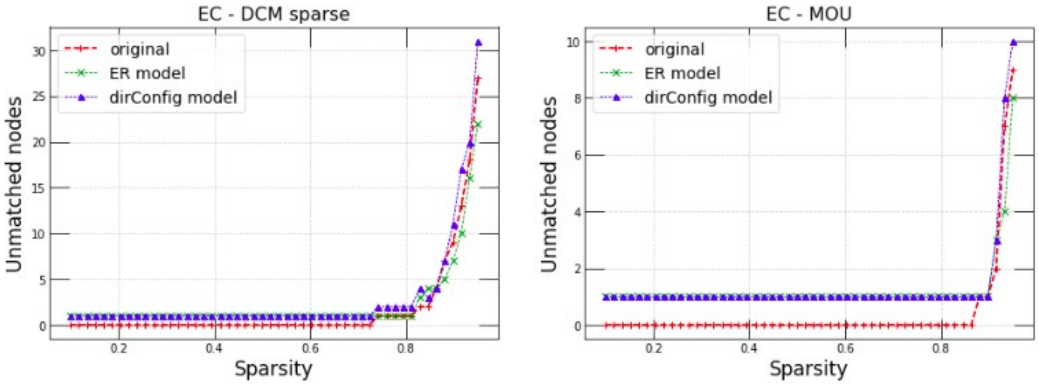
- **Use the best (linear) model of the data**
- ***A = EC   Effective connectivity matrix***
- Sparse Dynamic Causal Modelling (spDCM)   [Prando et al., NIMG 2021]
- Multivariate Ornstein Uhlenbeck(MOU) model   [Gilson et al., PLOS CB 2017]
- EC is computed by best fit on data of each individual subject
- Both models allow for asymmetric connections -> *directed graph*
- More accurate description of dynamics and possibility to define unmatched nodes

Single-node controllability (in theory)

K. Kabbur, …, S. Suweis, A. Bertoldo, M. Allegra, in prep.

- **All nodes are matched: the system is 'theoretically controllable' with a single node**
- EC networks are dense (40% sparsity)
- All nodes are matched unless sparsity is very high

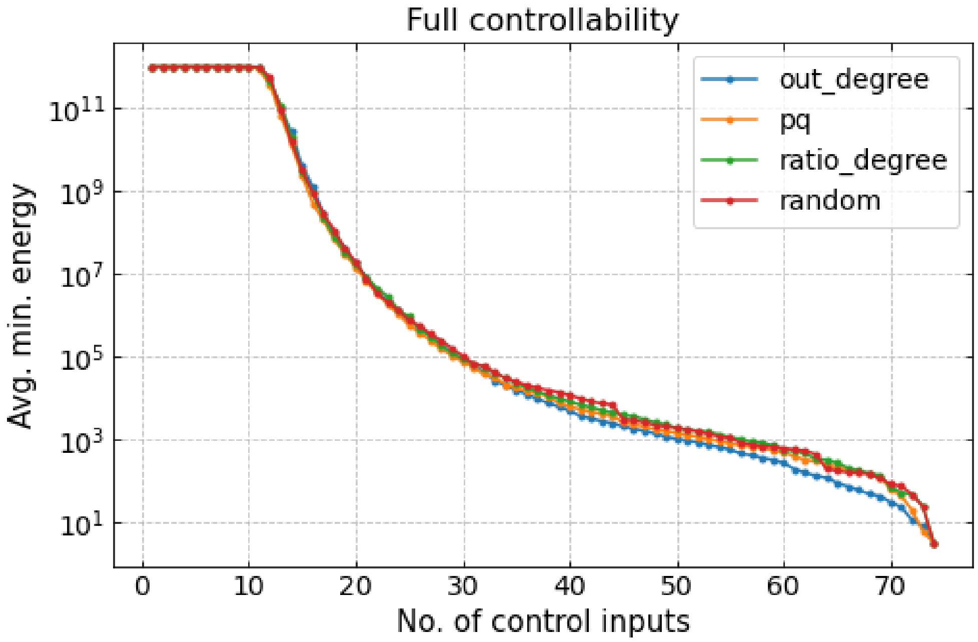


(a) (b)

Many nodes are needed (in practice)

K. Kabbur, ..., S. Suweis, A. Bertoldo, M. Allegra, in prep.

- **Full controllability requires to control at least 20% of nodes**

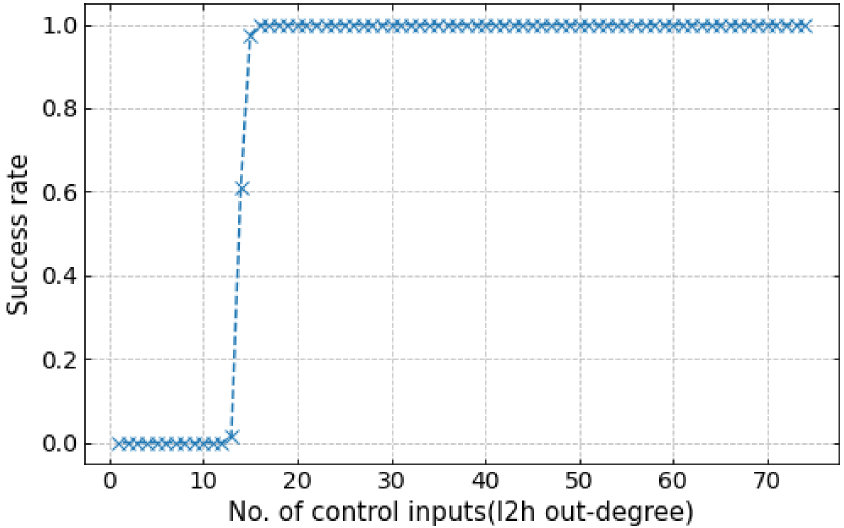


Many nodes are needed (in practice)

K. Kabbur, ..., S. Suweis, A. Bertoldo, M. Allegra, in prep.

- **Unless 20% of nodes are controlled, control is numerically unstable**

  [Gie Sun and Adilson E. Motter, Phys. Rev. Lett. **110**, 208701]

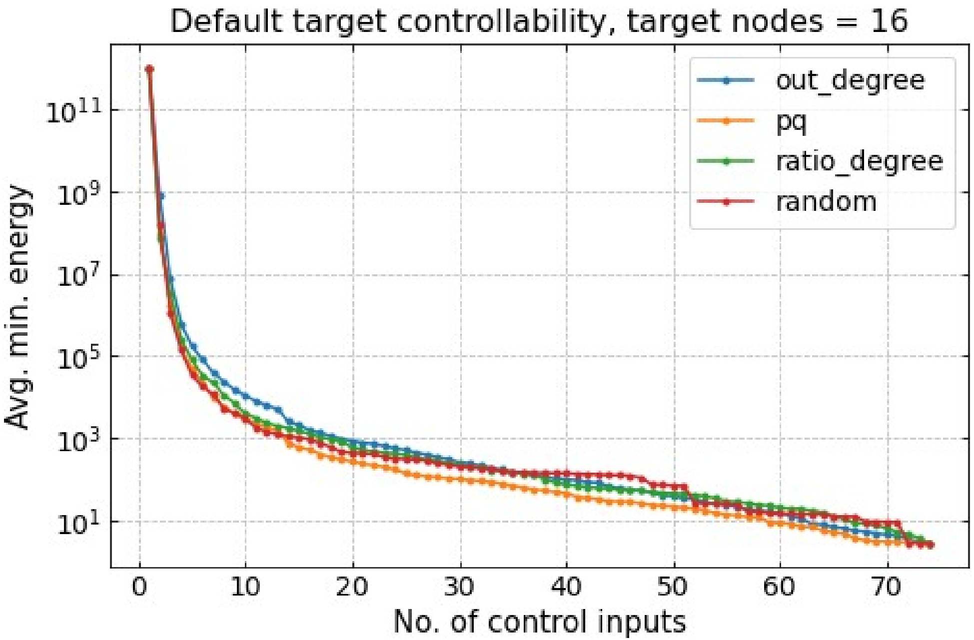


Restricting the target

K. Kabbur, ..., S. Suweis, A. Bertoldo, M. Allegra, in prep.

If we aim to control a small subset of nodes, control energy significantly decreases

[Gao, Jianxi, et al. "Target control of complex networks." Nat. Comm. 5.1 (2014): 1-8.]



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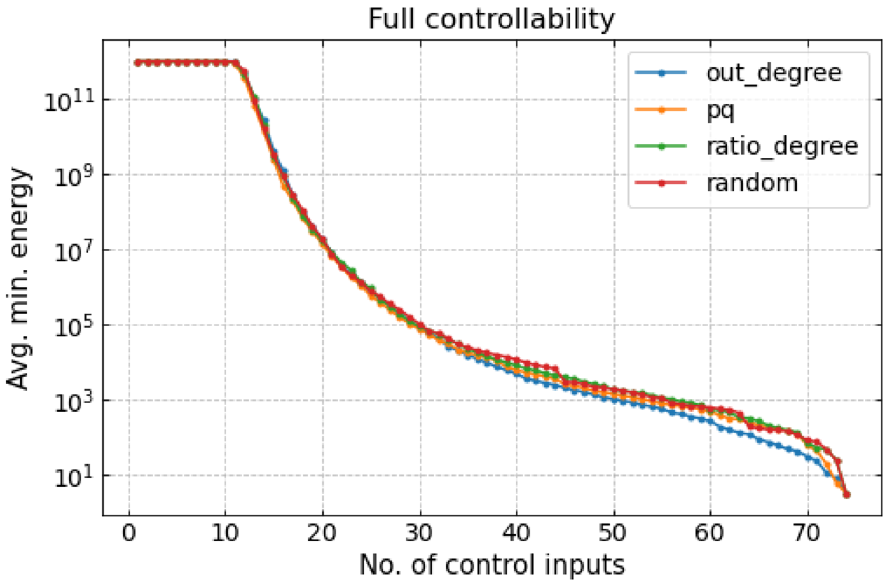

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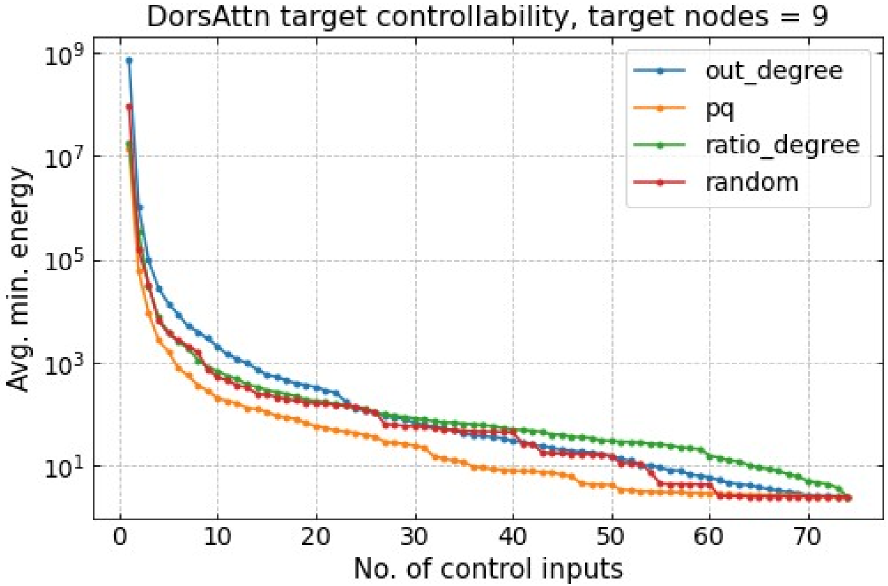

(pro-tempore) Conclusions

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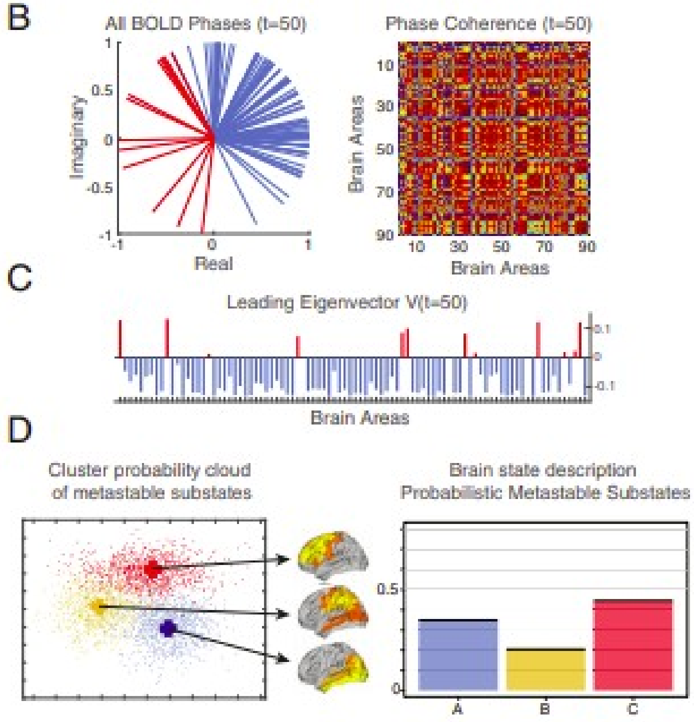
- look for a paradigm to design controlled interventions on brain dynamics
- *“control theory”* offers an interesting conceptual framework
- Applying control theory requires appropriate modeling of dynamics (EC)
- Qualitatively, results are robust w.r.t. choice of EC model
- Controllability properties mainly depend on connection sparsity rather than other topological features.
- Controlling brain’s activity globally by stimulating one or a few nodes appears practically unfeasible
- Controlling a subsystem may be more affordable but still significantly hard

An alternative approach to control?

Can we exploit dimensionality reduction to define an easier control objective?

- the target is not a "*microstate*" (activity state **x***), but a "*macrostate*" (an activity regime with specific features)
- E.g., try to control balance between dynamic connectivity patterns [Deco et al. PNAS 116.36 (2019): 18088-18097.]
- The probabilities of different states determine "macrostate"



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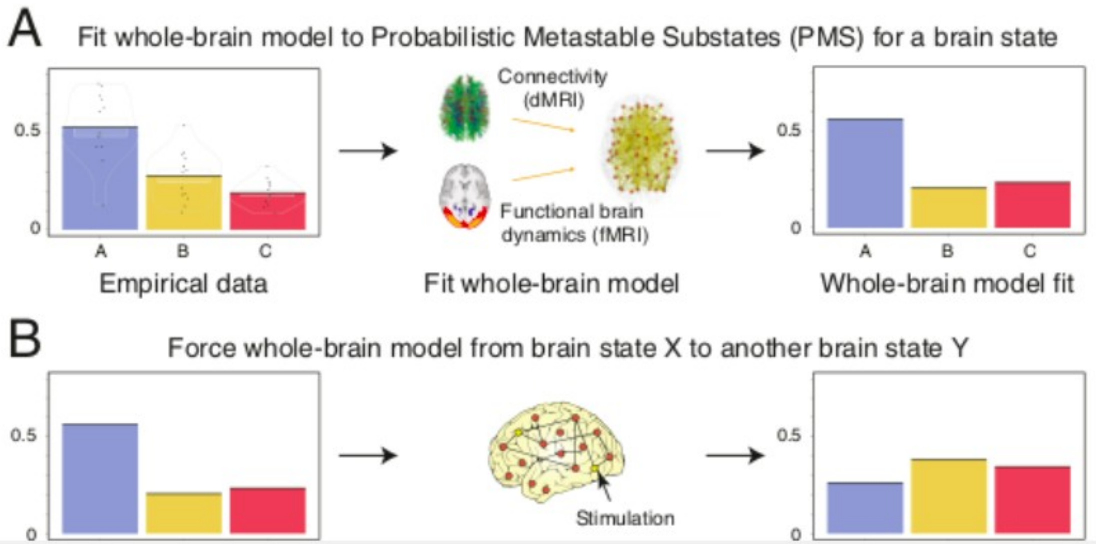

Acknowledgements

Karan Kabbur Hanumanthappa Manjunatha

Samir Suweis

Alessandra Bertoldo

Giorgia Baron

Dipartimento di Fisica e Astronomia Galileo Galilei

DIPARTIMENTO DI INGEGNERIA DELL'INFORMAZIONE

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Acknowledgements

IPM
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Thank you for your attention!!

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