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Micro-, Meso- and Macro-Dynamics of the Brain **Hippocampal Place Fields Space,Time and Memory in the Hippocampal Formation** Conditioned Fear Modulates Place Field Stability in Hippocampal Place Cells Through Activity of the Basolateral Amygdala The Neural Basis of Navigation **Dark and Magical Places: The Neuroscience of Navigation** Exploring how Spatial Learning Can Affect the Firing of Place Cells and Head Direction Cells **Inhibitory Synaptic Plasticity** The Neural Circuit for Spatial Representation The Hippocampus and Episodic Memory **The Hippocampus as a Cognitive Map** Human Spatial Navigation **The Hippocampus Book The Connected Hippocampus Head Direction Cells and the Neural Mechanisms of Spatial Orientation Hippocampal Microcircuits** *A Computational Model of Grid Cells based on a Recursive Growing Neural Gas* **Neuronal Dynamics Analysis and Modeling of Coordinated Multi-neuronal Activity** Beyond the Cognitive Map Contribution of Multisensory Stimuli to the Representation of Space in the Hippocampus and Medial Entorhinal Cortex **Discovering the Brain Effects of Context and Novelty on Place Cell and Grid Cell Spatial Firing** *Effects of Intraseptal Carbachol on Firing Characteristics of Hippocampal CA1 Place Cells* Development of Spatial Memory in the Entorhinal Cortex Through Neural Mechanisms of Self-organization **Sharpening the Spatial Tuning Curves of Place Cells in a Feed-Forward Network Brain and Space** *The Hippocampus* Adventures Between Lower Bounds and Higher Altitudes The Hippocampus in Clinical Neuroscience *The CA3 Region of the Hippocampus: How is it? What is it for? How does it do it?* **Effects of Cannabinoids and Novelty on Hippocampal Electrophysiology Modelling Environmental and Self-motion Influences on Grid Cell Firing** *Molecular Characterization of Autophagic Responses Part B* **The Dentate Gyrus: A Comprehensive Guide to Structure, Function, and Clinical Implications A Model of Goal-directed Spatial Navigation Based on Rodent Neurophysiological Data** Analysis of Hippocampal Place Cell Dysfunction in Mouse Models of Alzheimer's Disease Through Single Unit Electrophysiology and Calcium Imaging Techniques **Handbook of Neural Activity Measurement Space, Time and Number in the Brain Investigating the Relationship Between Hippocampal Theta Oscillations and Firing Properties of CA1 Time Cells**

This book brings together leading investigators who represent various aspects of brain dynamics with the goal of presenting state-of-the-art current progress and address future developments. The individual chapters cover several fascinating facets of contemporary neuroscience from elementary computation of neurons, mesoscopic network oscillations, internally generated assembly sequences in the service of cognition, large-scale neuronal interactions within and across systems, the impact of sleep on cognition, memory, motor-sensory integration, spatial navigation, large-scale computation and consciousness. Each of these topics require appropriate levels of analyses with sufficiently high temporal and spatial resolution of neuronal activity in both local and global networks, supplemented by models and theories to explain how different levels of brain dynamics interact with each other and how the failure of such interactions results in neurologic and mental disease. While such complex questions cannot be answered exhaustively by a dozen or so chapters, this volume offers a nice synthesis of current thinking and work-in-progress on micro-, meso- and macro- dynamics of the brain. This Festschrift volume is published in honor of Juraj Hromkovi? on the occasion of his 60th birthday. Juraj Hromkovi? is a leading expert in the areas of automata and complexity theory, algorithms for hard problems, and computer science education. The contributions in this volume reflect the breadth and impact of his work. The volume contains 35 full papers related to Juraj Hromkovi?'s research. They deal with various aspects of the complexity of finite automata, the information content of online problems, stability of approximation algorithms, reoptimization algorithms, computer science education, and many other topics within the fields of algorithmics and complexity theory. Moreover, the volume contains a prologue and an epilogue of laudatios from several collaborators, colleagues, and friends. Alzheimer's disease (AD) is a neurodegenerative disease characterized by progressive mnemonic deficits. Previous studies have established that AD causes neural dysfunction in hippocampal place cells in the form of decreased place cell stability and increased place field size in mouse models. Most such experiments, however, have been unable to record from specific layers of the hippocampus while mouse models complete goal-oriented spatial memory tasks. Here, we introduced a spatial memory task to allow electrophysiology recordings from the CA1, CA3, and DG regions of the hippocampus while transgenic AD mouse models completed the task. We also aimed to develop calcium imaging to analyze populations of place cells from the CA1 region and we hoped to compare data retrieved using calcium imaging to data acquired from tetrode wire electrophysiology. We found that CA1 and CA3 place cells showed impairments in firing rate, information score, and stability, while showing increased spatial correlation and place field size while animals completed hippocampal dependent memory tasks, particularly as animals got older. While our calcium imaging experiments were unsuccessful, we set the foundation for future calcium imaging experiments in this research. Our results thus point towards substantial CA1 and CA3 place cell dysfunction while AD mouse models complete hippocampal dependent spatial memory tasks. Furthermore, our experiments set the stage for using calcium imaging as method that can add to previously existing information about place cell dysfunction in AD and paint a more global image of hippocampal dysfunction in AD. Data from neuropsychological and animal research suggest that the hippocampus plays a pivotal role in two relatively different areas: active navigation, as well as episodic learning and memory. Recent studies have attempted to bridge these disparate accounts of hippocampal function by emphasizing the role that hippocampal place cells may play in processing the spatial contextual information that defines situations in which learned behaviors occur. A number of established laboratories are currently offering complementary interpretations of place fields, and this book will present the first common platform for them. Bringing together research from behavioral, genetic, physiological, computational, and neural-systems perspectives will provide a thorough understanding of the extent to which studying place-field properties has informed our understanding of the neural mechanisms of hippocampus-dependent memory. Hippocampal Place Fields: Relevance to Learning and Memory will serve as a valuable reference for everyone interested in hippocampal function. The hippocampus is one of the most intriguing structures of the human brain. Damage to this part causes symptoms ranging from transient disorders accompanied by tiny lesions to severely debilitating cognitive disorders with marked tissue loss. This publication provides a predominantly clinical approach to the complex workings of the hippocampus from different perspectives, ranging from basic principles to specific diseases. The first part of the book summarizes current knowledge regarding the structure and physiology of the hippocampus and establishes the ties to basic neuroscience. The second part deals with the function and assessment of the human hippocampus, including memory function, neuropsychological measures, and conventional and functional imaging studies. The chapters of the third part are devoted to the hippocampus in neurological disorders, e.g. the interaction between stress and memory function, and the pathological conditions of common as well as selected rare neurological diseases affecting the hippocampus. The book is highly recommended to clinical neurologists who wish to gain a broad understanding of this complex and fascinating organ in terms of basic principles, modern imaging findings, and specific diseases. This volume of Progress in Brain Research focuses on the Connected Hippocampus. This well-established international series examines major areas of basic and clinical research within neuroscience, as well as emerging subfields Abstract: Damage to the hippocampus specifically impairs episodic memory, defined as the ability to recall the precise details of unique personal experiences. In this thesis, the basic cognitive and neural processes that are mediated by the hippocampus in supporting episodic memory were further examined. Experiment one used an odor-based recognition memory task to address the role of the hippocampus in aging, which negatively affects hippocampal function and spatial memory. Recognition memory is widely viewed as having two components: episodic recollection, dependent on the hippocampus, and familiarity, dependent on surrounding cortical structures. Receiver Operating Characteristic analyses were used to examine the contributions of recollection and familiarity. Recollection estimates were similar between young and aged rats with intact spatial memory. Importantly, aged rats with poor spatial memory showed a selective loss of recollection. Familiarity levels were not different between groups, but there was a trend towards an increase in familiarity with aging. These results show that unsuccessful aging results also in a loss of episodic recollection, further supporting hypotheses that posit a specific role for the hippocampus in mediating retrieval processes that are characteristic of episodic memory. Experiment two examined firing correlates of hippocampal neurons while rats performed a task that required the disambiguation of two overlapping routes. The majority of recorded cells fired differentially in association with one of the two routes, despite the rats being in the same spatial location. Thus, the hippocampus encodes episodic information that differentiates events that occur within the same place. Experiment three compared place cell firing in the task used in experiment two with a delayed alternation task, where memory demands are greater. Some cells showed stronger trial-specific selectivity during delayed alternation, while other cells increased their firing prior to the delay. Both of these cell classes showed substantially less firing when errors were made during the delayed task. This merges hippocampal place fields with episodic memory function, showing that single hippocampal neurons can predict memory performance. Collectively, the results are consistent with a role for the hippocampus in mediating episodic recollection, and in creating neural representations that could underlie the formation of episodic memories. Underlying principles of the various techniques are explained, enabling neuroscientists to extract meaningful information from their measurements. Although hippocampal place cells have been extensively studied since their discovery in 1971, the cause of hippocampal pyramidal cells acquiring place specific firing remains unknown. Place cells are thought to be neural correlate of a cognitive map such that place cell firings are the internal representation of the external environment. Current models suggest that the internal representation is formed from an integration of contextual and non-contextual information. Non-contextual information is currently thought to only include orientation through head direction cells and distance travelled through grid cells. However, it is possible that emotional information is also incorporated into the non-contextual information. Since the amygdala is known to modulate emotional information in other brain regions including the hippocampus, it is possible that the amygdala modulates the incorporation of emotional information into place fields. This dissertation addresses this possibility by cue fear conditioning a rat in one environment and presenting the conditioned stimulus (CS) in a completely separate environment in which the firing of place fields was measured. This methodology allows for the association of the CS with the firing of specific place fields. Results showed that pairing the CS with the firing field of a place cell (in-field) resulted in an immediate disruption of the place field followed by restabilization in a new location. However, pairing the CS in an area outside of the place field (out-of-field) did not disrupt the place field stability. Temporary inactivation of the amygdala immediately after the CS was presented in-field resulted in an attenuation of place field disruption. These data suggest that emotional information is incorporated into the internal representation as seen as changes in place cell firing in a cell-specific manner, and the incorporation of this emotional information is driven by amygdala activity. This data provides valuable insight into the mechanisms involved in the encoding of emotional information into contextual representations. This solid introduction uses the principles of physics and the tools of mathematics to approach fundamental questions of neuroscience. Hippocampal place and time cells are thought to play a major role in the encoding of the spatial and temporal components of episodic memory. Extensive research in rodents has been performed studying the firing properties of hippocampal place cells. However, the firing properties of more recently discovered time cells are still not well understood. In this study, we performed electrophysiological recordings from CA1 time cells in rats as they performed a spatial working memory task on a figure-8 maze. The goal of this study was to better understand how differences in both the duration of the delay and running behavior influence the sequential activity of time cells. Time cells were recorded across two different delays of either 10 s or 30 s. The figure-8 maze was modified to contain an electric treadmill in the delay zone. The electric treadmill served to control behavior of rats during the delay zone and, depending on the extent of running, resulted in reduced theta oscillations. We found that a smaller proportion of time cells coded for later portions of the delay period. These late time cells were less stable both within and across corresponding blocks. However, when considering the entire population of time cells, CA1 time cell activity seemed to be stable between corresponding blocks irrespective of the delay length and the extent of theta oscillation during the delay period. Furthermore, the proportion of time cells did not differ depending between forced running blocks and blocks with the treadmill off, which suggests that the continuity of theta oscillations during the delay period was not necessary for the maintenance of time cell activity. Our experiment provides further insight into the mechanisms that govern the sequential activity of time cells. There are currently two major theories about the role of the hippocampus, a distinctive structure in the back of the temporal lobe. One says that it stores a cognitive map, the other that it is a key locus for the temporary storage of episodic memories. A. David Redish takes the approach that understanding the role of the hippocampus in space will make it possible to address its role in less easily quantifiable areas such as memory. Basing his investigation on the study of rodent navigation--one of the primary domains for understanding information processing in the brain--he places the hippocampus in its anatomical context as part of a greater functional system. Redish draws on the extensive experimental and theoretical work of the last 100 years to paint a coherent picture of rodent navigation. His presentation encompasses multiple levels of analysis, from single-unit recording results to behavioral tasks to computational modeling. From this foundation, he proposes a novel understanding of the role of the hippocampus in rodents that can shed light on the role of the hippocampus in primates, explaining data from primate studies and human neurology. The book will be of interest not only to neuroscientists and psychologists, but also to researchers in computer science, robotics, artificial intelligence, and artificial life. This volume will explore the most recent findings on cellular mechanisms of inhibitory plasticity and its functional role in shaping neuronal circuits, their rewiring in response to experience, drug addiction and in neuropathology. Inhibitory Synaptic Plasticity will be of particular interest to neuroscientists and neurophysiologists. The entorhinal cortex of rat contains neurons, called "grid cells", that exhibit a very peculiar behavior. Discovered about a decade ago, the activity of these cells was found to correlate with the allocentric position of the animal by forming a regular, hexagonal lattice of firing fields across the entire environment. Due to this unusual behavior and the proximity of the entorhinal cortex to other brain regions that also contain cells with spatially correlated activity grid cells are commonly recognized as an important element of a neuronal system for navigation. Existing computational models of grid cells share this view and typically describe the behavior of grid cells as a path integration component of such a system. This work presents a new, complementary computational model of grid cells. In contrast to existing models it does not assume that grid cells are a specialized component of a navigational system. Instead, it assumes that the activity of grid cells reflects a general principle by which neurons in higher order parts of the cortex process information. The proposed model extends the growing neural gas approach by Bernd Fritzke into a recursive algorithm that describes the joint behavior of grid cells in a group as well as the processes within each individual cell. The work demonstrates that the chosen approach is able to model the characteristic behavior of grid cells and other cells, that also exhibit grid cell-like firing patterns but whose activity does not correlate with the animal's location in the environment. Since information in the brain is processed by the exchange of spikes among neurons, a study of such group dynamics is extremely important in understanding hippocampus dependent memory. These spike patterns and local field potentials (LFPs) have been analyzed by various statistical methods. These studies have led to important findings of memory information processing. For example, memory-trace replay, a reactivation of behaviorally induced neural patterns during subsequent sleep, has been suggested to play an important role in memory consolidation. It has also been suggested that a ripple/sharp wave event (one of the characteristics of LFPs in the hippocampus) and spiking activity in the cortex have a specific relationship that may facilitate the consolidation of hippocampal dependent memory from the hippocampus to the cortex. The book will provide a state-of-the-art finding of memory information processing through the analysis of multi-neuronal data. The first half of the book is devoted to this analysis aspect. Understanding memory information representation and its consolidation, however, cannot be achieved only by analyzing the data. It is extremely important to construct a computational model to seek an underlying mathematical principle. In other words, an entire picture of hippocampus dependent memory system would be elucidated through close collaboration among experiments, data analysis, and computational modeling. Not only does computational modeling benefit the data analysis of multi-electrode recordings, but it also provides useful insight for future experiments and analyses. The second half of the book will be devoted to the

computational modeling of hippocampus-dependent memory. Abstract: This dissertation presents a biophysical model that combines evidence from neurophysiological studies of goal-directed spatial navigation in the rat into a single algorithm based on bidirectional graph search. Application of this algorithm allows the model to simulate behavioral and neurophysiological data from rats performing memory-dependent spatial tasks. The behavioral component is represented as a virtual animal in a virtual environment. The neurophysiological component is represented as a network of simulated neurons, which receives sensory input from the environment and directs the movement of the animal. The binding of the physiology and behavior in the model allows several experimental phenomena to be addressed, such as (1) activities of the principal cells in the hippocampal area are correlated with an animal's position in space; (2) this positional information degrades after a lesion that disconnects the hippocampus from the medial septum; (3) after lesions of the medial septum, reduction of hippocampal theta rhythm is correlated with an impairment in spatial tasks; (4) cells in the hippocampus tend to fire at a preferred phase of the theta cycle, and (5) the arrival of different inputs to the hippocampus corresponds to specific phases of the theta cycle. The model shows how these physiological properties allow such behavioral functions as successful navigation through various mazes towards a desired goal, selection of a goal on the basis of distance and salience, and reshaping its knowledge about the environment. The latter is based on a thoroughly analyzed spatially and temporally local spike-timing-dependent synaptic modification rule. Four types of gated learning are compared in the context of simulated behavior. Presynaptic and dual OR (triggered by either presynaptic or postsynaptic activity) gatings are more noise tolerant and produce experience-dependent changes in place cell firing patterns shown experimentally. Postsynaptic gating leads to a better competition between input patterns. Dual AND gating (based on the simultaneous presence of both presynaptic and postsynaptic activity) leads to stabilization of the network activity. Each of these gatings can be used to subserve different aspects of the exploratory behavior. The proposed model can be further extended to more general problem-solving based on classical graph search. Exposure to novel environments alters hippocampal cell and theta local field potential activity to support the formation of new or updated spatial representations. It induces remapping of place cell fields, a reduction in CA1 theta frequency and an increase in the spatial scale of entorhinal grid cell fields. A recent model proposes that a reduction in the slope of the theta frequency-running speed relationship (TFRSR) can account for these effects (Burgess, 2008, Hippocampus). In contrast, the model proposes that the Y-axis intercept of the TFRSR is unaffected by novelty but instead correlates with anxiety/arousal. Thus, the theta frequency reduction elicited by a wide range of anxiolytic drugs (Gray & McNaughton, 2000) is suggested to result from a decrease in the intercept. Cannabinoids are anxiolytic at low doses, reduce theta frequency and disrupt the theta-timescale dynamics of place cell firing. In contrast, environmental novelty elicits a coordinated shift in CA1 place cell firing to a later theta-phase. This thesis examines the electrophysiological effects of environmental familiarity or novelty in combination with a low, intraperitoneal dose of the cannabinoid agonist O-2545, or its vehicle, saline. It was found that exposure to novel environments reduced the slope of the TFRSR whereas the cannabinoid reduced the intercept, in agreement with the model. These effects were not due to decreased body temperature or changes in behaviour. Combining novelty and drug reduced both slope and intercept. Furthermore, the extent of novelty-induced place cell remapping correlated with the reduction in slope. The mean theta-phase of place cell firing shifted later in novelty, but this was disrupted by the cannabinoid. In contrast, the mean theta-phase of the interneuron population was stable across conditions, but novelty increased the dispersion of interneuron theta-phase preferences. These results help to elucidate the mechanisms underlying novelty processing and cannabinoid action in the hippocampus. Since the appearance of the John O'Keefe and Lynn Nadel book in which they proposed that the hippocampus provides an abstract, internal representation of the animal's environment, considerable conceptual progress in the area of navigational information processing has been achieved. The purpose of the current work is to consolidate recent data and conceptual insights related to navigational insight processing in a format useful to both practitioners and advanced students in neuroscience. The hippocampus is one of a group of remarkable structures embedded within the brains medial temporal lobe. Long known to be important for memory, it has been a prime focus of neuroscience research for many years. This volume offers an account of what the hippocampus does, and what happens when things go wrong.--[Source inconnue]. Properly tuned receptive fields in feed-forward networks depend on topographical input (afferent cells with properly tuned receptive fields connect topographically to their postsynaptic partners with little or no convergence/divergence) or on attractor network dynamics provided by specfic intra-layer lateral connections (recurrent excitation/inhibition). For hippocampal place cells neither might be availabe. We investigated how theta oscillation can transform the dynamics of a simple feed-forward network without topographical input or recurrent connections so that tuning curves of individual cells remain sharp in spite of the considerable convergence/divergence between layers. The mechanism is also shown to be appropriate for describing fine details of place cell firing. Rats learn to navigate to a specific location faster in a familiar environment (Keith and Mcvety 1988). It has been proposed that place learning does not require specific reward signals, but rather, that it occurs automatically. One of the strongest pieces of evidence for the automatic nature of place learning comes from the observation that place and head direction cells reference their receptive fields to prominent landmarks in an environment without needing a reward signal (O'Keefe and Conway 1978; Taube et al. 1990b). It has also been proposed that an allocentric representation of an environment would be bound to the landmarks with the greatest relative stability to guide its orientation (O'Keefe and Nadel 1978). The first two parts of this thesis explore whether place and head direction cells automatically use the most coherent landmarks for orientation. Head direction cells have been shown to orient their preferred firing directs coherently when being exposed to conflicting landmarks in an environment (Yoganarasimha et al. 2006). A model of head direction cells was thus used to explore the necessary mechanisms required to implement an allocentric system that selects landmarks based on their relative stability. We found that the simple addition of Hebbian projections combined with units representing the orientation of landmarks to the head direction cell system is sufficient for the system to exhibit such a capacity. We then recorded both entorhinal head direction cells and CA1 place cells and at the same time subjected the rats to repeated experiences of landmark conflicts. During the conflicts a subset of landmarks always maintained a fixed relative relationship with each other. We found that the visual landmarks retained their ability to control the place and head direction cells even after repeated experience of conflict and that the simultaneously recorded place cells exhibited coherent representations between conflicts. However, the 'stable landmarks' did not show significantly greater control over the place and head direction cells when comparing to the unstable landmarks. This argues against the hypothesis that the relative stability between landmarks is encoded automatically. We did observe a trend that, with more conflict experience, the 'stable landmarks' appeared to exert greater control over the cells. The last part of the thesis explores whether goal sensitive cells (Ainge et al. 2007a) discovered from CA1 of hippocampus are developed due to familiarity with the environment or from the demands for rats to perform a win-stay behaviour. We used the same win-stay task as in Ainge et al. and found that there were few or no goal sensitive cells on the first day of training. Subsequent development of goal sensitive activity correlated significantly with the rat's performance during the learning phase of the task. The correlation provides support to the hypothesis that the development of goal sensitive cells is associated to the learning of the win-stay task though it does not rule out the possibility that these goal sensitive cells are developed due to the accumulated experience on the maze. In summary, this thesis explores what kind of spatial information is encoded by place and head direction cells and finds that relative stability between landmarks without a reward signal is not automatically encoded. On the other hand, when additional information is required to solve a task, CA1 place cells adapt their spatial code to provide the necessary information to guide successful navigation. A comprehensive examination of head-direction signals and their importance in explaining orienting and navigation behaviors. Head direction cells—neurons that fire only when an animal orients its head in a certain direction—are found in several different brain areas, with different neurons selective for different head orientations; they are influenced by landmarks as well as motor and vestibular information concerning how the head moves through space. These properties suggest that head direction cells play an important role in determining orientation in space and in navigation. Moreover, the prominence, strength, and clarity of head direction signals indicate their importance over the course of evolution and suggest that they can serve as a vital key for understanding brain function. This book presents the latest findings on head direction cells in a comprehensive treatment that will be a valuable reference for students and researchers in the cognitive sciences, neuroscience, computational science, and robotics. The book begins by presenting head direction cell properties and an anatomical framework of the head direction system. It then looks at the types of sensory and motor information that control head direction cell firing, covering topics including the integration of diverse signals; the relationship between head direction cell activity and an animal's spatial behavior; and spatial and directional orientation in nonhuman primates and humans. The book concludes with a tutorial demonstrating the implementation of the continuous attractor network, a computational model of head direction cells, and an application of this approach for a navigational system for mobile robots. It had been known for decades that the hippocampus is involved in learning and memory. When an animal moves through an environment, the firing patterns of hippocampal pyramidal cells show spatial specificity or "place fields". When a rat is exposed to a familiar environment, the hippocampus displays the previously stored pattern for that environment; when the rat is introduced to a novel environment, a new pattern is displayed. It is hypothesized that the medial septal theta rhythm is the signal that switches the hippocampal activity from a recalling to an encoding state. The projection from the medial septum to the hippocampus has been shown to influence hippocampal electrophysiology, both in terms of population and single unit activity. Alteration of the septo-hippocampal input (by septal lesions, inactivation, or infusions of anticholinergic drugs) decreases hippocampal theta power, and intraseptal cholinomimetics increase hippocampal theta power. I infused a cholinergie agonist known to induce hippocampal theta into the medial septum, and recorded hippocampal CA1 pyramidal cells in young and old rats. The recordings were performed either in a familiar environment or in a novel configuration of the environment. I found a differential effect of medial septal activation under familiar and novel conditions; in young animals carbachol always caused instability of the hippocampal representation, while in aged animals carbachol caused instability in a familiar environment but improved the development of a representation under conditions of novelty. I propose that in a familiar environment CA1 cells reflect the previously stored CA3 input, and ignore minor sensory mismatches (small changes in auditory, olfactory, or visual stimuli). Increasing the degree of mismatch by moderately modifying the environment (i.e. our novel configuration) or increasing the septal modulation in a familiar environment results in CA1 reflecting extra-hippocampal input more than the previously stored CA3 input. A moderate modification of the environment accompanied by septal activity (signaling the significance of the situation) will also affect the CA3 representation, and will produce a new representation in the CA1 cell population. How the brain integrates information over multiple sensory modalities to encode highly complex stimuli is a central question of neuroscience. The mammalian brain structures that encode space provide a tractable system in which to explore this question, as there are several well-defined cell types that have spatially selective firing. Place cells in the hippocampus fire when an animal is in a particular location in the environment. Grid cells, found in the upstream medial entorhinal cortex (MEC), have multiple firing fields located on the vertices of a triangular grid. Also found in the MEC are border cells that fire along the boundaries of an environment, and head direction (HD) cells that fire when the animal's head is facing a particular direction. Using virtual reailty for rats, we explored the contribtion of multiple sensory modalities to the spatial selectivity of these cell types. The hippocampal cognitive map is thought to be driven by distal visual cues and self-motion cues. In VR place cells showed robust spatial selectivity, however a much smaller proportion were track active, compared to the RW. This indicates that distal visual and non-vestibular self-motion cues are indeed sufficient to provide selectivity, but vestibular and other sensory cues present in RW are necessary to fully activate the place cell population. Additionally, bidirectional cells preferentially encoded distance along the track in VR, but encoded absolute position in RW. Taken together these results suggest the differential contributions of sensory cues in shaping the hippocampal population code. Similarly, we also measured the activity of grid cells and head direction cells in open field environments in VR and RW. Here, we found that grid cells lost their spatial selectivity and periodicity, demonstrating that the cues available in the VR were insufficient. Most HD cells, likewise, did not retain their directional tuning in a body-fixed VR, suggesting that visual cues might maintain only a partial ability to update the firing directions of HD cells in the absence of reliable angular vestibular cues. However, a small portion of HD cells found to maintain their selectivity in the VR warrant further investigation. These results provide insight to the contributions of individual sensory modalities to the firing of spatially selective cell types, as well as the mental representation of space. Molecular Characterization of Autophagic Responses, Part B presents a collection of methods for the qualitative and quantitative evaluation of virtually all the morphological, biochemical, and functional manifestations of autophagy, in vitro, ex vivo and in vivo, in organisms as distant as yeast and man. Autophagy is an evolutionarily conserved mechanism for the lysosomal degradation of superfluous or dangerous cytoplasmic entities, and plays a critical role in the preservation of cellular and organismal homeostasis. Monitoring the biochemical processes that accompany autophagy is fundamental for understanding whether autophagic responses are efficient or dysfunctional. Offers a detailed overview of the protocols used to study autophagy and various aspects of autophagic responses Written in an accessible style by renowned experts in the field The CA3 hippocampal region receives information from the entorhinal cortex either directly from the perforant path or indirectly from the dentate gyrus via the mossy fibers (MFs). According to their specific targets (principal/mossy cells or interneurons), MFs terminate with large boutons or small filopodial extensions, respectively. MF-CA3 synapses are characterized by a low probability of release and pronounced frequency-dependent facilitation. In addition MF terminals are endowed with mGluRs that regulate their own release. We will describe the intrinsic membrane properties of pyramidal cells, which can sometimes fire in bursts, together with the geometry of their dendritic arborization. The single layer of pyramidal cells is quite distinct from the six-layered neocortical arrangement. The resulting aligned dendrites provides the substrate for laminated excitatory inputs. They also underlie a precise, diversity of inhibitory control which we will also describe in detail. The CA3 region has an especially rich internal connectivity, with recurrent excitatory and inhibitory loops. In recent years both in vivo and in vitro studies have allowed to better understand functional properties of the CA3 auto-associative network and its role in information processing. This circuit is implicated in encoding spatial representations and episodic memories. It generates physiological population synchronies, including gamma, theta and sharp-waves that are presumed to associate firing in selected assemblies of cells in different behavioral conditions. The CA3 region is susceptible to neurodegeneration during aging and after stresses such as infection or injury. Loss of some CA3 neurones has striking effects on mossy fiber inputs and can facilitate the generation of pathologic synchrony within the CA3 micro-circuit. The aim of this special topic is to bring together experts on the cellular and molecular mechanisms regulating the wiring properties of the CA3 hippocampal microcircuit in both physiological and pathological conditions, synaptic plasticity, behavior and cognition.We will particularly emphasize the dual glutamatergic and GABAergic phenotype of MF-CA3 synapses at early developmental stages and the steps that regulate the integration of newly generated neurons into the adult dentate gyrus-CA3 circuit. This is the 2nd edition of a very well received and popular book that reflects the current state-of-the-art of the ongoing research avenues concerning the hippocampus and processing units bridging the gap between single cell activity, network activity and global brain function. It aims to provide a methodology to anyone interested in developing microcircuit level models of the hippocampus. The book is divided into two thematic areas: (I) Experimental background and (II) Computational analysis. In part I, leading experimental neuroscientists discuss the morphological, physiological and molecular characteristics as well as the connectivity and synaptic properties of the various cell types found in the hippocampus. Behaviour-related ensemble activity patterns of morphologically identified neurons in anesthetized and freely moving animals provide insights on the function of the hippocampal areas. In part II, computational neuroscientists present models of the hippocampal microcircuits at various levels of detail (e.g. single cell level, network level, etc.). Synaptomics and connectomics models of hippocampal structures are initially discussed. Then, network models of memory, rhythm generation and spatial navigation are presented, followed by abstract and biophysical models of synaptic plasticity. Network models of hippocampal implicated disorders (epilepsy and schizophrenia) are then detailed and how their network topologies, connectivities and activities change in these diseases. Finally, two chapters are dedicated to describing simulator environments of single neurons and networks currently used by computational neuroscientists in developing their models and modelling tools to parametrically constrain them. This engaging volume is invaluable to experimental and computational neuroscientists, electrical engineers, physicists, mathematicians and others interested in developing microcircuit models of the hippocampus. Graduate level students and trainees in all of these fields can find this book a significant source of information. Abstract: How does the brain learn to navigate in the world? How do maps develop that can represent the large spaces in which animals navigate? Grid cells in the dorsal segment of the medial entorhinal cortex (dMEC) show remarkable hexagonal activity patterns as a rat navigates an open field. Furthermore, there exists a gradient of spatial scales along the dorsoventral axis of the dMEC, with neighboring cells sharing the same spatial scale but having offset spatial phases while maintaining the same orientation. Past studies have suggested multiple mechanisms explaining how grid cells firing fields can develop hexagonal structure. The GRIDSmap model that is introduced in this thesis contributes to an understanding of how such hexagonal structures may be

learned as an animal navigates through the world. In particular, the GRIDSmap model shows how hexagonal firing fields may be learned by a self-organizing map whose inputs come from multiple one-dimensional small-scale stripe cells that integrate linear velocity signals in different directions, and whose learned categories are grid cells in layer II of dMEC. GRIDSmap cells learn this hexagonal structure from a simple trigonometric property of space that is manifested in the most frequent co-occurrences of stripe cell firing. The GRIDSmap habituative dynamics that control map learning also generate membrane potential oscillations. Faster (slower) oscillations lead to learning of smaller (larger) grid scales, consistent with experimentally observed oscillations in dMEC layer II stellate cells. Such multiple scales of grid cells can induce learning of hippocampal place cell firing fields that represent much larger scales; namely, the least common multiple of the grid cell scales. This hierarchy of entorhinal and hippocampal maps clarifies how path integration signals may give rise to place fields capable of representing the large spaces that animals can successfully navigate. The study of mathematical cognition and the ways in which the ideas of space, time and number are encoded in brain circuitry has become a fundamental issue for neuroscience. How such encoding differs across cultures and educational level is of further interest in education and neuropsychology. This rapidly expanding field of research is overdue for an interdisciplinary volume such as this, which deals with the neurological and psychological foundations of human numeric capacity. A uniquely integrative work, this volume provides a much needed compilation of primary source material to researchers from basic neuroscience, psychology, developmental science, neuroimaging, neuropsychology and theoretical biology. The first comprehensive and authoritative volume dealing with neurological and psychological foundations of mathematical cognition Uniquely integrative volume at the frontier of a rapidly expanding interdisciplinary field Features outstanding and truly international scholarship, with chapters written by leading experts in a variety of fields The dentate gyrus is a part of the brain that has been a topic of intense interest since the beginning of neuroscience, and pioneering studies from the distant and recent past attest to this. One of the reasons for such interest is that this structure provides some of the most remarkable examples of plasticity within the nervous system. In addition, it is critical to normal cognitive function, although exactly how and when is still a question that eludes answers. Furthermore, abnormalities within the dentate gyrus appear to play a role in diverse clinical conditions, from depression to epilepsy and traumatic brain injury. The primary goal of this book is to provide a context, or background, upon which the detailed knowledge of the current era can be appreciated. A series of overviews are provided to clarify essentials related to structural organization and development, cellular components, neurotransmitters and neuromodulators, plasticity, and clinical relevance. * Covers the topic comprehensively from anatomy to cellular and systems perspectives * Includes basic research and addresses translational implications, so it will be useful to both researchers in the laboratory and clinicians who conduct experiments in humans * Chapters provide fundamentals, but also details and ample references for further review of the topic The first book to comprehensively explore the cognitive foundations of human spatial navigation Humans possess a range of navigation and orientation abilities, from the ordinary to the extraordinary. All of us must move from one location to the next, following habitual routes and avoiding getting lost. While there is more to learn about how the brain underlies our ability to navigate, neuroscience and psychology have begun to converge on some important answers. In Human Spatial Navigation, four leading expertstackle fundamental and unique issues to produce the first book-length investigation into this subject. Opening with the vivid story of Puluwat sailors who navigate in the open ocean with no mechanical aids, the authors begin by dissecting the behavioral basis of human spatial navigation. They then focus on its neural basis, describing neural recordings, brain imaging experiments, and patient studies. Recent advances give unprecedented insights into what is known about the cognitive map and the neural systems that facilitate navigation. The authors discuss how aging and diseases can impede navigation, and they introduce cutting-edge network models that show how the brain can act as a highly integrated system underlying spatial navigation. Throughout, the authors touch on fascinating examples of able navigators, from the Inuit of northern Canada to London taxi drivers, and they provide a critical lens into previous navigation research, which has primarily focused on other species, such as rodents. An ideal book for students and researchers seeking an accessible introduction to this important topic, Human Spatial Navigation offers a rich look into spatial memory and the neuroscientific foundations for how we make our way in the world. This work presents the work of leading authorities on spatial relationships and cognition, describing the latest medical research and new theoretical insights. The authors explore problems concerning the way space is represented in the brain, and how spatial relationships are encoded in the neural network, creating a framework for our perceptions that enables them to guide our actions. Although these fascinating questions have generated endless philosophical debate over the years, it is only recently that neurophysiology has advanced sufficiently to provide a sound scientific basis for understanding the subject. Among the topics examined here are oculomotor control, neural control of skeletal movements, the contribution of the cortical parietal association areas to mapping spatial information, the role of hippocampal structures in cognitive mapping and spatial memory, and the ways neural networks generate internal representations of the physical world. In addition to researchers and advanced students in neurophysiology, neuropsychology, and cognitive psychology, this state-of-the-art work will interest scientists in the fields of artificial intelligence and robotics. The hippocampus is an important brain region, a true central hub for memory of various kinds and other processes. Neuropsychiatric disorders such as Alzheimer's disease, drug addiction, and schizophrenia are characterized by hippocampal alterations. The dentate gyrus of the hippocampus is a site exhibiting adult neurogenesis. This book covers the topic of the hippocampus from various perspectives. It discusses adult neurogenesis, effect of enriched environments on hippocampal plasticity, and long-term potentiation-associated gene expression. The book also addresses multiscale representations of complex environments and strategies in the hippocampus-dependent spatial tasks. Finally, insight into the hippocampus as a link between negative affect and relapse to psychostimulants is provided. The book collects evidence of various hippocampal functions in healthy and disordered brain. The discovery of new cell types, such as grid and time cells, in the hippocampus has been accompanied by major anatomical and theoretical insights in the recent years. This book provides comprehensive, up-to-date information about the hippocampal formation and especially the neural basis of episodic memory, spatial location (the formation of the cognitive map) and temporal representation. The first part of the book describes the information flow from pre-hippocampal areas into the hippocampus, the second part discusses the different types of hippocampal processing and finally, the third part depicts the influence that the hippocampal processing has on other brain structures that are perhaps more closely tied to explicit cognitive or behavioral output. This book is intended for neuroscientists, especially for those who are involved in research on the hippocampus, as well as for behavioral scientists and neurologists. The brain ... There is no other part of the human anatomy that is so intriguing. How does it develop and function and why does it sometimes, tragically, degenerate? The answers are complex. In Discovering the Brain, science writer Sandra Ackerman cuts through the complexity to bring this vital topic to the public. The 1990s were declared the "Decade of the Brain" by former President Bush, and the neuroscience community responded with a host of new investigations and conferences. Discovering the Brain is based on the Institute of Medicine conference, Decade of the Brain: Frontiers in Neuroscience and Brain Research. Discovering the Brain is a "field guide" to the brainâ€"an easy-to-read discussion of the brain's physical structure and where functions such as language and music appreciation lie. Ackerman examines: How electrical and chemical signals are conveyed in the brain. The mechanisms by which we see, hear, think, and pay attentionâ€"and how a "gut feeling" actually originates in the brain. Learning and memory retention, including parallels to computer memory and what they might tell us about our own mental capacity. Development of the brain throughout the life span, with a look at the aging brain. Ackerman provides an enlightening chapter on the connection between the brain's physical condition and various mental disorders and notes what progress can realistically be made toward the prevention and treatment of stroke and other ailments. Finally, she explores the potential for major advances during the "Decade of the Brain," with a look at medical imaging techniquesâ€"what various technologies can and cannot tell usâ€"and how the public and private sectors can contribute to continued advances in neuroscience. This highly readable volume will provide the public and policymakersâ€"and many scientists as wellâ€"with a helpful guide to understanding the many discoveries that are sure to be announced throughout the "Decade of the Brain." How do we find our way? The discovery of medial entorhinal cortex grid cells in 2005 stimulated a wide variety of experimental, theoretical and computational work aimed at elucidating the neural circuit underlying spatial representations in the entorhinal cortex. However, grid cells act in concert with place cells, head direction cells and border cells, each playing a part in the spatial navigation circuit. The aim of this Research Topics is to solicit contributions from leading researchers in the field of spatial navigation and spatial memory to present new experimental data, computational modeling or discussion on mechanisms underlying the neural encoding of space in the parahippocampal cortices. How the brain helps us to understand and navigate space—and why, sometimes, it doesn’t work the way it should. Inside our heads we carry around an infinite and endlessly unfolding map of the world. Navigation is one of the most ancient neural abilities we have—older than language. In Dark and Magical Places, Christopher Kemp embarks on a journey to discover the remarkable extent of what our minds can do. Fueled by his own spatial shortcomings, Kemp describes the brain regions that orient us in space and the specialized neurons that do it. Place cells. Grid cells. He examines how the brain plans routes, recognizes landmarks, and makes sure we leave a room through a door instead of trying to leave through a painting. From the secrets of supernavigators like the indigenous hunters of the Bolivian rainforest to the confusing environments inhabited by people with place blindness, Kemp charts the myriad ways in which we find our way and explains the cutting-edge neuroscience behind them. How did Neanderthals navigate? Why do even seasoned hikers stray from the trail? What spatial skills do we inherit from our parents? How can smartphones and our reliance on GPS devices impact our brains? In engaging, engrossing language, Kemp unravels the mysteries of navigating and links the brain’s complex functions to the effects that diseases like Alzheimer’s, types of amnesia, and traumatic brain injuries have on our perception of the world around us. A book for anyone who has ever felt compelled to venture off the beaten path, Dark and Magical Places is a stirring reminder of the beauty in losing yourself to your surroundings. And the beauty in understanding how our brains can guide us home.

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