nature

BOOKS & ARTS

Where are the switches on this thing?

Asking the big questions in neuroscience.

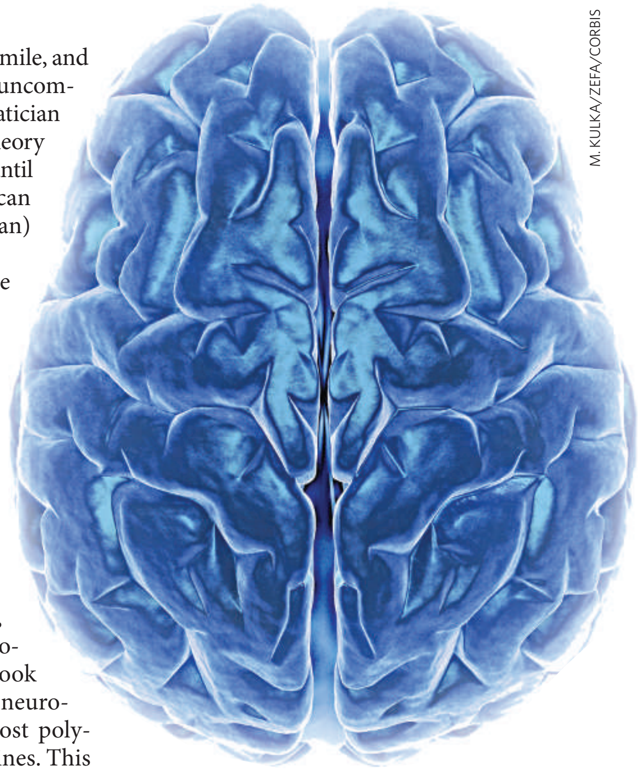
23 Problems in Systems Neuroscience
edited by J. Leo van Hemmen & Terrence J. Sejnowski
Oxford University Press: 2006. 530 pp. £49, $79.95

Kevan A. C. Martin

David Hilbert, in his opening address at the International Congress of Mathematicians in Paris in 1900, presented his colleagues with 23 problems whose investigation he thought would provide the major advances in mathematics in the twentieth century. Although about half of the problems remain unsolved, history shows that mathematicians rose splendidly to the challenge.

Neuroscience has a rather briefer history than mathematics, but Leo van Hemmen and Terry Sejnowski felt that it was nonetheless mature enough for them to organize a meeting on 'Problems in Neuroscience' a century after Hilbert's address. This printed version of their meeting, *23 Problems in Systems Neuroscience*, has taken six years to arrive, but it is not too late and certainly not too little. In the place of one Hilbert are 40 problem-posers who have collectively contributed the 23 chapters, grouped into sections that sum up 5 current concerns: How have brains evolved? How is cerebral cortex organized? How do neurons interact? What can brains compute? How are cognitive systems organized? With such an attractive list of topics, this book is sure to find a wide audience at every level of interest, from lay readers to students and academics.

For most of the contributors, the operations of the cerebral cortex pose the principal problems to be solved. It is refreshing, then, to feel the frank blast of Gilles Laurent's irritation on page 1 when he asks: "Why this obsession with cortex?" From his locust-brain perspective, it seems to Laurent that "most scientists act as if King Cortex appeared one bright morning out of nowhere, leaving in the mud a zoo of robotic critters, prisoners of their flawed designs and obviously incapable of perception, feeling, pain, sleep, or emotions, to name but a few of their deficiencies. How nineteenth century!" This opening salvo is exactly the energetic and uncompromising tone required to sweep the reader onwards through the sparkling debates that fuel this book and to help define the most important questions in neuroscience.



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Neuroscience would be much easier if we had a detailed circuit diagram of the brain.

The writing frequently made me smile, and often it comes close to realizing the uncommon view of an old French mathematician retold by Hilbert: "A mathematical theory should not be considered complete until you have made it so clear that you can explain it to the first man (or woman) whom you meet on the street."

Like Hilbert, the authors assume that their problems can and will be solved. However, unlike mathematical problems, those of systems neuroscience will not be solved by pure reason, but will require the integration of experiment and theory, and perhaps even a new science that incorporates the subjective. In this context it would be interesting to know how many of the authors originally trained as neuroscientists or even biologists. If, as I suspect, card-carrying neurobiologists are in the minority, then this book exposes the deep, dark secret that neuroscience has become one of the most polymathic of modern scientific disciplines. This is as it should be, because neuroscience faces the most intractable questions in modern science and we need all hands on deck if we are to find a safe passage through the problems raised here.

However, most contemporary experimental neuroscience is done at the molecular and cellular level, where most of the hard problems discussed in the book need not be faced. Although the book does not consider molecular and cellular techniques, it seems increasingly clear that they will be central to the approaches required to solve many of the systems-level problems.

Similarly, although Cathy Carr and her colleagues do discuss some structurally significant adaptations of neurons in the auditory system, questions of the relevance of structure to systems neuroscience are hardly addressed here at all. Jim Watson and Francis Crick emphatically demonstrated that some otherwise intractable problems in biology can be cracked by solving structures. But structural neuroscience has limited sex-appeal for the editors of leading journals. This, together with the granting agencies' blind-spot for structure, has resulted in a lack of knowledge about the fine structure of the nervous system of every model animal, *Caenorhabditis elegans* excepted, and this remains a major impediment to progress. Sejnowski points to a related problem when he asks: "What are the projective fields of cortical neurons?" The receptive fields of neurons, which result from the convergent input of many neurons, have been well studied for decades. The projective fields — the influence of the output of a neuron on its many targets — are largely unknown but would be much better understood if we had a detailed circuit diagram of the cortex and its related structures.

Several of the authors have produced entertaining and provocative critiques of the state of current techniques and thinking. A sharp intake of breath will no doubt be heard from many readers of the piece by Bruno Olshausen and David Field. They make the seemingly outrageous claim that we are ignorant of 85% of the functions of the primary visual cortex, area V1, the cortical area that most textbooks present as being essentially solved. But this provocative view does not go unsupported by experimentalists for, as Amiram Grinvald and

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colleagues show, their techniques for recording large numbers of neurons in the primary visual cortex with fine spatial and temporal resolution inevitably drive new concepts of cortical function. Fortunately, discussions of the visual cortex do not dominate the book. Perhaps this is because the key themes that run through it are questions of what the neural code is, and how time is represented in the brain, and both questions apply equally well to the brains of creatures great and small. These two questions are also considered in virtuoso solos by Carl van Vreeswijk and Andreas Herz.

A prize for the wittiest title goes to Larry Abbott who asks: "Where are the switches on this thing?" He points out that the problem of self-regulated switching is solved for digital computers, which are the most complex machines we have built, but when it comes to the flow of information through a brain we know only that there are ways of biasing the flow by mechanisms such as neuromodulation or inhibition. Thus, with a motivation certain to warm the heart of every invertebrate physiologist, he recommends that we study any reasonable candidate mechanisms for switching in a brain.

Hilbert stated that "the importance of a scientific work can be measured by the number of previous publications it makes it superfluous to read". Answers to some of the questions raised here will no doubt make the literature reviews of most PhD theses shorter, but what will we really understand even if all 23 problems in systems neuroscience are solved? This is the most difficult question of all, and its answer has a significance that goes far beyond even the ambitious goal of understanding the workings of a brain. Hilbert's vision for mathematics was carved on his tombstone — "Wir müssen wissen, wir werden wissen" ("We must know, we shall know") — but for those who study brains, even if we must, will we? ■

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Seeking meaning in the void

The View from the Center of the Universe: Discovering Our Extraordinary Place in the Cosmos
by Joel R. Primack & Nancy Ellen Abrams
Riverhead Books: 2006. 400 pp. $25.95

Simon Singh

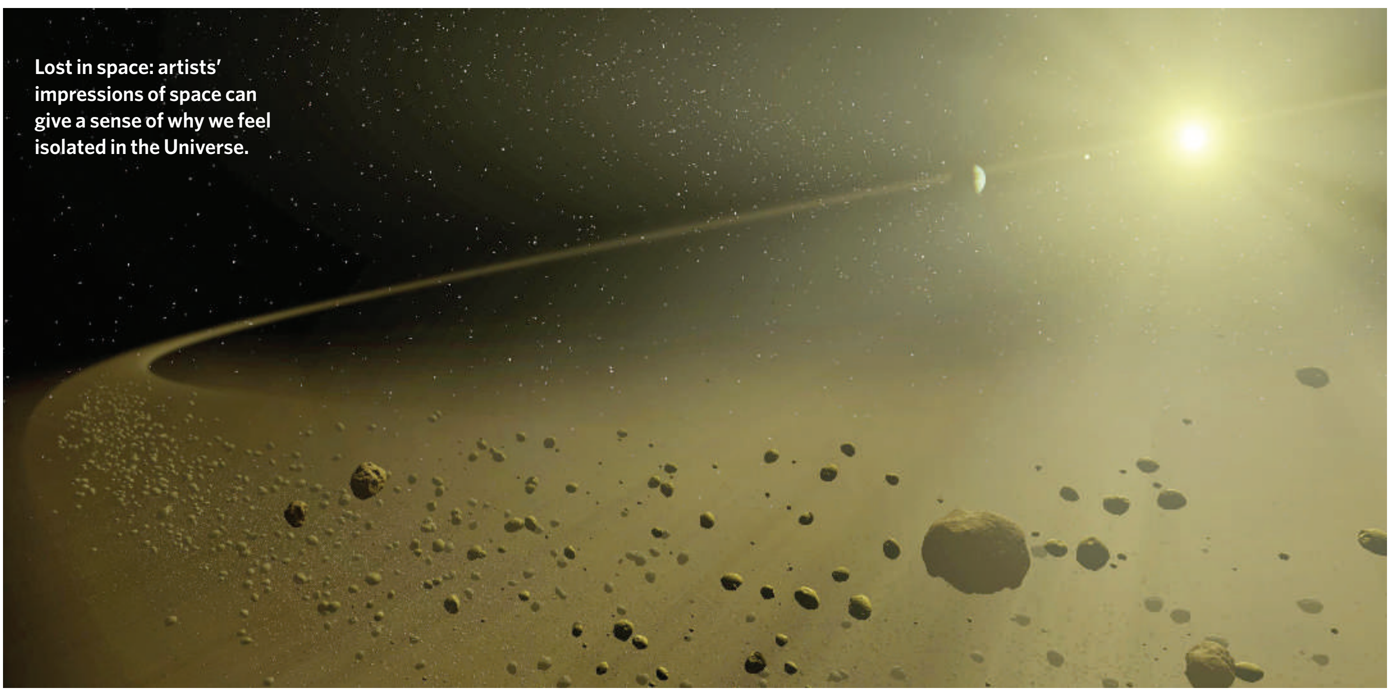
The married couple of philosopher Nancy Ellen Abrams and cosmologist Joel R. Primack are uniquely placed to discuss how our understanding of the Universe affects how we perceive our role in it. The ancient creation myths provide comfort and meaning, but they are fantasies. In contrast, modern cosmology offers a glimpse of reality but leaves many people cold. In *View from the Center of the Universe*, Abrams and Primack challenge themselves to try and get the best of both world views.

In the distant past, we convinced ourselves that we had a special place in the Universe. Geographically we were at the centre of space, with everything revolving around us, and biologically we thought that humans were an exceptional creation. But as each century passed, we realized that we are less and less special. Today, we see ourselves as insignificant in the context of the whole Universe. The copernican revolution relegated and redefined Earth as just another planet, and made the Sun the hub of the Universe. Then astronomers showed that the Sun is not even at the centre of the Milky Way, and eventually it became clear that there are billions of other galaxies, which made Earth seem trivial.

The problem with becoming increasingly insignificant was appreciated as far back as the seventeenth century by the French philosopher Blaise Pascal: "I feel engulfed in the infinite immensity of spaces whereof I know nothing and which know nothing of me. I am terrified…The eternal silence of these infinite spaces alarms me."

The existence of dark matter only further relegated humanity, as Primack pointed out in 1984: "Yet another blow to anthropocentricity: not only is man not the center of the universe physically (as Copernicus showed) or biologically (as Darwin showed), it now appears that we and all that we see are not even made of the predominant variety of matter in the universe!"

But Abrams and Primack argue that humans still hold a central and special position in the Universe, perhaps not geographically but in many other ways. For example, we are special because we are made of the rarest material in the Universe, namely large atoms. Also, we live at a central time, because most nearby galaxies are past their violent youths but are not yet senescent. And we live at the midpoint of our planet's life, which is a few billion years old, and which has a few billion more years before it will be roasted by our Sun swelling into a red giant. And humans have a reasonably central size, roughly halfway between the smallest length scales (10^{-33} cm) and the distance to the cosmic horizon (10^{28} cm).



Lost in space: artists' impressions of space can give a sense of why we feel isolated in the Universe.

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