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Introduction

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Introduction to the theme issue 'Cerebral cartography: a vision of its future'

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I was very pleased to have been invited to guest-edit this special issue of *Philosophical Transactions of the Royal Society B*, as part of the celebration of the 350th anniversary of the institution of the first peer-reviewed journal in the world.

When Editor-in-Chief of *Philosophical Transactions B*, I prepared a special issue on *Cerebral Cartography*, published in 2005. It was to commemorate the centenary of the publication of three influential works on the brain, Alfred Campbell's *Histological Studies of Cerebral Function* [1], *Paul Flechsig's Gehirnphysiologie und Willenstheorien* [2] and, above all, Korbinian Brodmann's work on cortical cytoarchitectonics [3]. Cytoarchitectonics was, and continues to be, a controversial guide to the organization of the cerebral cortex. But, in spite of its many inadequacies and in spite of the many criticisms levelled at it, including criticisms of Brodmann's work, that paper and a subsequent book by Brodmann have had a lasting influence [4]. In the state of our imperfect knowledge, it has proved to be a more or less reliable anatomical guide, if not a functional one, for locating brain activity. In spite of its inadequacies, it is still used today by many, especially in the field of brain imaging. However imperfect a guide to the organization of the cerebral cortex cytoarchitectonics may be, its sheer longevity has proved its usefulness. Equally, Flechsig's myelogenetic studies, though not as widely quoted today as Brodmann's work, has had a recent renaissance with the increasing emphasis on developmental studies in health and in disease.

That issue of *Philosophical Transactions B* was, therefore, a look into the present through the past.

This issue is different in the sense that it looks largely at the future through the present. For that reason alone, it was a more difficult enterprise. How can anyone foresee what future conceptual and technical developments there will be and how they will change the nature of the answers that we seek, if not the questions themselves? How can anyone foretell whether an approach that is regarded as insignificant today, and therefore not covered in these pages, or not adequately covered, will not assume centre stage in the future. After all, as early as 1877, Pierre Paul Broca had proposed using thermometers attached to the scalp to detect differences in temperature to infer changes in cerebral blood flow (which we today accept as an index of brain activity) during mental activity [5,6]. The idea seemed outrageous then; it was widely suspected and denounced in an editorial published in *The Lancet* in 1880 as "a supposition which is quite inconceivable" [7]. The essential validity of this approach was taken up by Roy & Sherrington in 1890 [8] but, up to about the 1980s, nowhere was the issue seriously discussed again until the advent of brain imaging techniques.

I therefore invited all contributors, not to write scholarly articles but to speculate freely and in an informed way about the future of brain studies, as seen through the prism of their own work and techniques, restricting themselves to the next 25 years, beyond which all speculation becomes idle. The result is this collection of papers.

Rich societies are currently spending vast fortunes on brain studies, for which they expect some kind of return. It was therefore important to cover the aspirations of the three major brain initiatives—in the USA, Europe and Japan—by those who are leading them. I am aware that such initiatives have been controversial and have had their supporters and their detractors. All the more reason, therefore, to lay out, for neurobiologists worldwide, the details of these programmes from those who are leading them (Jorgenson *et al.* [9], Frackowiak & Markram [10] and Okano *et al.* [11]). Whether one approves of such large initiatives or not, they are destined to play leading roles in brain studies worldwide and these comprehensive articles will ensure that future debates about these initiatives will be well informed. It is unlikely that any of them will continue rigidly in their present form; new advances will almost certainly result in one aspect or another of these programmes changing course, or so one hopes. But what is presented here is the backbone of what those leading the initiatives think the neurobiological community can develop and achieve in the future in the light of present knowledge.

Within this overall initiative, there are specific areas that are likely to be of increasing importance in the future. Connectomics, dedicated to mapping at very high resolution the connections that underlie nervous activity, is covered here by one of the key players in it (Olaf Sporns [12]). Connectomics links, in a sense, the past with the present and the future; its emphasis is not simply charting in very intimate detail the connections in the brain but also in how these connections change with time. What the German anatomist Bernhard von Gudden wrote in 1886, 'Anatomy first and then physiology, but if physiology first then not without anatomy' remains true today, although the methods of addressing the question have changed beyond recognition.

There are, of course, new departures of looking at the brain. The advent of brain imaging techniques has led to an unprecedented explosion in studies of brain activity that underlies sensation, action and, perhaps above all, cognitive states in health and disease. Yet, in an important sense, these activities are departures from the on-going intrinsic activity of the brain which, itself, may not be the same at all times. It is, above all, highly organized and, as one of the founders of brain imaging techniques (Raichle) explains here [13], understanding the rules that govern that organization will be an important element in future brain studies.

Comparing the past and the future viewed through the present, it is significant to note that many of the core issues that exercised the attention of neurobiologists in the past, and continue to do so today, will also extend into the future. But the approach will be significantly different. It is, for example, highly interesting to note, in all the articles here, the important emphasis being put on studying the timing of activity in the brain and its role in one of the most elusive problems in brain studies—of the past, the present and future—namely, how activity in the different, specialized parts of the brain are integrated. The increasing sophistication of imaging techniques, and the rapid improvements in magneto-encephalography, means that brain activity can be studied in the microsecond and millisecond range and related to the location of brain areas, thus giving in unprecedented detail the dynamics of interactions between them. One of the pioneers of magneto-encephalography and her colleague (Hari and Parkkonen) address this here [14] as does (Zeki) [15] in his discussion of the asynchronous brain. The time factor is also critical in the papers by another pioneer of imaging studies, Karl Friston and his co-workers [16], which looks at brain activity computationally, emphasizing in particular attention and the ubiquitously important predictive coding, as well as in the paper by Gollo *et al.* [17], which looks at the synchronization of activity that is critical in mood and introspection. Finally, the overall and seemingly intractable problem of consciousness, never far in any profound thinking about the brain, is covered here by two central figures (Tononi and Koch) in the study of consciousness [18] in the context of Integrated Information Theory.

Intriguingly, what the papers collectively reveal is the continuity from the past to the future of the fundamental questions that we ask about the brain. The fact that, over 150 years since neurology and neurobiology began as a distinct discipline, the grand, overall, questions have remained much the same illustrates what an enormous challenge it is to study the brain. But the papers also reveal how these questions, and the methods used to address them, have been refined to unprecedented levels, giving us hope that the next 25 years will see as well an unprecedented sophistication in the answers we obtain.

Of course, there are important areas that we have not covered. This is due partly to limitations of space and partly to unforeseen circumstances which led some to withdraw their contributions. But, together, the articles here provide an inspiring and intriguing look into the future of brain studies from the perspective of the present. Not everyone will agree with all that has been written, which in itself is a healthy sign of the ongoing debate within our field. But this glimpse into the future of brain studies will, I hope, inject important insights into that debate.

References

1. Campbell AW. 1905 *Histological studies on the localisation of cerebral function*. Cambridge, UK: Cambridge University Press.
2. Flechsig P. 1905 *Gehirnphysiologie und Willenstheorien*, translated by G. von Bonin (1960). In Some Papers on the Cerebral Cortex. Springfield, IL: CC Thomas.
3. Brodmann K. 1905 Beitrage zur histologischen lokalisation der Grosshirnrinde. III. Die rindenfelder der niederen affen. *J. fur Psychol. un Neurol.* **4**, 177–226.
4. Zilles K, Amunts K. 2010 Centenary of Brodmann's map–conception and fate. *Nat. Rev. Neurosci.* **11**, 139–145. (doi:10.1038/nrn2776)
5. Broca P. 1877 Sur la thermometrie cerebrale. *Rev. Sci.* **13**, 257.
6. Broca P. 1879 Sur les temperatures morbides locales. *Bull. Acad. Med.* **25**, viii.
7. Editorial. (1880) *The Lancet*, pp. 303–304.
8. Roy CS, Sherrington CS. 1890 On the regulation of the blood supply to the brain. *J. Physiol.* **11**, 85–108. (doi:10.1113/jphysiol.1890.sp000321)
9. Jorgenson LA *et al.* 2015 The BRAIN Initiative: developing technology to catalyse neuroscience discovery. *Phil. Trans. R. Soc. B* **370**, 20140164. (doi:10.1098/rstb.2014.0164)
10. Frackowiak R, Markram H. 2015 The future of human cerebral cartography: a novel approach. *Phil. Trans. R. Soc. B* **370**, 20140171. (doi:10.1098/rstb.2014.0171)
11. Okano H, Miyawaki A, Kasai K. 2015 Brain/MINDS: brain-mapping project in Japan. *Phil. Trans. R. Soc. B* **370**, 20140310. (doi:10.1098/rstb.2014.0310)
12. Sporns O. 2015 Cerebral cartography and connectomics. *Phil. Trans. R. Soc. B* **370**, 20140173. (doi:10.1098/rstb.2014.0173)
13. Raichle ME. 2015 The restless brain: how intrinsic activity organizes brain function. *Phil. Trans. R. Soc. B* **370**, 20140172. (doi:10.1098/rstb.2014.0172)

14. Hari R, Parkkonen L. 2015 The brain timewise: how timing shapes and supports brain function. *Phil. Trans. R. Soc. B* **370**, 20140170. (doi:10.1098/rstb.2014.0170)
15. Zeki S. 2015 A massively asynchronous, parallel brain. *Phil. Trans. R. Soc. B* **370**, 20140174. (doi:10.1098/rstb.2014.0174)
16. Kanai R, Komura Y, Shipp S, Friston K. 2015 Cerebral hierarchies: predictive processing, precision and the pulvinar. *Phil. Trans. R. Soc. B* **370**, 20140169. (doi:10.1098/rstb.2014.0169)
17. Gollo LL, Zalesky A, Hutchison RM, van den Heuvel M, Breakspear M. 2015 Dwelling quietly in the rich club: brain network determinants of slow cortical fluctuations. *Phil. Trans. R. Soc. B* **370**, 20140165. (doi:10.1098/rstb.2014.0165)
18. Tononi G, Koch C. 2015 Consciousness: here, there and everywhere? *Phil. Trans. R. Soc. B* **370**, 20140167. (doi:10.1098/rstb.2014.0167)