Memory: From Mind to Molecules. Edited by Larry R. Squire and Eric R. Kandel. Scientific American Library, New York, 1999. Pp xi+235, ISBN 0-7167-6037-1 (paperback).

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Article Outline

The authors of this book hardly need any introduction. The back-cover lists some of the many prestigious awards they have won. To this list can now be added the year 2000 Nobel Prize in medicine to Eric Kandel.

In the preface, Squire and Kandel state that a goal of their book was to create a new synthesis; a molecular biology of cognition. This is a synthesis between the molecular biology of signalling and the cognitive neuroscience of memory. They also state that they did not try to provide an exhaustive coverage of the field, but emphasized research that they themselves had been directly involved in or research that had a direct influence on their thinking. A final statement from the preface that serves to define the book is that they wrote this book for a broad audience, foremost nonscientific readers without specialized backgrounds for the topics of the book.

The book has ten chapters. The first chapter (From Mind to Molecules) serves as an introduction. It includes brief discussions of pioneers in the study of memory, significant discoveries in biology, and genetic studies. I particularly enjoyed the treatment of the landmark work by Brenda Milner with patient H.M. The second chapter (Modifiable Synapses for Nondeclarative Memory) is concerned with the simplest case of nondeclatative memory, habituation. A highly readable treatment of neurons, synapses, and synaptic plasticity is given before studies of habituation in Aplysia are presented in some detail. A beautiful series of studies is reviewed that lead up to the conclusion that habituation relies on a weakening of the strength of pre-existing synaptic connections. Chapter three (Molecules for Short-Term Memory) addresses the issue of the molecular mechanisms whereby synapses are altered in strength. Here, studies of sensitization are considered. This form of nonassociative memory results from an increase in synaptic strength. This is mediated by modulatory interneurons, the most important one using serotonin as its transmitter. A critical factor is the type of receptor to which the transmitter binds, and the authors describe how metabotropic receptors and the second (intracellular) messenger system they activate are crucial for the synaptic changes that underlie sensitization. The chapter also considers associative memory in the form of classical conditioning. Interesting parallels between sensitization and classical conditioning are noted, but the crucial importance of the timing of CS-US pairings for conditioning is emphasized.

Chapter four (Declarative Memory), five (Brain Systems for Declarative Memory), and six (A Synaptic Storage Mechanism for Declarative Memory) are concerned with memory for knowledge that can be declared (also called explicit or conscious memory). In chapter four, cognitive aspects of the major sub-processes of declarative memory (encoding, storage, retrieval) are discussed, as are forgetting and distortion. Chapter five is focused on the medial temporal lobe system. A nice overview of amnesia is presented, followed by the presentation of an animal model of human amnesia. Considerable evidence for a

temporary role of the medial temporal lobe system is reviewed. In chapter six, the authors address possible differences in the basic storage mechanisms that underly nondeclarative and declarative memory. Long-term potentiation (LTP) is introduced as a possible storage mechanism for declarative memories. Some basic work on LTP is covered, before studies on the specific role of LTP for declarative memory are discussed. This includes studies using inhibitors as well as studies with genetically modified mice (knockouts and transgenics). Finally, evidence is reviewed that suggest that LTP is required for the formation of a stable internal representation of space in the hippocampus.

Chapter seven (From Short-Term Memory to Long-Term Memory) deals with how short-term memories are transformed into long-term memories. Evidence is reviewed that suggests that the switch of short-term memory into long-term memory is crucially dependent on protein synthesis. That is, whereas retention of memories over the short term (up to an hour, or even more, cf., p. 85) does not require new protein synthesis, memory over the long term rests on anatomical changes that require new protein synthesis. A major part of the chapter is devoted to a fairly detailed description of studies designed to uncover and explore the genes and proteins required for the conversion of short-term memory into long-term memory and how they are activated. This includes studies of nondeclarative as well as declarative forms of memory. An important conclusion is that there is a surprising degree of similarity in the switch used to convert short-term to long-term memory for nondeclarative and declarative forms of memory.

Chapter eight (Priming, Perceptual Learning, and Emotional Learning) and nine (Memory for Skills, Habits, and Conditioning) focus on the kinds of nondeclarative memory that have been discovered in human beings and how these kinds of memory are organized in the brain. The first part of chapter eight deals with priming, an unconscious form of memory that is intact in amnesic subjects. This indicates that priming does not depend on the medial-temporal lobe system, and data generated by PET show that (visual perceptual) priming is associated with decreased activity in regions in posterior visual cortex. Thereafter, perceptual learning is discussed (e.g. increased discrimination between line drawings as a function of repeated attempts at discriminating). This form of nondeclarative memory, too, appears to be mediated by changes in early visual areas. Finally, emotional learning is discussed. Here the important role of amygdala is highlighted, and it is suggested that interactions between amygdala and hippocampus can explain why emotionally arousing events usually are remembered well. Chapter ten starts out with a discussion of memory for motor skills. Parts of the basal ganglia (neostriatum) are important for this form of memory, as are parts of motor cortex. In addition, early on, before a skill has been well learned, regions in prefrontal and parietal cortices as well as the cerebellum seem to be important. Studies of habit learning also point to an important role for the neostriatum. Patients with Huntingson's or Parkinson's disease show impaired ability to learn habits (measured with the weather-prediction task). A review of studies of category learning indicates that such learning can develop independently of the medial-temporal lobe memory system. Instead, investigations with fMRI indicate that the processing of visual category members is associated with decreased activity in early visual areas — a pattern that resembles that for perceptual priming. Finally, different forms of classical conditioning are discussed. Studies on (nondeclarative) eyeblink conditioning point to an important role of the cerebellum for this form of memory. This is also true for (declarative) trace conditioning, but in addition, trace conditioning seems to rely on hippocampus. The latter may be an example of a situation when two learning circuits need to operate in parallel for learning to take place.

The final chapter, chapter ten (Memory and the Biological Basis of Individuality), includes discussion of how experience can modulate brain organization. The chapter also includes a discussion of age-related memory impairment and the cognitive impairment that accompany Alzheimer's disease, including consideration of the neural bases for such impairments. In the concluding part of the chapter (and the book) it is noted that the

new synthesis — the molecular biology of cognition — has the potential to yield a number of important implications, including the development of effective treatments for age-related memory loss and for Alzheimer's dementia.

This, to me, is a great book. In the preface the authors expressed their belief that the time is ripe for a treatment of memory that covers the full range of the topic. As I hope my review has illustrated, this book actually spans the gap from molecule to mind. Of course, no book is perfect. I felt that their treatment of the prefrontal cortex was a bit sparse. Although the book has a unique coverage of the field, and the authors explicitly stated in their preface that they did not try to provide an exhaustive coverage of the field, I would have appreciated more discussion of the role of the prefrontal cortex in declarative memory. From 1994 and onwards, a number of PET and fMRI studies have been conducted that collectively show: (i) that prefrontal cortex is generally involved in declarative memory; (ii) that different forms/systems of declarative memory (episodic and semantic) are associated with specific prefrontal regions; (iii) that encoding and retrieval of episodes engage distinct prefrontal regions; and (iv) that specific component processes of encoding and retrieval are associated with specific prefrontal activation. Little or none of this work is reflected in the section on episodic and semantic memory in chapter five. Rather, the section may give readers the impression that prefrontal regions are not involved in semantic memory, or that the only role of prefrontal regions in episodic memory relates to memory for source. There is considerable evidence to suggest that such an impression is incorrect. A related topic concerns the role of prefrontal brain regions in working memory. I think the discussion of the neural correlates of working memory in chapter five would have become even more informative if some of the imaging work on domain- and process-specificity had been included.

These are two examples of topics that I would have liked to see treated in more detail, but again, the coverage of the book is impressive indeed. Indeed, to my knowledge, no other book covers as many aspects of the study of memory as the present one. Moreover, it presents the many topics in a highly accessible format, using very informative illustrations. The authors have truly lived up to their ambition to write a book for a broad audience. This is not to say that the general reader will grasp everything. I think even readers with specialized backgrounds will need to put in effort to fully digest specific parts of the book, such as the discussion of the genetical basis for the switch from short-term to long-term memory in chapter seven. Other parts, too, will require some effort from most readers, and I therefore believe that the book indeed qualifies to be used, in whole or in part, in various undergraduate and graduate programs. Finally, I honestly think that active memory researchers can learn a lot from this book. Thus, it is a book for 'everybody' or as Dan Schacter put it on the back-cover: 'Essential reading for anyone who has ever wondered about how we remember or why we forget'.