Available online at www.sciencedirect.com

ScienceDirect

Physics of Life Reviews 15 (2015) 124–127

PHYSICS of LIFE reviews

www.elsevier.com/locate/plrev

Comment

Complex-system causality in large-scale brain networks
Comment on "Foundational perspectives on causality in large-scale brain networks" by M. Mannino and S.L. Bressler

Luiz Pessoa [a,*], Mahshid Najafi [b]

[a] *Department of Psychology, University of Maryland, College Park, MD 20742, USA*
[b] *Department of Electrical and Computer Engineering, University of Maryland, College Park, MD 20742, USA*

Received 5 October 2015; accepted 12 October 2015

Available online 23 October 2015

Communicated by L. Perlovsky

Keywords: Causality; Complex systems; Networks; Modularity; Functional MRI

Mannino and Bressler [1] discuss foundational issues related to understating causality in a complex system such as the brain. We largely agree with their main point that standard versions of causality, such as those espoused in classical physics, provide an inadequate basis to support the understanding of complex systems. In a nutshell, instead of thinking that one event causes another, it is more fruitful to think that the occurrence of one event *changes the probability* of occurrence of other events. Such probabilistic notion of causation is, we believe, an important step in attempting to unravel the workings of the brain.

Although we strongly support the approach advocated by Mannino and Bressler, we would prefer referring to it as "complex system causality" instead of "probabilistic causality." This is because, even though a probabilistic account should still be used, neutral terminology could help fend off inevitable counter reactions related to the "inherent" nature of the brain. As Mannino and Bressler state, their formalism is agnostic with respect to the question of whether the brain operates deterministically or stochastically. In any case, below, we briefly discuss our views on understanding causality in the brain.

1. Causation

To a great extent, the mission of neuroscience is to understand the nature of signals observed in different parts of the brain, and to attempt to *disentangle* the potential contributions to those signals. But here lies the problem, too. The problem can be illustrated by considering a type of reasoning prevalent in neuroscience, what can be called the *billiard ball* causal model (Fig. 1A). In this model, force applied to a ball leads to its movement on the table until it hits the

DOI of original article: http://dx.doi.org/10.1016/j.plrev.2015.09.002.

* Corresponding author at: Department of Psychology, Biology–Psychology Building, University of Maryland, College Park, MD 20742, USA.
E-mail address: pessoa@umd.edu (L. Pessoa).

http://dx.doi.org/10.1016/j.plrev.2015.10.009

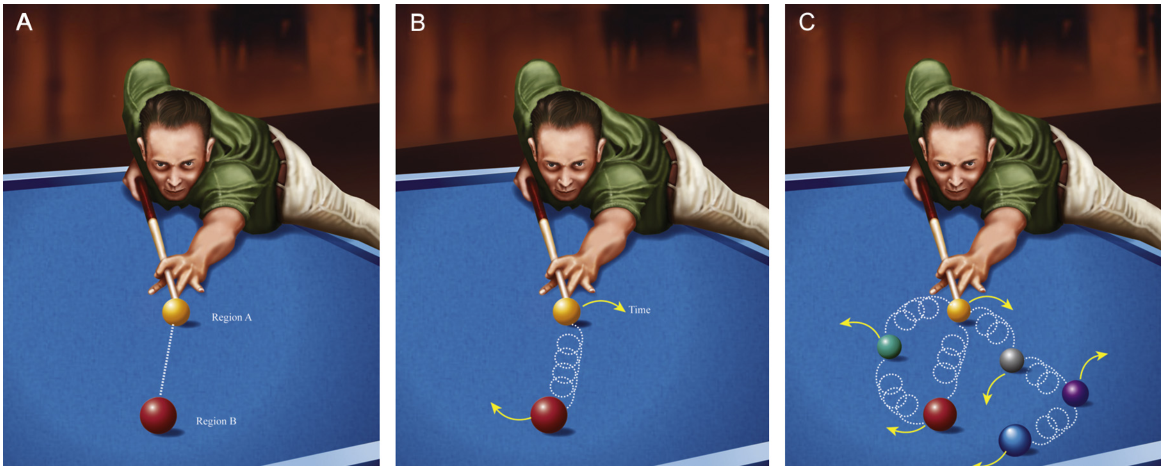

Fig. 1. Schematic representation of causal frameworks. (A) Billiard ball scheme. Complex system scheme with two (B) or many "particles" (C). In complex systems like the brain, standard causation conceptualizations fail to capture the interdependent nature of signals across regions.

target ball. In this case, the reason the target ball moves is obvious: the first ball hits it, and via the force applied to the target ball, the target ball moves. But this mode of thinking, which has been very productive in the history of science, is too impoverished when complex systems – the brain for one – are considered.

To illustrate why, consider two brain "systems," such as emotion and cognition. One possibility is that these systems are *decomposable*. Emotion processes (and brain circuits) operate separately from cognitive processes (and brain circuits). The separation may be partial; for example, anatomical connections may link the two. But the overall system with emotion and cognition is decomposable in that each subsystem operates according to its own intrinsic principles, independently of the other [2]. A second scenario can be called *nondecomposable*, because the interrelatedness in the brain of the subsystems (via extensive anatomical connectivity) is such that they are no longer isolable – interfering with one, will influence the other, and vice versa. Of course, in between these two extremes lies a continuum of possible organizations [3].

The contention that we make is that brain "systems" are *not* isolable from one another. This is *not* to say that the associated mental processes are so interrelated as to become one and the same thing. But when systems are not isolable, understanding the interrelatedness between "subsystems" means that we should consider interactions between systems and integration of signals as the central elements to be unraveled [3].

This is where standard frameworks of causation do not provide useful intuition. Let's return to the billiard-ball model discussed above. Its simplicity lies in the existence of two spatially separate billiard balls that make simple contact with each other. We can think here of typical diagrams seen in neuroscience papers that place mental processes in separate boxes (like billiard balls) that can affect each other in direct, simple ways (like a ball hitting another), as diagrammed by arrows connecting the boxes. But this analogy will not be helpful in nondecomposable systems – like the brain. Whereas thinking of causation in complex systems is much more challenging, consider the modification illustrated in Fig. 1B. Here, the two balls are connected by a spring, and the goal of explanation is not to explain where ball 2 ends up. Instead, when the initial force is applied to ball 1, the goal is to understand the evolution of the ball_1–ball_2 *system* as the two balls interact with each other. More generally, a series of springs with different coupling properties links the multiple elements in the system, and we are interested in understanding the evolution of a large "multi-particle" system (Fig. 1C).

2. Dynamic brain networks

The upshot is that simple ways of reasoning about causation are inadequate when unraveling the workings of a complex system such as the brain. Therefore, we suggest that, instead of focusing on causation as the inherent goal of explanations in neuroscience, a fruitful research avenue is to develop formal tools that describe the *multivariate covariance structure of brain data*. In other words, we are interested in describing the joint state of a set of brain regions, and how this joint state evolves through time. Consider the set of activation strengths for a set of brain