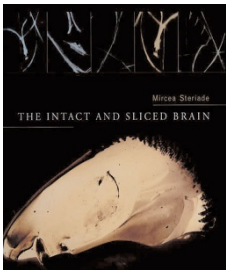
To slice or not to slice?



The Intact and Sliced Brain

by Mircea Steriade
MIT press, Cambridge, Massachusetts, 2001. $55.00
hardcover, pp 382
ISBN 0-262-19456-2

Reviewed by David A. McCormick

It is the dream of neuroscience to integrate the incredibly diverse range of information available about the brain into a coherent understanding. This approach requires crossing discipline boundaries to tie together seemingly disparate results into a unique and powerful story of brain function. In the field of thalamocortical physiology, sleep, arousal and epilepsy, we have witnessed this type of integration over the last 20 years or so—from genes to networks to behavior. Mircea Steriade has been actively investigating these topics for several decades, and in *The Intact and Sliced Brain*, he reviews the work of his laboratory in a very personal way.

With the great success and agreement of information within the field of thalamocortical physiology from laboratories working at multiple levels (not only *in vivo* and *in vitro*, but also at the genetic level), one might imagine that this book would be a crowning moment of glorious integration—a tale of inspiration that would urge and encourage new (and old) investigators to follow in the footsteps of those before them. However, when reading the pretext of the book on the inside cover, one finds rather that the author intends to challenge the notion that "global brain functions, normal or pathological, [can be inferred] from the properties of single neurons or simple networks." He states that "Studies on extremely simplified preparations ... led to a climate in which isolated neuronal networks and even single neurons are sometimes considered responsible for complex physiological processes that arise naturally from interconnections between many brain structures." Raised eyebrows, and thoughts along the lines of 'this should be interesting' abound among the readers of these statements. It goes without saying that the brain is a complex organ that operates through the interaction of many cells. But is it really the case that investigations on 'simplified networks' have led to an inaccurate and oversimplified view of the normal and abnormal operation of the brain?

The book thus has two purposes: to give the author a forum to review and comment on the work of his laboratory (which uses *in vivo* neurophysiological techniques), and to demonstrate how the *in vitro* slice technique has led to dangerously oversimplified thinking.

In the first chapter, the author leads us on a fascinating (although at times difficult to follow) historical journey, highlighting the development of a view of the brain as a complex machine. In the second chapter, the author briefly reviews the "Evolution of methods in brain studies." This, as the name suggests, is a laundry list of many, but not all, techniques that monitor activity in the brain. Presumably the author included this chapter in preparation for the following one entitled "Similar and contrasting results from studies in the intact and sliced brain"— the section of the book that aims to answer the query, 'To slice or not to slice?' First the author describes the similarities of results obtained from brain slices and *in vivo* physiology experiments, as he sees them. Curiously, this occupies only 18 of the chapter's 86 pages. The author reduces the similarities to a few electrophysiological properties and the presence of spindle waves *in vivo* and *in vitro*. Is this really all the similarities there are? I was surprised by the brevity of this section, for the wealth of *in vitro* and *in vivo* findings in the thalamus and cortex that confirm and complement each other could easily fill the entire book!

For the next 68 pages, the author outlines differences (and some similarities) in results obtained with *in vivo* and *in vitro* techniques in the thalamocortical system. Here, the implicit assumption is that all data obtained in anesthetized or immobilized cats *in vivo* is 'correct,' and data obtained *in vitro* that is at all at variance with the *in vivo* data is somehow 'incorrect'. As a user and advocate of both *in vitro* and *in vivo* techniques, and one who believes that they each have advantages and limitations, I read this section with great interest. Unfortunately, I found the author's arguments to be largely unconvincing. Although some of the differences he points out (for example, the rapid propagation of spindle waves *in vivo* versus the slow propagation of these oscillations *in vitro*) are surely due to the reduced connectivity of the slice, others are not so clear. (For example, the lack of spindle waves in the isolated thalamic reticular nucleus *in vitro* is blamed on a lack of connectivity, but it is equally or even more likely that the results obtained *in vivo* have been misleading owing to complex interactions). Furthermore, relatively little credit is given to the exceptional body of information that has been obtained using *in vitro* techniques that has allowed for the interpretation and inspiration for experiments done *in vivo*. As a user of *in vivo* techniques, I would love to have a well-thought-out portrayal of why reluctant students in my lab should perform such experiments. Unfortunately, in an attempt to illustrate the "misleading simplicity of the *in vitro* slice," the author himself is guilty of oversimplifying the issues in his favor.

In the next chapter, "Building blocks of synaptic networks underlying normal and paroxysmal states," the author reviews his lab's extensive studies on sleep activity and seizure generation *in vivo*. It is well known that spike-wave activities (which underlie diverse epileptic seizures such as those in absence seizures and Lennox-Gastaut syndrome) are generated either within the cortex or as an interaction between the thalamus and cortex. Here, the author outlines his lab's data on the spike-wave seizures of cortical origin, and illustrates how these are different from thalamocortical seizures. Many readers will note the curious lack of reference to the vast body of information on the cellular basis of cortical epilepsy that comes from prior *in vitro* studies. The final chapter is a primer on the problems of trying to give mechanistic detail to the statement 'consciousness arises from the brain.'

So, has the author succeeded in the two tasks of the book? Yes and no. This book offers a personal viewpoint covering the extensive and important work of the author and his colleagues, and should be read by anyone interested in this topic. The book fails, however, to support the author's claim that work on slices has yielded an oversimplified view of the brain. Aren't things always simpler when you begin to understand them, whatever techniques you use?

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