

BOOK REVIEWS

living system. It brings to the forefront, as many call it, the 'big picture' which is often forgotten in the detailed nitty-gritty of everyday experimental systems. Finally, this book also shows indirectly that modern research is not necessarily married to capital-intensive, off the shelf sophisticated instrumentation. Rather, it is the beauty of experimental design within the constraints of what is measurable, that is more important in scientific exploration especially in modern biology.

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Annual Review of Neuroscience, 2008.

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The Annual Review of Neuroscience has over the years come to be a much-anticipated yearly enterprise because it has traditionally provided the neuroscience community with a combination of timely reviews with an emphasis on those areas of research with a sufficiently built up knowledge base and hence controversies that require some degree of untangling and simplification, necessary for the field to move forward. In this respect, these books not only serve as a repository of critical and authoritative reviews, but provide readers with a 'scientific weathercock' so to speak. Consequently, these books become necessary reading for researchers wanting to be well informed about the latest developments at least in their respective fields. For the student of neuroscience, the exhaustive list of references can serve as a useful starting point to begin their research. The basis of excellence for the *Annual Reviews* is simple; build a collection of reviews by getting the most distinguished and active researchers in their fields to participate. This job is facilitated by the presence of a distinguished editorial board. This year's editorial board led by Prof. Steve Hyman of Harvard and supported by Profs. Thomas Jessel of Columbia University, Carla

Shatz of Stanford University and Charles Stevens of the Salk Institute continues the tradition of excellence set by their predecessors. In putting this review together I have taken the liberty to reorganize the presentation of chapters, emphasizing functional links where possible. I hope this approach might be of greater value to a reader of this meta-review interested in getting a gist of the breadth of issues being examined in the 2008 edition, rather than just evaluating the reviews in their order of presentation in the volume, or segregating the reviews into areas such as molecular, cellular, systems, behavioral/cognitive and computational neuroscience as is typically done in many neuroscience journals these days.

Neural development, plasticity and the acquisition of higher cognitive functions.

It is now well established that neural circuits are specified by the spatiotemporal gradients of certain molecules. One such class of molecules referred to as Wnt (pronounced as *wint*) are known to be critical regulators of neural development. The review by Salinas *et al.* (Wnt signalling in neural circuit assembly; pp. 339–358) discusses the role of distinct signalling cascades of Wnt and reports how these may support the diverse roles hypothesized for Wnt in influencing distinct aspects of neural circuit development such as migration, polarity and axon path finding. A particular interesting case of neural circuit development is provided by the well known decussation of fibres constituting the optic tract. The article by Petros *et al.* (Retinal axon growth at the optic chiasm: To cross or not to cross; pp. 295–316) reviews the molecular mechanisms underlying the axonal pathfinding in this circuit. In addition to molecular cues, a number of studies since the work of Hubel and Wiesel have shown the critical role that electrical activity plays in the development of neural circuits as well. Understanding the roles that signalling molecules and activity play in the development of topographic maps and receptive field properties in the visual system is the focus of the article by Huberman *et al.* (Mechanisms underlying development of visual maps and receptive fields; pp. 295–316). The article by Flavell and colleagues (Signaling mechanisms linking neuronal activity to gene expression and plasticity of the nervous system; pp. 563–590) attempts to address how patterns of electrical activity are translated

into patterns of gene expression that help build and modify neural circuits. Work in this important area may finally provide answers to our understanding of how the brain develops under the influence of both nature and nurture. While not entirely obvious, it is now clear that electrical activity continues to play an important role in dynamically reshaping neural circuits right through adulthood. The article by Caporale and Dan (Spike timing dependent plasticity: A Hebbian learning rule; pp. 25–46) describes mechanisms by which this might occur. A critical site where plasticity manifests itself is the dendritic spine. In the hippocampus these changes in spine morphology form the structural basis of our current understanding of learning and memory and provide the central theme of the review by Bourne and Harris (Balancing structure and function at hippocampal dendritic spines; pp. 25–46). The article by Briggman and Kristan (Multifunctional pattern-generating circuits; pp. 271–294), drawing examples invertebrate physiology, describe the architecture of circuits that are endowed with multifunctional dynamics endowing them with the ability to take part in distinct behaviours. These sort of circuits, the authors argue, may provide the basis for understanding how circuits are dynamically reconfigured by subtle changes in the external and internal states of an organism. Ultimately, the need for such flexible circuits arises because our brain needs to support complex cognitive functions such as language. The article by Kuhl and Rivera-Gaxiola (Neural substrates of language acquisition; pp. 511–534) reviews the much expanding literature on the development of language in infants drawing on non-invasive techniques such as evoked response potentials and functional magnetic resonance imaging. While flexibility may be a hallmark of learning, one paradoxical consequence of over-learning may be the generation of habits that are stereotypical behaviours that may override higher-order deliberative behaviours. The article by Graybiel (Habits, rituals and the evaluative brain; pp. 359–388) discusses the neural representations underlying such behaviours and suggests that the basal ganglia may play a critical role in their expression and modulation.

Information processing in neural circuits. As is usually the case, a number of articles in the 2008 edition have been devoted to reviews that are pegged

at a systems level understanding of brain function using primarily electrophysiological techniques in awake behaving animals. A particularly provocative article is the review by Bell *et al.* (Cerebellum-like structures and their implications for cerebellar function; pp. 1–24) in which the authors use comparative neurobiology to suggest that the information processing performed by the cerebellum and cerebellar-like structures seen in lower vertebrates and invertebrates may be comparable, allowing comparative neurobiology to advance our understanding of the intricate computations performed by these circuits. The article by Tsao and Livingstone (Mechanisms of face perception; pp. 411–438) is interestingly the sole review dealing with purely sensory representations in the brain. The focus of this article is face processing and it advocates the hypothesis that face processing is a two-stage process; an initial one that determines whether the object of interest is a face; this process is thought to act like a gate enabling a second process which elaborates on the primitives producing a holistic representation of the face. The article by Britten (Mechanisms of self-motion perception; pp. 389–410) reviews progress made towards understanding how the brain processes motion signals in the retina to distinguish motion caused by the organism as distinct from those caused by external motion. This article points to relatively recent work that describes the combined role of vestibular and tactile information, in addition to optic flow signals, in our perception of self-motion and highlights the deficiencies in current models. The article by Angelaki and Cullen (Vestibular system: The many facets of a multimodal sense; pp. 125–150) highlights the role of the vestibular system in particular, emphasizing its multimodal nature that appears to be critical in our understanding of our sense of spatial orientation. At the other end of the spectrum, the article by Lemon (Descending pathways in motor control; pp. 195–218) re-evaluates the comparative functions of different descending motor pathways and highlights possible species differences. The article by Sommer and Wurtz (Brain circuits for the internal monitoring of movements; pp. 317–338) reviews a story that began with a prediction by Helmholtz, and recently validated by the authors, of a specialized oculomotor circuit in which the usual information flow is reversed; i.e. where information from

the motor system is fed back into sensory representations. Such a reverse flow of information, the authors argue, can be used to generate sensory consequences of upcoming movements, implementing a so-called forward model predicted by computational motor theorists. In addition to sensory and motor circuits, neurophysiologists have also described circuits that are of more cognitive nature. The article by Moser *et al.* (Place cells, grid cells, and the brain's spatial representation system; pp. 69–90) describes how cells in the hippocampus, called place cells, and cells in the entorhinal cortex, called grid cells (incidentally discovered by the authors) together might generate our (i.e. rodents) sense of space. The second such article that discusses the nature of a cognitive representation is by Sakai (Task set and prefrontal cortex; pp. 219–246). He describes experiments from human functional imaging and monkey neurophysiology that have attempted to show how selectivity of prefrontal cortex conforms to what cognitive theorists define as a task set that implements that rules that govern our goal directed behaviours.

Neurobiology of Brain Disorders. Given the importance of understanding brain dysfunction, which is a large contributor to the disease burden in modern society, it is not surprising to find a number of articles that are devoted to our current understanding of brain disorders. The major conceptual challenge in this area is to distinguish cause and consequence of the brain damage; these are invariably coupled in complex systems, such as the brain, and it is therefore not surprising that radically different points of view persist. For example, while DiMauro and Schon (Mitochondrial disorders in the nervous system) highlight the role of the mitochondria and oxidative stress, DeVos *et al.* highlight the role of axonal transport deficits in the accumulation of abnormal proteins in causing neurodegenerative diseases (Role of axonal transport in neurodegenerative disorders; pp. 151–174). A radically different hypothesis concerning the role of abnormal prion protein accumulation in certain kinds of neurodegenerative disorders highlights the likely possibility that different diseases are likely to have very different causative agents (see Aguzzi *et al.*, The prions elusive reason for being; pp. 439–478). In addition to distinguishing cause and effect, the complexity of brain diseases is such that in some

cases even their nature is debatable. This point is highlighted in the article by Trapp and Klaus-Armin Nave (Multiple sclerosis: An immune or neurodegenerative disorder; pp. 247–270) who discuss whether the demyelination, typically seen in patients with multiple sclerosis, is primary or secondary to the disease process. Based on the evidence presented, these authors instead argue that multiple sclerosis is better understood as a neurodegenerative disease. These controversies notwithstanding, some progress has been made towards treatment of some neurodegenerative disorders. A potentially promising route could be immunotherapy. Brody and Holtzman (Active and passive immunotherapy for neurodegenerative disorders; pp. 175–194) discuss some of the challenges in this field that need to be overcome for effective treatment of disorders such as Alzheimer's disease using immunotherapy.

Taken together, all these controversies highlight one important fact – that basic research is imperative if we are to understand and cure diseases. The article (Axon-glial signaling and the glial support of axon function; pp. 535–562) by the same authors of the article on multiple sclerosis is in keeping with such spirit.

In conclusion, I believe that the breadth and depth of articles presented in the 2008 *Annual Review of Neuroscience* necessitates its inclusion in the library of every active neuroscientist. For students wishing to delve into the intricacies of neuroscience research, it will be very informative and useful. In addition, I particularly liked the idea of the index section in this review, which lists the chapter titles at the end of the book, allowing the interested reader to quickly identify his/her area of interest and be able to access the earlier reviews in the area.

However, aside from the positives I did notice the absence of articles in the area of membrane channels and articles using the techniques of slice recordings, that are useful to understand links between cellular neurophysiology and a systems level of understanding. To make the annual reviews more inclusive I hope that these areas find adequate representations in future editions.

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