Brainy Days in Jerusalem 2: An Interdisciplinary Celebration
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Abstracts:

Charles Zuker, Columbia University, USA
From Receptors to Behavior
The taste system is one of our fundamental senses, responsible for detecting and responding to sweet, bitter, umami, salty, and sour stimuli. In the tongue, the five basic tastes are mediated by separate classes of taste receptor cells each finely tuned to a single taste quality. In the cortex, each taste quality is represented in its own separate cortical field, revealing the existence of a gustotopic map in the brain. We study the logic of taste coding as a platform to understand how our brain creates an internal representation of the outside world and transforms sensory signals at the periphery into percepts, actions and complex behaviors.

Noam Sobel, Weizmann Institute of Science, Israel
Predicting Odor Perception from Odor Structure: Pleasantness as a Reflection of the Physical World

Liqun Luo, Stanford University, USA
Genetic Dissection of Neural Circuit Assembly and Organization
This talk will discuss recent work on the development and function of neural circuits in flies and mice. Discussion of development will focus on cellular and molecular mechanisms that mediate the establishment of wiring specificity between pre- and postsynaptic partners. Discussion of function will focus on applications of the TRAP method to interrogate circuits involved in remote memory.

Michal Rivlin-Etzion, Weizmann Institute of Science, Israel
The Computation of Motion Direction in the Retina: Recalculating
Direction selective retinal ganglion cells (DSGCs) fire robustly in response to motion in one (preferred) direction, and poorly to motion in the opposite (null) direction. Starburst amacrine cells (SACs) mediate this computation via two mechanisms – they form asymmetric inhibitory connections onto DSGCs; and their processes display directional preference. Surprisingly, we have found that DSGCs can overcome the circuit's anatomy and reverse their directional preference following a short repetitive visual stimulation. We used this reversal in DSGCs to shed new light on the mechanisms that contribute to the computation of motion direction in the retina. Using

two-photon targeted patch clamp techniques and various moving stimuli we find that SACs' processes change their response properties following repetitive stimulation to support the reversed computation. In addition, we discover that directional preference of DSGCs depends on stimulus type, and that DSGC responses to a given stimulus may contain multiple phases that are tuned to opposite directions. Our results reveal new mechanisms that act in orchestra to support the computation of motion direction in DSGCs, and add to recent findings demonstrating that the computations performed by anatomically-defined neuronal circuits can be altered by dynamic circuit mechanisms that are guided by visual experience.

Jonathan Pillow, Princeton University, USA

Low-Dimensional Dynamic Encoding in Prefrontal Cortex during Decision-Making

A growing body of evidence indicates that the inherent dimensionality of neural population activity is far smaller than the number of neurons that can be recorded with current technology. However, it is also clear that single neurons often represent multiple kinds of information simultaneously, a phenomenon known as "mixed selectivity", indicating that neural population activity represents complex mixtures of sensory, cognitive, and behavioral variables. In this talk, I will describe new statistical techniques for uncovering low-dimensional latent structure from high-dimensional neural datasets. Our work represents an extension of "Targeted Dimensionality Reduction" (Mante et al, 2013), which seeks to identify subspaces that carry information about distinct task variables. We have applied our method to neural population data from macaque prefrontal cortex during a context-dependent perceptual discrimination task. It reveals the existence of independent multi-dimensional subspaces of neural activity space devoted to the coding of sensory, context, and decision-related variables on multiple timescales. I will discuss implications of this and related approaches for understanding the dimensions of neural activity underlying complex behaviors.

Eilon Vaadia, The Hebrew University of Jerusalem, Israel

Volitional Control of Neuronal Activity in Brain Machine Interface

Richard Axel, Columbia University, USA

Representations of the Olfactory World in the Brain: Beyond the Piriform Cortex

Bert Sakmann, Max Planck Institute for Neurobiology, Germany

From Single Cells & Single Columns to Cortical Networks - Coincidence Detection and Synaptic Transmission in Brain Slices and Brains

While patch pipettes were initially designed to record elementary current events from muscle and neuronal membrane (e.g. Sakmann, 1992) the whole-cell and cell-attached recording configurations proved to be useful tools for examining signaling within and between nerve cells. In this lecture I will summarize first work on electrical signaling within single neurons, describing communication between its dendritic compartments, soma and nerve terminals via forward and backward propagating action potentials. The newly discovered dendritic excitability endows neurons with the capacity for coincidence detection of spatially separated subthreshold inputs. When these are occurring during a time window of tens of milliseconds this information is broadcasted to other cells by the initiation of bursts of action potentials (AP-bursts). The occurrence of AP bursts critically impacts signaling between neurons that are controlled by target cell specific transmitter release mechanisms at downstream synapses even in different terminals of the same neuron. This can in turn determine the induction of synaptic plasticity mechanisms if AP bursts occur both presynaptically in terminals and postsynaptically in dendrites, within a short time window.

A fundamental question that arises from these findings is: ”What are the possible functions of active dendritic excitability with respect to network dynamics in the intact cortex of behaving animals”?

To answer this question I will highlight in this review the functional and anatomical architectures of an averaged cortical column in the vibrissal (whisker) field of somatosensory cortex (vS1), with an emphasis on the role of layer 5 thick tufted cells (L5tt) embedded in this structure. Synaptic and unit responses of these major cortical output neurons to a whisker deflection are compared with responses of afferent neurons in primary somatosensory thalamus (VPM) and of one of their efferent targets, the secondary somatosensory thalamus (POm). Coincidence detection mechanisms appear to be implemented in vivo as judged from the occurrence of AP-bursts. Three-dimensional reconstructions of anatomical inputs that could provide separate dendritic inputs suggest that inputs from several combinations of thalamocortical projections and intra-columnar connections could trigger the dendritic mechanisms that lead to the generation of AP-bursts. Finally, recordings from target cells of a column reveal the importance of AP bursts for signal transfer to these cells .

The observations lead to the hypothesis that in vS1 cortex the sensory afferent sensory code is transformed, at least partially, from a rate to an interval (burst) code that broadcasts the occurrence of sensory stimuli to different targets of L5tt cells. In addition the occurrence of pre- and postsynaptic AP-bursts may, in the long run, alter sensory representation in cortex.

Jackie Schiller, Technion – Israel Institute of Technology, Israel
Motion Related Activity in the Different Layers of the Primary Motor Cortex during a Hand Reach Task

Idan Segev, The Hebrew University of Jerusalem, Israel
What Makes Human Cortical Neurons Distinctive?

Mickey London, The Hebrew University of Jerusalem, Israel
Adrenergic Modulation Regulates Dendritic Excitability of Layer 5 Pyramidal Neurons In Vivo

The excitability of the apical tuft of layer 5 pyramidal neurons plays a crucial role in behavioral performance and in synaptic plasticity. Here we show that the excitability of the apical tuft and the coupling between the tuft and the perisomatic region, are sensitive to adrenergic neuromodulation. Using two-photon dendritic Ca^{2+} imaging and *in vivo* whole cell recordings from layer 5 pyramidal neurons in awake mice we show that application of the α2A-adrenoceptor agonist guanfacine increases the probability of dendritic Ca^{2+} events in the tuft and lowers the threshold for dendritic Ca^{2+} spikes. We further show that these effects are likely to be mediated by the dendritic hyperpolarization activated current I_h. Compartmental modeling shows that the modulation can either serve as an on-off switch of dendritic excitability or provide a gradual control of it, depending on the baseline availability of I_h. These findings suggest that adrenergic neuromodulation affects cognitive processes such as sensory integration, attention and working memory by regulating the sensitivity of layer 5 pyramidal neurons to top-down inputs.

Sabine Kastner, Princeton University, USA
Neural Dynamics of the Primate Attention Network

The selection of information from our cluttered sensory environments is one of the most fundamental cognitive operations performed by the primate brain. In the visual domain, the selection process is thought to be mediated by a static spatial mechanism – a 'spotlight' that can be flexibly shifted around the visual scene. This spatial search mechanism has been associated with a large-scale network that consists of multiple nodes distributed across all major cortical lobes and includes also subcortical regions. To identify the specific functions of each network node and their functional interactions is a major goal for the field of cognitive neuroscience. In my lecture, I will challenge two common notions of attention research. First, I will show behavioral and neural evidence that the attentional spotlight is neither stationary nor unitary. In the appropriate behavioral context, even when spatial attention is sustained at a given location, additional spatial mechanisms operate flexibly in parallel to monitor the visual environment. Second, spatial attention is assumed to be under 'top-down' control of higher order cortex. In contrast, I will provide neural evidence indicating that attentional control is exerted through thalamo-cortical interactions. Together, this evidence indicates the need for major revisions of traditional attention accounts.

Galit Yovel, Tel Aviv University, Israel

Beyond Faces: A Comprehensive Framework for Person Recognition

Humans are considered experts in person recognition. However, the study of person recognition has primarily focused on static images of unfamiliar faces, whereas in real life we typically need to recognize familiar people that are often seen in motion. Thus, to understand person recognition as it happens in real life, we need to consider additional sources of information that has so far been neglected. In the first part of my talk I will show that both perceptual and conceptual information should be considered to account for human expertise in face recognition. In the second part of my talk I will explore the conditions under which body and motion contribute to person recognition. At the end, I will discuss the neural mechanisms that may underlie dynamic whole person recognition. Overall, our studies move beyond the static image of a face and provide a comprehensive framework for the study of person recognition as it happens in real life.

Jack Gallant, University of California, Berkeley, USA

The Interface between Vision and Language (based on work by Alexander G. Huth, Sara F. Popham and Natalia Y. Bilenko)

One of the unique aspects of the human brain is our facility with language. Our linguistic capabilities interact closely with the primary sensory systems that we share with other primates. In recent studies we have explored the relationship between semantic representations of linguistic information and semantic representations of perceptual information in the human brain. Information about semantic categories in narrative speech is represented across much of the posterior temporal and parietal lobes, while information about visual categories is represented across much of anterior occipital cortex. These two types of representation meet at the boundary of visual cortex. We investigated the spatial relationship between these types of representation by examining voxel-wise models that predict BOLD fMRI responses based on semantic properties of visual and linguistic stimuli. Examination of the region around the linguistic-visual boundary reveals that by means of fMRI and voxel-wise modeling shows that for nearly any broad linguistic noun category that is represented on the anterior side of the border, an adjacent representation of the same visual category appears on the anterior side of the border. This suggests that the boundary of visual cortex constitutes both an anatomical and functional interface between perceptual representations of visual semantic information and linguistic, conceptual and/or amodal representations of related information. We expect that this systematic functional relationship reflects an underlying relationship of anatomical connectivity.

James DiCarlo, Massachusetts Institute of Technology, USA

Reverse Engineering Primate Visual Object Perception

Neuroscience is hard at work on one of our last great scientific quests — to reverse engineer the human mind and its intelligent behavior. Yet neuroscience is still in its infancy, and forward engineering approaches that aim to emulate human intelligence in artificial systems (AI) are also still in their infancy. The challenges of reverse engineering the human mind machine can only be solved by tightly coupling the efforts of brain and cognitive scientists (hypothesis generation and data acquisition), with forward engineering efforts using neurally-mechanistic computational models (hypothesis instantiation and data prediction). As this approach discovers the correct neural network models, those models will not only encapsulate our understanding of complex brain systems, they will be the basis of next-generation computing and novel brain interfaces (chemical, genetic, optical, electronic, etc.) for therapeutic and augmentation goals (e.g, brain disorders). To make this vision concrete, I will discuss one aspect of perceptual intelligence — object categorization and detection — and I will describe how work in brain science, cognitive science and computer science has converged to create deep neural networks that have recently made dramatic leaps: Not only are these neural network models reaching human performance for many images and tasks, but we have found that their internal workings largely emulate the previously mysterious internal workings of the primate ventral visual stream. Yet, our recent results show that the primate ventral visual stream still outperforms current generation artificial deep neural networks, and they point to what is importantly missing from current deep neural network models. More broadly, we believe that the community is poised to embrace a powerful new paradigm for systems neuroscience research.

Yair Weiss, The Hebrew University of Jerusalem, Israel

Neural Networks, Graphical Models and Image Restoration

This talk discusses some of the history of graphical models and neural networks and speculates on the future of both fields with examples from the particular problem of image restoration.

Hamutal Slovin, Bar Ilan University, Israel

Encoding Local Stimulus Attributes and Higher Visual Functions in V1 of Behaving Monkeys

One of the main tasks of the visual system is to combine edges and surfaces of individual objects into a perceptual group, and thus create a representation of visual scenes in which multiple objects are segregated from background and from other objects. In this talk we will review our recent findings on cortical processing of edges and surfaces and specifically how color-defined square surfaces and luminance-defined square surfaces are encoded in the macaque's primary visual cortex (V1). Using voltage-sensitive dye imaging to measure neuronal responses in V1 of behaving monkeys we found that regions corresponding to the squares' edges exhibited higher activity than those corresponding to the center. Responses to black were higher than to white, and the square-evoked activation patterns exhibited spatial modulations along the edges and corners. A model comprised of neural mechanisms that compute local contrast, local luminance temporal modulations in the black and white directions, and cortical center-surround interactions, could explain the observed population activity patterns in detail. In addition we found that cortical responses of figure-ground segregation are divergent, comprised from figure enhancement and background suppression and further investigation of a more realistic natural scene with multiple objects suggests that separate objects are labeled by different response amplitude.

Daphna Shohami, Columbia University, USA

How Memory Guides Value-Based Decisions

Learning is central to adaptive behavior. From robots to humans, the ability to learn from experience turns a rigid response system into a flexible, adaptive one. How are decisions shaped by past experience? What are the neurobiological and cognitive mechanisms that allow experiences to change the way we perceive and act in the world? I will present evidence for a critical role for memory mechanisms in the hippocampus in biasing value-based decisions, focusing on two distinct mechanisms. The first concerns the integration of information across discrete past events to support generalization of past experience towards novel decisions. The second concerns the retrieval and use of memories for rare, "one shot" events when making decisions about reward. Finally, I will discuss how results emerging from this work challenge the traditional view of learning systems and advance understanding of how memory biases decisions in both adaptive and maladaptive ways.

Yonatan Loewenstein, The Hebrew University of Jerusalem, Israel

Intertemporal Conflicts – From Past to Future

Much misery is the outcome of choice behaviors that seem self-defeating. We eat to excess, do not exercise and procrastinate; we are vulnerable to addictions, to alcohol, tobacco and drugs. In the first part of my talk I will use a normative theory of choice to show that such seemingly counterproductive behaviors, often stochastic, emerge as the only self-consistent choice patterns in intertemporal conflicts. Specifically, I will show how the temporal direction of the conflict (past vs. future), the sign of the payoff (benefits vs. costs) and the shape of the temporal discounting function of the decision maker (hyperbolic vs. anti-hyperbolic) determine the nature of the self-defeating behavior. In the second part of my talk I will consider rats in a particular intertemporal conflict, a waiting task. Behavior of animals in this task is highly stochastic, in line with the normative theory. Intriguingly, electrophysiological recordings from two regions necessary for this behavior, medial prefrontal cortex and secondary motor cortex indicate that waiting time is determined by a two-stage process: stochastic components of action timing decisions are injected by circuits downstream of those carrying deterministic bias signals.

Shlomit Yuval-Greenberg, Tel-Aviv University, Israel
The Temporal Dynamics of Visual Exploration

Leon Deouell, The Hebrew University of Jerusalem, Israel
Visual Categorical Perception Beyond Onsets

Angela Friederici, Max Planck Institute for Cognitive and Brain Sciences, Leipzig, Germany
The Neural Language Network: Structure and Function
Language is a uniquely human capacity. It is in particular the processing of complex syntax that is specific to humans, and therefore considered to be the core of language. I will describe the different syntax-related brain regions in the temporal and inferior frontal cortex as well as the white matter fiber tracts connecting these different brain regions and their contributions to syntax processing. The data suggest two networks: a ventrally located network connecting the inferior frontal cortex and the anterior temporal cortex which supports the combination of adjacent elements and a dorsally located network connecting the posterior portion of Broca’s area and the posterior temporal cortex which subserves the processing of syntactically complex sentences. These networks will be discussed against the background of recent ontogenetic and phylogenetic studies on the language-brain relationship. These studies suggest that it is the dorsal network, responsible for complex syntax, emerges late both in phylogeny and in ontogeny. This network may thus be viewed as the essential part of the neural basis underlying the human faculty of language.

Wolfram Schultz, University of Cambridge, UK
Getting the Best Reward: Neuronal Mechanisms for Utility Maximisation
Rewards induce learning (positive reinforcement), approach behaviour, economic decisions and positive emotions and mental states (pleasure, desire). We investigate basic neuronal reward signals during learning and decision-making, using behavioural and neurophysiological methods. We use specific behavioural tools to establish formal economic utility functions that constitute mathematical representations of behavioural preferences and predict the animal's choices. We find that the dopamine reward prediction error (RPE) signal codes economic utility, which may explain the maximisation of utility required for evolutionary beneficial behaviour. RPEs have specific valences whereby they act in specific directions; a positive RPE increases, and a negative RPE reduces, the frequency of actions that led to that RPE. Given that

electrical and optogenetic activation of dopamine neurones mimicks positive RPE, decision makers would seek situations leading to positive RPEs and avoid negative RPEs, thus increasing the rewards they are getting. Such an ever-increasing reward profile would amount to utility maximisation.

Hagai Bergman, The Hebrew University of Jerusalem, Israel

<u>The Subthalamic Nucleus and the Striatum – Driving Force vs. Fine Tuning of Downstream Basal-Ganglia Networks</u>

The basal ganglia (BG) main axis is built as three layers neural network, where the striatum and the subthalamic nucleus (STN) constitute the BG input stage and together innervate the BG downstream structures (GPe and GPi/SNr) using GABA and glutamate, respectively. However, the respective contribution of these two distinct BG input nuclei in shaping downstream activity in health and parkinsonism is still unknown. Comparison of the neuronal activity in BG input and downstream structures reveals that subthalamic, not striatal, activity fluctuations correlate with modulations in the increase/decrease discharge balance of BG downstream neurons during classical condition task with short and long delays. After striatal dopamine depletion and induction of parkinsonism with MPTP, abnormal low beta (8-15 Hz) spiking and local field potential (LFP) oscillations emerge and resonate across the BG network. Nevertheless, LFP beta oscillations entrain spiking activity of STN, striatal cholinergic interneurons and BG downstream structures, but do not entrain spiking activity of striatal projection neurons. Together, these results highlight the pivotal role of STN glutamatergic and divergent projections in BG physiology and pathophysiology and provide sound explanation for the widespread choice of the STN as the prime target along the BG network for DBS in patients suffering from Parkinson's disease and other basal ganglia related disorders.

Kathleen Cullen, Johns Hopkins University, USA

<u>Neural Representations of Natural Self Motion: Implications for Perception & Action</u>

The vestibular system detects self-motion and in turn generates reflexes that are crucial for our daily activities - such as stabilizing the visual axis (gaze) and maintaining head and body posture – as well as our subjective sense of movement and orientation in space. The loss vestibular function due to aging, injury, or disease produces dizziness, postural imbalance, and an increased risk of falls – all symptoms that profoundly impair quality of life. In this talk, I will describe how the brain processes vestibular information in natural conditions. Notably, our work has established how early stages of processing encode vestibular stimuli and integrate them with extra-vestibular cues – for example proprioceptive and premotor information to ensure accurate perception and behaviour. Our experiments have revealed that while vestibular afferents respond identically to externally-generated and actively-generated self-motion, this is not the case at first central stage of sensory processing. Neurons mediating the vestibulo-spinal reflexes, as well as ascending thalamocortical pathways, are robustly activated during externally-generated motion, however their sensory response are cancelled during actively-generated movements. Our work has further revealed that this cancellation of actively-generated vestibular input occurs only in conditions where the actual sensory signal matches the brain's internal estimate of the expected sensory consequences of active movement. Moreover, when unexpected vestibular inputs becomes persistent during voluntary motion, a cerebellar-based cancellation mechanism is rapidly updated to re-enable the vital distinction between self-generated and externally-applied stimulation to ensure the maintenance of posture and stable perception. In contrast, vestibular pathways mediating the vestibulo-ocular reflex, employ a different strategy. In this pathway, head velocity is robustly encoded whenever the goal is to stabilize gaze, but when the goal is to voluntarily redirect gaze an efferent copy of the gaze command suppresses the efficacy of this reflex pathway. Taken together, these findings have important implications for understanding the neural basis of perception and action during self-motion.

Michael Long, New York University School of Medicine, USA
How Does the Brain Generate Behavioral Sequences?
Zebra finches learn to sing in much the same way that infants learn to speak, but circuit-based mechanisms that underlie the existing parallels between human speech and song production remain unknown. To address this directly, we use focal cooling to manipulate the circuits underlying birdsong and human speech production, and we examine the effects on the fine structure of these vocalizations to establish a functional map for these behaviors. In the songbird, we then examine dynamics within a key forebrain premotor structure using 2-photon imaging in the singing bird, and we looked at the underlying circuitry using a combined electron-light microscopy approach. Using these observations, we have begun to test circuit-level models of sequence generation that are likely to be involved in a range of neural computations.

Ronen Segev, Ben Gurion University, Israel
What Can Fishes Teach Us About the Brain?
Fishes have diverged in evolution from the mammalian linage some 450 million years ago and as a result fishes' brain structure is different from the fundamental design of the mammalian, reptilian and avian brains. This raises the question what can we learn from the ability of fishes to solve different tasks. I will discuss aspects of how visual search and navigation are implemented in different fishes brains and the implications of our findings.

Yossi Yovel, Tel Aviv University, Israel

From Sensory Perception to Foraging Decision Making - The Bat's Point Of View

Bats are extreme aviators and amazing navigators. Many bat species nightly commute dozens of kilometres in search of food, and some bat species annually migrate over thousands of kilometres. Studying bats in their natural environment has always been extremely challenging because of their small size (mostly <50 gr) and agile nature. In the past four years, we have developed novel miniature technology to GPS-tag small bats, thus opening a new window to document their behaviour in the wild. However, the movement of an animal alone is not sufficient for studying its decision processes. We therefore equipped our miniature GPS devices with an ultrasonic microphone which allows monitoring the sonar and social communication of freely behaving bats. Because echolocating bats rely on sound emission to perceive their environment, on-board recordings enable us to tap into their sensory 'point of view' and to monitor fundamental aspects of their behaviour such as attacks on prey and interactions with conspecifics. This intimate description of behaviour allows us to examine bat decision making under natural conditions. We used this approach to study several systems of which I will focus on three: (1) I will discuss how a social bat species (*Rhinopoma microphyllum*) that searches for ephemeral prey benefits from a collective search in a group. (2) I will compare two *Myotis* bat species that exhibit very different foraging strategies, resulting from the nature of the prey they seek, and (3) I will describe dramatic differences in the foraging behaviour of city vs. country fruitbats (*Rousettus aegyptiacus*). Finally I will also present our current effort to include more on-board sensors for the study of bat neuro-ecology including acceleration, EEG and physiology sensors.

Yaniv Ziv, Weizmann Institute of Science, Israel

Multiplexing Information About Where and When in Hippocampal Neural Codes for Long Term Memory

Episodic memory relies on the hippocampus, whose neurons are thought to encode information about *where* and *when* events have occurred. Whereas ample knowledge exists regarding the encoding of location, relatively little is known about the neural mechanisms that enable the encoding of the time in which events occur. We performed time-lapse imaging of thousands of neurons over weeks in the hippocampal CA1 of mice as they repeatedly visited two distinct environments. Longitudinal analysis exposed ongoing environment-independent evolution of episodic representations, despite stable place field locations and constant remapping between the two environments. These dynamics time-stamped experienced events via neuronal ensembles that had cellular composition and activity patterns unique to specific points in time. Temporally close episodes shared a common timestamp regardless of the spatial context in which they occurred. Temporally remote episodes had distinct timestamps, even if they occurred within the same spatial context. Our results suggest that days-scale hippocampal ensemble dynamics could support the formation of a mental timeline in which experienced events could be mnemonically associated or dissociated based on their temporal distance. Overall, our ensemble-level analyses point to a plausible mechanism by which information about where and when can be simultaneously and independently encoded in episodic representations.

Edvard Moser, Kavli Institute for Systems Neuroscience, Norway

Organization of the Medial-Entorhinal Space Network

The brain's medial entorhinal cortex is part of a neural system for mapping of self-location. One of the first component to be detected in this internal map was the grid cell. Grid cells fire electric impulses when animals are at particular locations that together tile the environment in a periodic hexagonal pattern, like in a Chinese checkerboard. The circuit was soon found to include a wider spectrum of functional cell types, such as head direction cells, speed cells, and border cells, intermingled among the grid cells. In this lecture, I will first show that additional specialized cell types are present when spatial behavior is tested in environments with salient objects or landmarks. A subset of medial entorhinal cells fires in a vector-like manner at distinct distances and directions from objects inserted in the recording enclosure, irrespective of where in the enclosure the object is located, and irrespective of the identity of the object. In the second section of the talk, I will show that grid cells retain spatial relationships not only across recording environments but also from awake exploration to sleep, consistent with the idea that grid cells, and the entorhinal network as a whole, are part of a network-generated continuous attractor-like representation of local space. I will discuss possible roles of inhibitory networks in this representation and show that different functional cell types may be regulated by distinct classes of GABAergic interneurons. Finally, in the third part of the talk, I will discuss how the entorhinal-hippocampal navigational circuit evolves during the formation of the nervous system during the first weeks and months of life and I will discuss how immaturity of the circuit at early developmental stages may influence properties of medial entorhinal cell types.