

## The path the brain takes – a closer look at the temporal evolution of functional states in a network control theoretical framework

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## Abstract:

Network Control Theory (NCT) is a powerful methodological toolbox that models how a dynamical system might maintain and traverse between various functional states [1]. Applied to neuroscience, it allows investigations into how the brain's structural connectome constrains function, how specific brain regions or networks might control dynamics via functional "control inputs", and into how these characteristics change in clinical samples [1].

Among various other factors, the energy needed by the brain to traverse between a start and target brain state is associated with specifics of the target state, i.e. some functional target states are much more costly to be reached than others [2,3]. Much less is known about the temporal aspect of the dynamics - that is, about the path of intermediate brain states the brain takes from the start state to arrive at the target state.

We here analyse specifics of these trajectories, based on 123 meta-analytically derived brain states from the Neurosynth database. With dynamics constrained by a group-averaged structural connectome calculated from the Human Connectome Project subset of unrelated participants, we conduct full NCT analyses between all pairs of brain states. We then project all 123 states, as well as all trajectories onto a shared geometrical space determined by the full set of principal components (PCs) of the 123 Neurosynth states.

Transitions between brain states might be optimized with regard to energetic costs, as well as with regard to directness of the path between start and target [2]. We show that trajectories optimized for directness also closely correspond to straight line segments

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between states in PC space. In practice, these direct, but also highly costly transitions are not always feasible in biological systems geared to energy minimisation (such as the brain) [3]. We show that a more balanced consideration of both cost as well as directness is indeed associated with more curved, that is, indirect, trajectories in PC space. Both the direction into which trajectories are deflected in respect to a direct path, as well as the magnitude of the deflection, are initially influenced both by the start and the target state. Over time, the influence of the target state increasingly diminishes, with trajectories ultimately only being influenced by the state from which they started. We show that this finding is persistent across NCT parameter settings and hypothesize that it is related to the brain's energy landscape, with energetically balanced trajectories explicitly avoiding traversal through energetically costly areas of the PC space (i.e. explicitly evolving via intermediate brain states that are energetically easier to reach, even if they might be not be located on the direct path between start and target state).

Our results suggest that a model of the brain's dynamics that is informed by biological plausibility needs to take into account not only target-state specifics and energetic cost of transitions, but necessarily also start-state specifics and characteristics of the temporal evolution of functional states – of the trajectories themselves.

Note: A descriptive figure is attached in the pdf document.