Proposal for PhD position

Working Group: **Intrinsic Brain Activity and Behavior**
Members (https://pnc.unipd.it/category/people/):

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Marco Zorzi	(PNC & Department of General Psychology, coordinator)

List of activities carried out by the Working Group and how they were communicated and promoted within the PNC from 27/2/2023 to today:

- 1st meeting on 30/3/2023
- Proposed research activities reported at: https://docs.google.com/document/d/1E4El_yFs1v2R3viSwbCfgV8SIiKCMn7jB9kGhtH8UWc/edit
- Meetings to discuss a possible project for a PNRR call (bando a cascata partenariato esteso MNESYS);
- Drafting and submission of proposal for MNESYS call
- 1 paper: Manjunatha KKH, Baron G, Benozzo D, Silvestri E, Corbetta M, Chiuso A, Bertoldo A, Suweis S, Allegra M "Controlling target brain regions by optimal selection of input nodes" PLoS Comput Biol. (2024) J12;20(1):e1011274.

Proposal:

Title of the PhD project: *Organization and dynamics of healthy and pathological brains*

Abstract:
Brain activity at rest shows fluctuations over time that can be described in terms of ordered transitions between multiple modes. A leading hypothesis is that spontaneous activity is the manifestation of top-down dynamics of generative models detached from action–perception cycles, which is consistent with the finding that functional brain connectivity at rest is predictive of both task-related activity and behavioral performance. Nevertheless, brain dynamics depend on the structural organization of white matter pathways (i.e., the physical connections between brain regions) and require large energy consumption (glucose metabolism), which pose significant constraints on brain functioning.

Together, brain functional, metabolic and structural organization support the complex neural computations that drive behavior and cognition. This complex organization can be modelled as a complex multimodal network and investigated by using graph theory and dynamical systems theory. Graph-based measures allow to describe the architecture of the brain analyzing the information encoded in the so-called adjacency matrix. System theory allows to characterize

important properties of a system such as stability, controllability, and observability. More specifically, control theory methods can be used to investigate the ability of a specific region to steer the brain dynamics from one state to another, for example, from rest to task. Therefore, exploring the control properties of different brain regions and their correlation with the traditional graph measures can improve our understanding of whether and how regional hubs (as defined by graph metrics) may be able drive the brain from any initial state to a desired state, with profound implications for the design of intervention in neurological or psychiatric conditions.

This project has **two aims**: i) enrich the directed brain network, as described by dynamic casual modeling, with structural and metabolic information; ii) use tools from control and network theory to offer a mechanistic explanation for how the brain moves between cognitive states by also considering the network organization of white matter microstructure and glucose consumption. The final aim is to develop a subject-specific approach to investigate the differences in brain networks of healthy and impaired individuals (e.g., stroke patients) based on a multimodal directed connectome complemented by both graph-based and system theory-based biomarkers.

Potential supervisors: To be defined within the Working Group

Description of the expected background of the PhD student:
The PhD student is expected to have a strong quantitative background with interest in computational neuroscience and in an interdisciplinary study of the nervous system's structure, physiology, information processing, and cognitive abilities. An interest in applying system theory, graph theory and mathematical multi-scale models to physiology will be helpful in pursuing the aims of the proposed project.

Description the multidisciplinary training path planned for the student's career:
In addition to the regular training activities of the PhD program, the PhD student will collaborate and discuss with the “Intrinsic Brain Activity and Behavior” Working Group, which includes several senior scientists (beyond the PhD supervisor and co-supervisors). This will ensure that the student will receive truly interdisciplinary training as well as regular input from scientists from diverse disciplines (statistical physics, bioengineering, computer science, cognitive and behavioral neuroscience). The student will attend regular meetings of the Working Group and present progress reports. Publications will primarily target high-impact multidisciplinary journals. A period abroad with one of the various collaborators of the PIs of the WG will complete the training.

References:

1) Benozzo D, Baron G, Coletta L, Chiuso A, Gozzi A, Bertoldo A (2024). Macroscale coupling between structural and effective connectivity in the mouse brain. *Scientific Reports*, 14(1):3142. doi: 10.1038/s41598-024-51613-7.
2) Pezzulo G, Zorzi M, Corbetta M (2021). The secret life of predictive brains: what's spontaneous activity for? *Trends in Cognitive Science*, 25(9):730-743. doi: 10.1016/j.tics.2021.05.007

3) Prando G, Zorzi M, Bertoldo A, Corbetta M, Zorzi M, Chiuso A (2020). Sparse DCM for whole-brain effective connectivity from resting-state fMRI data. *Neuroimage,* 208:116367. doi: 10.1016/j.neuroimage.2019.116367.
4) Rocha RP, Koçillari L, Suweis S, De Filippo De Grazia M, de Schotten MT, Zorzi M, Corbetta M (2022). Recovery of neural dynamics criticality in personalized whole-brain models of stroke. *Nature Communications*, 13(1): 3683. doi: 10.1038/s41467-022-30892-6
5) Tu C, Rocha RP, Corbetta M, Zampieri S, Zorzi M, & Suweis S (2018). Warnings and caveats in brain controllability. *Neuroimage*, 176, 83-91. doi: 10.1016/j.neuroimage.2018.04.010