

OPINION

Rethinking segregation and integration: contributions of whole-brain modelling

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Abstract | The brain regulates information flow by balancing the segregation and integration of incoming stimuli to facilitate flexible cognition and behaviour. The topological features of brain networks — in particular, network communities and hubs — support this segregation and integration but do not provide information about how external inputs are processed dynamically (that is, over time). Experiments in which the consequences of selective inputs on brain activity are controlled and traced with great precision could provide such information. However, such strategies have thus far had limited success. By contrast, recent whole-brain computational modelling approaches have enabled us to start assessing the effect of input perturbations on brain dynamics *in silico*.

Evolution has led to the development of many different strategies for the survival of species. The relative evolutionary success of mammals has been made possible by sophisticated brains that can combine information from current stimuli with memories to predict the future and to adapt behaviour accordingly. The healthy human brain segregates and integrates information from sensory modalities, the body and memories. Take the example of a tennis player, who effortlessly integrates their memories with the colour, movement and shape of a tennis ball and segregates this information from the changing background of the tennis court and the crowd. These processes enable the player to predict the trajectory of the ball and to plan how best to position their body and tennis racket to return the ball beyond the reach of their opponent. The integrated information can be formally defined as the information a system has besides the information that is available from the sum of its parts^{1,2}. Such integration of information has been linked to consciousness, but it can also proceed without awareness³. However, we still lack a full understanding of the principles that underlie this fundamental process.

The most direct way to discover the brain mechanisms that underlie segregation and integration would be to use neuroimaging methods to map whole-brain structure and function. Much important progress has been made in this regard using sophisticated meta-analyses that have pooled data from thousands of task-related neuroimaging studies that probed and tested the brain in many

different ways⁴. However, such meta-analyses present many important potential confounds, including their cross-sectional nature. Instead, neuroimaging methods would ideally be used in the same individual to map the structural and functional pathways from each of the very large number of possible unimodal and multimodal inputs to integrate this information in a final common pathway and to map the underlying spatiotemporal dynamics. However, it is nearly impossible for human participants to sit through experiments that could both explore a vast range of diverse inputs and control the full dynamics of the human brain. The use of direct causal brain interference methods such as transcranial magnetic stimulation (TMS) also provides a promising approach to study brain networks. However, there are notable ethical problems associated with causally interfering with the human brain^{5,6}.

The difficulty in controlling the full range of inputs to an individual brain is another reason why neuroimaging-based investigations of information segregation and integration have so far focused on the topological aspects of brain organization and/or resting-state activity, which is based on processing and coordinating internal rather than external input⁷. However, the relatively poor spatiotemporal resolution (which is typically on the timescale of seconds) and the indirect nature of whole-brain neuroimaging measures (such as functional MRI (fMRI)) have thus far limited the use of these methods for examining the dynamics of segregation and integration in the brain.

In this Opinion article, we argue that whole-brain computational modelling based on and constrained by neuroimaging data can be used to gain new insights into segregation and integration. We describe the currently available topological measures that are obtained from neuroimaging studies of connectomics using graph theory and that support the notion of segregation and integration of input information. We propose that whole-brain computational modelling can improve these measures, and we provide a brief description of the fundamental principles of whole-brain models. By systematically perturbing model networks, such models can be used to improve our understanding of the dynamics of input processing and thereby provide new useful measures of segregation and integration. These models can also provide new information about how the processes of segregation and integration change over time. In particular, we propose new dynamic measures for the integrative ‘binding’ of information over time (FIG. 1). These measures are different from existing ‘rich clubs’ of structural connectivity hubs, which are, by their very nature, more static. Importantly, we show how the new perturbational measures of segregation and integration can be applied to distinguish between states of consciousness and between health and disease. Finally, we discuss how generative whole-brain computational models may increase our understanding of the fundamental principles of human brain function in health as well as their breakdown in neuropsychiatric disorders.

Topological brain measures

Neuroimaging methods that can map the structural and functional connectivity of the human brain have started to map the architecture of the structural and functional networks in the human brain⁸. An important goal of these studies is to establish the human connectome, which is defined as “the complete description of the structural connectivity (the physical wiring) of an organism’s nervous system” (REF. 7). Here, we argue that this purely structural description could be amended to include the functional connectivity of the connectome, and such combined knowledge may enable us to understand the complex segregation and integration of relevant information over time.

Collecting topological and functional data. Neuroimaging methods can be used to study brain activity on several timescales and with varying degrees of spatial precision. In humans, the most popular