iNAV 2018

Organizers: Jeffery Taube, Thomas Wolbers, Kate Jeffery, Laure Rondi-Reig, David Dickman, Mayank Mehta

2nd Interdisciplinary Navigation Symposium

25 – 29 june 2018
Quartier Tremblant | Canada

Contents

Taxis 3
Poster Presentations 3
Outings 3
Welcome Reception 4
Conference Dinner 4
Schedule of Daily Events 5
Registered Participants iNav 2018 12
Poster Session – Abstracts iNAV 2018 16
Blitz Session - Abstracts iNAV 2018 78

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Taxis

Those that do not drive to Mont Tremblant will most likely use the public transportation, resort shuttle or a Mont Tremblant taxi service. It is very easy to get a taxi in Tremblant, however during summer season we suggest you make your transportation arrangements ahead of time.

TAXI LOCAL DE MONT-TREMBLANT
1-819 808-8294 (TAXI)
monttremblanttaxi@hotmail.com
http://taximonttremblant.com

TAXI MONT-TREMBLANT
819 425-3212
taxilocal@hotmail.com
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TAXI EXPRESS
819-429 9119 (for taxi in Tremblant)
819-425 4436 (for limousine or airport transportation)
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Poster Presentations

For those presenting a Poster during the conference please put up your poster by **15:00 on the day of your poster (either Tuesday or Wednesday)**. Look for your name on the poster boards and place your poster there. Pins are provided. The proper format for the poster is A0 format (841 x 1189 mm, or 33.1 x 46.8 inch). This can be either in the landscape or portrait format. Poster Presenters are asked to be present at their posters during their allotted slot: **either Tuesday, 26th 17.30-18.30** or **Wednesday, 27th 18.30-19.30** (see schedule of events).

Reminder: Please take down your poster at the end of the session!

Outings

On Thursday, 28 June 2018 between 14:30 – 17:30 we have planned some time for outings, such as guided hikes, zip-lining, canoeing, cruise, e-Biking.

Enrollment:
dTour Tremblant
info@dtourtremblant.com | Phone: 819-430-TOUR (8687)

Meeting point: The Fairmont Hotel

Bring appropriate clothing for the activity you choose.

Everyone should be sure to pick up their free gondola ticket to the top of the mountain. This ticket is good for one round-trip ride to the top of the mountain during the conference. Be sure to check the times the gondola is open.

Welcome Reception

To meet your colleagues before the conference starts you are invited to our Welcome Reception with drinks and snacks (included in registration fee).

When: **Monday, 25 June, 18.00 - 20.00**
Where: Le Shack, 3035 Chemin de la Chapelle
How: Within walking distance (5 min) from hotels and conference center

Conference Dinner

The conference dinner will be held on the last evening after the end of the conference (included in registration fee).

When: **Friday, 29 June 19.30**
Where: Le Pont Couvert, 10, Rue du Centenaire, La Conception, Quebec
How: Buses will be leaving from the Basecamp starting at 19.00

Schedule of Daily Events

Monday 25 June 2018		
18:00 - 20:00	**Registration & Welcome Reception:** Le Shack, 3035 Chemin de la Chapelle	
Tuesday 26 June 2018		
8:00 - 8:45	**Registration**	
8:45 - 9:00	Introduction	
9:00 - 10:30	**Session 1**	**Large Scale Navigation**
	Nadasdy, Zoltan	Environment-dependent scaling of neuronal representations of space in the human entorhinal cortex
	Creem-Regher, Sarah	How does home city structure influence navigation preference and performance?
	Ulanovsky, Nachum	Neural codes for natural navigation in the hippocampal formation of bats
	Suthana, Nanthia	Medial temporal theta dynamics during ambulatory spatial navigation in humans
10:30 - 11:00	Break	
11:00 - 12:30	**Session 2**	**Path Integration**
	Chrastil, Elizabeth	Perceptual inputs and neural mechanisms of human path integration
	Dizio, Paul	Angular path integration in self-balancing
	Knierim, James	Recalibration of the path integrator gain in an augmented reality environment
	Stern, Chantal	fMRI Studies of Memory and Navigation
12:30 - 14:00	Lunch	
14:00 - 15:30	**Session 3**	**Virtual Space**
	Kelly, Jon	Teleporting through virtual environments
	Wirth, Sylvia	The coding of a virtual space in monkey hippocampus
	Ekstrom, Arne	How virtual and altered reality can help us understand the neural basis of human spatial navigation
	Lewis, Rick	Spatial orientation in peripheral and central vestibular disorders: prosthetics and psychophysics
15:30 - 16:00	Break	
16:00 - 17:00	**Session 4**	**Neural Dynamics**
	Allen, Kevin	Head-direction cells escaping attractor dynamics in the parahippocampal region
	Frank, Loren	Continuous sub-second alternation between divergent spatial representations in the hippocampus
	Ji, Daoyun	Recall fear in a space: role of place cells and awake replay

17:00 - 18:00	**Data Blitz Session 1**	
	Bellmund, Jacob	Distorting the metric of spatial memory
	Peer, Michael	Spatial representation at different scales along the parahippocampal-retrosplenial axis
	Vanderelst, Dieter	Sonar-based mapping in bats: data, models and robots
	Zhao, Jiayan	Walking and Learning in a Large-Scale Mediated Space: Impacts of viewpoint transition and body-based cues on spatial learning in virtual reality
	Julian, Joshua	Grid realignment predicts human contextual memory
	Bott, Jean-Bastien	Imaging of medial septal glutamatergic neurons during freely behaving navigation in mice in a dry version of the Star-Maze task
	Chebat, Daniel-Robert	The Neural Correlates of Navigation via a Simplistic Sensory Substitution Device.
	Kelly, Debbie	Age affects spatial working memory in pigeons
	Navarro Schröder, Tobias	Electrophysiological markers of grid cell population activity across species
	Boone, Alexander	Do task instructions matter? Individual differences in navigation strategy in virtual environments
	Hejtmánek, Lukáš	Enriched body-based cues and transfer to real-world environments
	Kang, Louis	A geometric attractor mechanism for the self-organization of entorhinal grid modules
	Phillips, John	Spontaneous association of magnetic and visual landmark cues
18:00 - 19:00	**Poster Session 1**	

Wednesday 27 June 2018		
9:00 - 10:30	**Session 5**	**Cue Integration**
	Giacomo, Lisa	Principles governing the integration of landmark and self-motion cues in entorhinal cortical codes for navigation
	McNamara, Timothy	Cue combination in human navigation
	Cacucci, Francesca	The role of sensory information in building and supporting cognitive maps
	Burgess, Neil	Combining environment and self-motion in neural Self-Localisation And Mapping
10:30 - 11:00	Break	
11:00 - 12:30	**Session 6**	**(Re-) Orientation**
	Montello, Dan	What does it mean to be lost?
	Muzzio, Isabel	Neural codes of reorientation
	Laurens, Jean	The three-dimensional Head Direction cells system in mammals
	Cullen, Kathleen	Neural mechanisms for perceptual stability during voluntarily-generated self-motion

12:30 -14:00	Lunch	
14:00 - 15:30	**Session 7**	**Computational**
	Warren, William	A test of cognitive graph theory
	Lee, Albert	The statistical structure of hippocampal representations
	Maimon, Gaby	Computations underlying spatial navigation in Drosophila
	Barry, Caswell	Are grid cells really a spatial metric?
15:30 - 15:45	Break	
	Topic Discussion 1:	
15:45 - 16:30	Small vs. Large Scale Environments: Differences in Spatial Processing Discussants: Dan Montello, Nora Newcombe, Francesco Savelli	
16:30 - 17:45	**Data Blitz Session 2**	
	Dudchenko, Paul	Place cell repetition
	Maidenbaum, Shachar	Grid-like Hexadirectional Modulation of Theta Power in Human Entorhinal Cortex during Virtual Navigation
	Zutshi, Ipshita	Hippocampal Neural Circuits Respond to Optogenetic Pacing of Theta Frequencies by Generating Accelerated Oscillation Frequencies
	Bae, Crystal	Collaborative Route Planning and Navigation in a Novel Environment
	Lee, Sang Ah	Spatiotemporal continuity in episodic memory: A developmental approach
	Viana da Silva, Silvia	Genetically targeted expression of APP to CA3 subpopulation of hippocampal principal neurons leads to neuronal network dysfunction and memory impairment
	Gönner, Lorenz	Step-like movement of place-cell sequences: evidence for discrete attractor dynamics, or a decoding artefact?
	Doore, Stacey	Natural-language spatial cues for learning and navigating indoor environments
	Agrawal, Yuri	Vestibular loss is associated with impaired spatial navigation in Alzheimer's Disease
	Grübel, Jascha	EVE: A framework for running virtual reality experiments in neuroscience
	Sabariego, Marta	Spatial working memory performance and intrahippocampal processing recover after mEC lesions
	Becú, Marcia	Age-related preference for geometric cues during real-world navigation: behavioral and neuroimaging correlates
	Penazzi, Lorene	OLM interneurons activation during spatial navigation
	Quirk, Clare	Effects of manipulating theta frequency on medial entorhinal cells
	Barhorst-Cates, Erica	Active and passive learning of real-world environments with simulated restricted field-of-view
	Holmes, Corinne	Sequential memory, spatial integration, and observer movement: A new perspective on spatial memory

17:45 - 18:45	**Poster Session 2**	

Thursday 28 June 2018

9:00 - 10:30	**Session 8**	**Medial Temporal Lobe Computations**
	Barnes, Carol	Interrogating the navigation circuit: Many paths to the final destination
	Epstein, Russell	Perceiving the local spatial environment
	Hasselmo, Michael	Coding of space and time in the entorhinal cortex
	Jacobs, Josh	Electrophysiology of spatial navigation and memory in the human medial temporal lobe
10:30 - 11:00	Break	
11:00 - 12:30	**Session 9**	**Grid Cells**
	Leutgeb, Stefan	The function of medial entorhinal inputs to hippocampus
	Doeller, Christian	Grid-like coding for vision and navigation in human entorhinal cortex
	Sargolini, Francesca	Flexibility of the grid cell spatial code
	Hussaini, Abid	Cognitive dysfunction in Alzheimer's disease
12:30 - 14:00	Lunch	
14:30 - 17:30	Optional Outings	Departing from The Fairmont Hotel

Friday 29 June 2018

9:00 - 10:30	**Session 10**	**Developmental/Plasticity**
	Lever, Colin	Trace memory of vector coding in the subiculum
	Nardini, Marko	Development and learning of new navigational skills
	Burgalossi, Andrea	Single-cell stimulation in freely-moving rodents: insights into the plasticity of spatial representations
	Newcombe, Nora	Assessing Individual Differences and Malleability in Navigational Skills
10:30 - 11:00	Break	
11:00 - 12:30	**Session 11**	**Alternative Cues**
	Hoffman, Kari	Revising brain-behavior classifications for exploration, movement, and vigilance states in primates.
	Fujisawa, Shigeyoshi	Spatial representations of self and other in the hippocampus during observational behavior
	Jacobs, Lucia	Rhinencephalon redux: the role of allocentric olfaction in navigation
	Sirota, Anton	Exploratory behavior modulation of hippocampal representation of space
12:30 - 14:00	Lunch	

14:00 - 15:30	**Session 12**	**Cognitive Mapping**
	Nitz, Douglas	Spatial periodicity and distance mapping in the retrosplenial cortex
	Taylor, Holly	Measuring uncertainty and what It means for navigation performance
	Smith, Paul	Transmission of vestibular information to the hippocampus and striatum in rats
	O'Keefe, John	How rats navigate: some recent studies on the place and grid cells of the hippocampal formation.
15:30 - 16:00	Break	
16:00 - 17:30	**Session 13**	
	Dickman, Dave Jeffery, Kate Mehta, Mayank Rondi-Reig, Laure Taube, Jeffrey Wolbers, Thomas	**Organizer Symposium** **Navigation: A Look to the Future**
17:30 – 18:15	**Topic Discussion 2**: The disconnect in metrics between recordings from spatial cells and human behavior. Discussants: Liz Chrastil, Doug Nitz	
18:15 – 18:30	**Wrap-up & Final Thoughts**	
19:30	**Conference Dinner:** Le Pont Couvert, 10, Rue du Centenaire, La Conception, Quebec	

Poster Session 1

Castegnaro, Andrea
Brandon, Mark P.
Alexander, Andy
Zhou, Ruojing
Weisberg,Steven
Etter, Guillaume
Ball Danny
LaChance, Patrick
Miller, Jonthan
Mao, Dun
Mussells Pires, Peter
Giudice, Nicholas
de Cothi, William
Lei, Xuehui
Kornienko, Olga
Liang, Mingli
Harootonian, Sevan
Zhang, Ningyu
Rekers, Sophia
Omer, David
Riemer, Martin
Huffman, Derek
Savelli, Francesco
Aarse, Janna
Keinath, Alexandra
Gurau, Oana
Chen, Guifen
Cheng, Han
Paradis, Anne-Lise
Geerts, Jesse
Jacob, Pierre-Yves
Moore, Jason
Rozeske, Robert

Poster Session 2

Umiltá, Alberto
Brandon, Mark
Street, James
Rondi-Reig, Laure
Cheng, Lilian (You)
Cherep, Lucia
He, Chuanxiuyue
Nazareth, Alina
Ball, Danny
Gönner, Lorenz
Segen, Vladislava
Kim, Soyoun
van der Veldt, Suzanne
Hinman, James
Viejo, Guillaume
Duszkiewicz, Adrian
Tsitsiklis, Melina
Bennett,Christopher
Giudice, Nicholas
Sheynikhovich, Denis
Maimon, Shir
Wunderlich, Anna
Mou, Weimin
Lefeldt, Nele
Constantinescu, Alexandra
Ajabi, Zaki
Hilton, Christopher
Bonner, Michael
Qasim, Salman
Ferris, Bennet
Zhang, Ningyu
Maimon, Gaby
Shelley, Laura

Registered Participants iNav 2018

Janna Aarse | Baylor College of Medicine
Yuri Agrawal | Johns Hopkins University
Zaki AJABI | McGill University
Hessameddin Akhlaghpour | Rockefeller University
Andy Alexander | Boston University
Kevin Allen | University of Heidelberg
Sandybel Angeles-Duran | McGill University, Montreal Neurological Institute
Crystal Bae | University of California, Santa Barbara
Erica Barhorst-Cates | University of Utah
Carol Barnes | University of Arizona
Caswell Barry | UCL
Joshua Bassett | University College London
Marcia Bécu | UPMC - Institut de la Vision - Sorbonne Universités
Jacob Bellmund | Kavli Institute for Systems Neuroscience, NTNU, Trondheim, Norway
Michael Bonner | University of Pennsylvania
Alexander Boone | University of California - Santa Barbara
Jean-Bastien Bott | McGill University - Douglas Institute
Thackery Brown | Georgia Institute of Technology
Andrea Burgalossi | CIN - University of Tübingen
Neil Burgess | UCL Inst of Cognitive Neuroscience
Francesca Cacucci | UCL
Andrea Castegnaro | University College London
Daniel Chebat | Ariel University
Guifen Chen | UCL
You Cheng | University of California, Santa Barbara
Han Yin Cheng | Institute of Behavioral Neuroscience, University College London
Lucia Cherep | Iowa State University
Elizabeth Chrastil | University of California, Santa Barbara
Alexandra Constantinescu | University College London
Sarah Creem-Regehr | University of Utah
Kathleen Cullen | Johns Hopkins University
William de Cothi | UCL
David Dickman | Baylor College of Medicine
Paul DiZio | Brandeis University
Christian Doeller | NTNU
Stacy Doore | Vemi Lab, UMaine
Yu Du | Department of Psychology, University of Alberta
Paul Dudchenko | University of Stirling
Adrian Duszkiewicz | McGill University
Arne Ekstrom | UC Davis
Russell Epstein | University of Pennsylvania
Guillaume Etter | McGill University & Douglas Mental Health Research Institute
Corey Fernandez | Stanford University
Bennett Ferris | Rockefeller University
Loren Frank | HHMI / UC San Francisco
Shigeyoshi Fujisawa | RIKEN Brain Science Institute
Tamara Gedankien | Columbia University
Jesse Geerts | Sainsbury Wellcome Centre
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Roddy Grieves | UCL

Jascha Grübel | ETH Zuŕich - Chair of Cognitive Science
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Sevan Harootonian | University of California Davis
Michael Hasselmo | Boston University
Chuanxiuyue He | University of California, Santa Barbara
Mary Hegarty | University of California, Santa Barbara
Lukáš Hejtmánek | UC Davis
Christopher Hilton | Bournemouth University
James Hinman | Boston University
Kari Hoffman | Vanderbilt University
Corinne Holmes | Trinity College Dublin
Derek Huffman | Center for Neuroscience University of California, Davis
Abid Hussaini | Columbia University Medical Center
Itzel Ishida | The Rockefeller University
Pierre-Yves Jacob | Laboratory of Cognitive Neurosciences - Aix-Marseille University
Joshua Jacobs | Columbia University
Lucia Jacobs | University of California, Berkeley
Kate Jeffery | University College London
Daoyun Ji | Baylor College of Medicine
Joshua Julian | Kavli Institute for System Neuroscience, NTNU
Louis Kang | University of California, Berkeley
Alexandra Keinath | Douglas Hospital Research Center / McGill University
Jon Kelly | Iowa State University
Debbie Kelly | University of Manitoba
Soyoun Kim | Korea Institute of Science and Technology
Brooke Klatt | Johns Hopkins University
Olga Kornienko | Department of Clinical Neurobiology and University of Heidelberg
Patrick LaChance | Dartmouth College
Jean Laurens | Baylor College of Medicine
Sang Ah Lee | Korea Advanced Institute of Science and Technology
Albert Lee | HHMI Janelia Research Campus
Nele Lefeldt | Baylor college of medicine
Xuehui Lei | University of Alberta
Stefan Leutgeb | University of California, San Diego
Colin Lever | Durham University
Richard Lewis | Massachusetts Eye & Ear (MEEI)
Mingli Liang | UC Davis
Eleonora Lomi | Oxford
Shachar Maidenbaum | Columbia University
Shir Maimon | Weizmann Institute of Science
Gaby Maimon | The Rockefeller University
Dun Mao | Baylor College of Medicine
Timothy McNamara | Vanderbilt University
Mayank Mehta | UCLA
Jonathan Miller | Columbia University
Meredith Minear | University of Wyoming
Uma Mohan | Columbia University
Dan Montello | UC Santa Barbara
Jason Moore | UCLA
Weimin Mou | University of Alberta
Marie Müller | University of Zurich
Peter Mussells Pires | Rockefeller University
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Adrien Peyrache | McGill University
John Philbeck | The George Washington University
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Salman Qasim | Columbia University
Clare Quirk | University of California San Diego
Sophia Rekers | Berlin School of Mind and Brain, Humboldt Universitaet zu Berlin
Martin Riemer | German Center for Neurodegenerative Diseases (DZNE), Magdeburg
Jennifer Robinson | Boston University
Sebastien Royer | Korea Institute of Science and Technology
Robert Rozeske | Douglas Hospital Research Centre, McGill University
Laure Rondi-Reig | CNRS, Paris
Marta Sabariego Collett | UCSD
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Jan Wiener | Bournemouth University

Sylvain Williams | McGill University, Douglas University Institute
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Ningyu Zhang | UCL
Jiayan Zhao | Penn State University
Ruojing Zhou | German Center for Neurodegenerative Diseases
Ipshita Zutshi | University of California, San Diego

Poster Session - Abstracts iNAV 2018

MVPA REVEALS DIFFERENT NEURONAL CODES FOR THE ACCUMULATION OF SPATIAL DISTANCE, TRAVEL TIME AND NUMEROSITY

Martin Riemer 1,2,3

Esther Kühn 1,2

Thomas Wolbers 1,2

1 Aging & Cognition Research Group, German Center for Neurodegenerative Diseases (DZNE), Magdeburg, Germany

2 Center for Behavioral Brain Sciences, 39118 Magdeburg, Germany

3 Medical Faculty (FME), Otto-von-Guericke University, Magdeburg, Germany

The compelling interdependency between the perception of space, time and numerosity is especially evident in the domain of spatial navigation, because moving in space requires time and is usually associated with a higher amount of encountered events. Knowledge about the length of a covered distance contains valuable information about the corresponding travel time and vice versa.

We used fMRI to identify the neuronal networks underlying the processing of traveled distance, travel time and numerosity. Twenty-five healthy, young participants were tested in a virtual environment, walking along a straight path, while their attention was directed either to travel time, traveled distance, or to the amount of blinking dots appearing on the surface of the path. An adaptive testing strategy was employed to ensure equal difficulty between the conditions, which could be verified by behavioral performance parameters.

When compared to a perceptual control condition, space, time and numerosity trials recruited common neuronal networks in the right intraparietal sulcus (IPS) and the right inferior frontal gyrus (IFG). Despite these overlapping activations, however, we were able to decode information about space, time and numerosity from the multivariate patterns in both regions.

Together, our results demonstrate that neuronal networks in the right IPS and the right IFG, which are recruited during the processing of different magnitudes, still contain domain-specific information and challenge the idea of a dimension-independent generalized magnitude system.

INVESTIGATING SPATIAL NAVIGATION IN AMNESIC PATIENTS: A COMPARISON BETWEEN IMMERSIVE AND COMPUTER-BASED VIRTUAL REALITY

Oana Gurau-University of Oxford, Nuffield Department of Clinical Neuroscience

Alexander von Klemperer-University of Oxford, Department of Pharmacology

Prof Kia Nobre-University of Oxford, Department of Experimental Psychology

Dr Chris Butler-University of Oxford, Nuffield Department of Clinical Neuroscience

Assessing spatial memory is important in hippocampal disease. Immersive virtual reality (iVR) confers tight experimental control in a multi-sensory environment and may offer advantages over traditional, computer based VR (cVR). We used iVR/cVR to study object location memory in a circular arena. We recruited young and old healthy subjects and amnesic patients. Preliminary results show that in both elderly controls and amnesic patients, spatial precision is improved by using the immersive environment. Patients nonetheless demonstrate a memory-specific deficit in item location. iVR may be a clinically useful tool for studying navigation deficits in neurological patients.

REPRESENTATION OF VOLUMETRIC SPACE IN THE RAT HIPPOCAMPUS

Roddy M. Grieves and Kate J. Jeffery

Institute of Behavioural Neuroscience, Division of Psychology and Language Sciences, University College London, London, WC1E 6BT, UK

Place cells are neurons in the hippocampus that increase their firing rate when an animal visits specific regions of its environment, these regions of high firing rate are known as ‘place fields’. When place cells are recorded in flat, horizontal environments each cell typically exhibits one or two place fields which have a round shape and small size (around 20cm diameter). The spatial activity of place cells is thought to underlie an animal’s ability to localise itself in space. This is supported by the fact that an animal's position can be inferred using the activity of only a handful of place cells.

How might these cells represent three-dimensional volumetric space? Do place fields extend into the vertical domain and if so, how? The round place fields recorded in flat environments may be slices through spheres. Such a representation would allow an animal to localise itself equally well in all dimensions. In contrast they may be slices through columns or other vertically elongated shapes. Representations like this would provide less spatial information about the vertical dimension.

We investigated this issue in rats freely exploring a three-dimensional volumetric space; a cubic honeycomb composed of horizontal and vertical climbing bars. Place fields recorded here had normal horizontal characteristics but many were elongated vertically, forming stretched spheres or elongated ellipsoids. Decoding the position of animals in this maze using only the activity of place cells revealed lower spatial information in the vertical dimension. These results suggest that place cells represent three-dimensional volumetric space unequally, or anisotropically, with vertically elongated place fields.

Place cells recorded in freely flying bats have been shown to exhibit near spherical place fields, suggesting that these animals have an isotropic (equal in all dimensions) representation of volumetric space. Why might the place cells of rats differ? Based on previous findings, it seems that grid cell odometry (and by implication path integration) may be impaired in the vertical domain, perhaps largely due to body movements which are perpendicular to the axis of the animal's body. Future experiments will look to explore the effects of such body movements on spatial representations more closely.

PATH INTEGRATION IN LARGE-SCALE SPACE AND WITH NOVEL GEOMETRIES

Harootonian S.K., Ziskin E., Erlenbach E., and Ekstrom A.D.

University of California, Davis

Path integration is an important mechanism that can function with no visual input and involves employing vestibular, proprioceptive, and somatosensory inputs to track direction and distance. Theoretical models suggest that importance of error accumulation in both direction and distance to path integration in humans, although these issues have been difficult to fully test in the small-scale (roomed-sized) environments employed in most studies. The triangle completion task is one important method for studying path integration, which involves participants integrating the distance and direction traveled through two guided legs to complete a third unguided leg, with participants returning to the origin with no visual or auditory information. Employing the triangle completion task also allows testing of the effect of different shapes of triangles (scalene vs. equilateral vs. isosceles), allowing determination of whether participants employ geometric templates (e.g., equilateral triangle) to compensate for incomplete path integration knowledge . Here, we used an omni directional treadmill to test accumulation of direction and distance errors, testing a larger range of distances and triangle types than past studies. Experiment 1 focused on scalene triangles of different distances (unguided leg: 15m, 25m, 125m, 250m and 500m perimeters). In Experiment 2 we tested participant on seven different triangles (2 scalene, 1 equilateral, 1, right angle, 1 isosceles, and 1 right isosceles) while the lengths of the triangles are held constant at ~25m. Our preliminary results show an underestimation of distance with the error scaling linearly with the size of the triangle, replicating findings from past studies with smaller-sized triangles. We also found an overestimation of the turn independent of the triangle configuration, also consistent with past studies using the triangle completion task. We did find, however, that equilateral triangles showed the lowest direction and distance error overall, consistent with the possibility that these particular triangles involve the least memory load. Overall, our findings suggest that the properties of path integration do not change substantially over longer distances yet there may be a bias for certain triangle types to be more readily learned than others.

DISSECTING THE ROLE OF MEDIAL SEPTAL CIRCUITS IN THE HIPPOCAMPAL CODE FOR TIME

Yong, H. (1) & Brandon, M. P. (2)

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Recent work has shown that hippocampal neurons code for the time spent in the delay period on a delayed spatial alternation task. These 'time cells' have been shown to require input from the medial septum(MS) as muscimol inactivation of the MS disrupted the activity of time cells and impaired memory. However, the exact role of the MS in time cell function remains unclear as the inactivation persisted for the full duration of the behavior task. It is possible that time cells may require information computed outside of a delay zone by other areas that rely on the MS. Also, the inactivation silences the activity of all septal neurons, thus it is unclear which cell populations within the MS supports the time cell activity. We, therefore, pursued an optogenetic approach to selectively silence genetically defined cell populations within the MS only when animals ran on the treadmill in the delayed spatial alternation task. Here, we specifically tested the role of GABAergic neurons in the MS, which are believed to have a role in the generation of the hippocampal theta rhythm. We injected the VGAT::Cre animals with AAVDJ-EF1a-Flex-ArchT-eGFP. They were trained to alternate in the Tmaze, and to run on the treadmill for 10s between each alternation. Activity of time cells was recorded from CA1 region of the hippocampus, and the MS was silenced when animals ran on the treadmill. We found that optogenetic inactivation of the septal GABAergic neurons cause a 70-80% reduction in theta power, similar to results observed with the muscimol inactivation. Also, the optogenetic inactivation had heterogeneous effects on the activity of time cells. However, their memory performance remained intact. Next, we plan to assess the role of the remaining cell types in the MS including cholinergic and glutamatergic neurons. Together, this data will reveal which MS populations are important for time cell function, and this will shed light on the underlying mechanisms of these time cells.

SPATIAL NAVIGATION IN NORMAL AGING

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Spatial navigation is known to be susceptible to cognitive aging as well as associated with the onset of Alzheimer's disease. Component navigation skills are dependent on different cortical regions and comparing their rates of decline could elucidate this vulnerability. Motivated by recent findings of this kind, e.g., age-related decline in path integration on a triangle completion task (Stangl, et al., 2018), the current study aimed to characterize aging effects in route learning and route integration. We used a virtual navigation paradigm that has been previously used to test children and young adults (Nazareth et al., 2018) and has been effective in categorizing different types of navigators. Data from a subset of the targeted sample have been analyzed so far (21 older adults aged 65-79 and 24 young adults aged 18-30). Participants viewed a first-person recording of the VE along two main and two connecting routes and were asked to remember locations of 8 target buildings. They then performed a within-route pointing task that assessed route representation, a between-route pointing task that assessed route-integration, and a model-building task that tested the accuracy of the participant's overall representation. Participants also completed a mental rotation (MR) task. Preliminary analysis suggests that young adults performed significantly better than older adults on both the within- and between-route pointing tasks (d= 1.31 and .61 respectively), as well as on MR (d = 1.36). There were no significant age differences on the model-building task, although the younger sample did somewhat better (d = .54). MR was correlated with the large-scale VE measures in both age groups. Our findings suggest age-related deficits in both route learning and route integration. Analyses of the full sample will be available for iNAV and will include working memory and episodic memory measures.

VARIANT RESPONSES OF RETROSPLENIAL BI-DIRECTIONAL CELLS IN A CUE-RICH ENVIRONMENT

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(The following is a revised one)

A classic limbic head direction (HD) cell fires whenever the rat faces a particular direction and stays inactive in others. The recent discovery of bi-directional (BD) cells in rat retrosplenial cortex (RSC) reveals a dominance of visual landmarks in part of the HD circuit. A BD cell fires when the rat faces in either of two opposing directions in a symmetrical black box that consists of two connected identical compartments, each scented with a unique odour and adorned with a cue card on opposing sides of the wall. Two reversed firing peaks of BD cell constitute BD tuning curves in the whole box, and 2/3 of cells reserved a BD pattern in single enclosures. However, it is unclear what primarily drives the responses of BD cell and whether they emerge specifically from the symmetrical box. We hypothesised that if the directionality of BD cell is principally driven by visual inputs, then they may show directional tuning to global cues even in an asymmetric space; or BD cell may lose tuning due to changes of visual cues and/or configuration. Thus, in addition to the box, where BD cells were identified, we recorded RSC directional cells in a circular open arena surrounded by rich distal cues, before and after the box trials. We found mixed responses of 23 BD cells in the open field - 4 cells showed stable directional tuning, and 4 were responsive and tuned only in the last trial, where 4 of the 8 maintained a BD pattern; whereas 2/3 were considered non-directional, including 7 that were active in both trials but directionally tuned only in either trial, and the rest that fired in all directions. In contrast, 22 HD cells behaved coherently as normal, firing uni-directionally across environments. Variant responses of BD cells suggest a subtle effect of distal landmarks - may not be as effective as the controlled intra-maze cues in serving as directional anchors of BD cells. Our results showed generalised distinct responses of BD cell from HD cell in a cue-rich open space.

TOWARDS A NEURAL UNDERSTANDING OF LOCAL SEARCH BEHAVIOR IN DROSOPHILA

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Central place foragers, such as desert ants and honeybees, are able to return from a foraging excursion by reference to an internal estimate of their position relative to the nest. The paths they take suggest that a vector addition process occurs in their brains, termed path integration. However, the neural substrate for path integration has proven difficult to study in these organisms due, in part, to the lack of genetic tools. We have developed a simple 2D navigation task for Drosophila by exploiting a walking pattern that fruit flies execute after consuming food, called search behavior. Searching flies accurately return to the food consumption location, often dozens of times, during a search, suggesting that they remember the food location and return to it via a process similar to path integration. To study the neural substrate of search behavior in real time, we developed a tethered version of this behavioral task, allowing us to image and manipulate neuronal activity while the fly executes a local search in a virtual reality environment. We hypothesized that the central complex, a region of the Drosophila brain that harbors head-direction-like signals, might be used to guide returns to the food location. In preliminary experiments, we have explored the activity of subsets of neurons in the central complex during search behavior and found sucrose responsive neurons in the fan-shaped body. The anatomy of these neurons suggests they are well-poised to convey information about the timing of a feeding event to head-direction-like neurons in the central complex, and thus they may serve a role in shaping search behavior.

TESTING HYPOTHESES OF HOW MULTISENSORY SELF-MOTION SIGNALS UPDATE THE HEAD DIRECTION NETWORK.

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The navigation system's ability to path integrate depends on multisensory self-motion signals. Understanding the interplay of visual, vestibular, somatosensory and efference copy signals in generating these signals is a crucial step for comprehending spatial navigation and designing virtual reality (VR) systems.

In the last decades, a series of quantitative models have emerged (Oman 1982; Glasauer 1992; Merfeld 1995; Laurens 2007; Karmali 2012; Laurens and Angelaki 2011, 2017, 2018) that assume the brain processes multisensory information using dynamic Bayesian inference and an internal model of self-motion. These models have been extensively validated by simulating a wide panel of behavioral and neuronal responses in humans and non-human primates during active and passive motion. Here we demonstrate that these models also account for the generation of multisensory rotation signals to update the Head Direction (HD) network in rodents.

We recorded HD cells in the Cortex and Thalamus of mice that were installed in a VR system mounted on a 6D motion platform. We applied a battery of classical visuo-vestibular paradigms that are designed to reveal the transformation of multisensory information (vestibular, visual and graviceptive) into rotation signals. Importantly, we found that HD cells robustly encode head direction with similar firing as during active motion when rotating passively in the presence of visual landmarks. In contrast, long-duration rotations with restricted visual information lead to inaccurate but predictable self-motion signals, whose gain and dynamics can be simulated by Bayesian models. We found that HD responses correspond to the temporal integration of the predicted rotation signals.

We conclude that the HD network integrates self-motion signals that are governed by well-established quantitative models of central visuo-vestibular information processing. These models apply to rodents, and in particular to VR environments.

ORIENTING IN A VISUAL WORLD: AN INTACT CORTICAL VISUAL PATHWAY IS NECESSARY FOR LANDMARK ANCHORING OF RAT HEAD DIRECTION CELLS

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In solving navigational tasks, rats must integrate rich visual scenes into their cognitive map so as to align their representations of space with the world. These spatial representations in the brain include head direction (HD) cells, which encode the azimuth bearing an animal faces in an environment, and provide a likely neural substrate for a 'sense of direction'. Although HD cell activity is maintained using vestibular information, visual information can be used to reorient cell activity through 'landmark anchoring' to prominent cues.

Which features within a visual scene are integrated into the HD signal, and through what pathway does this information enter the HD system? Do the cortical and subcortical visual pathways perform different roles in processing landmarks? We hypothesised that, if the HD system receives information solely from the cortical pathway, anchoring would be impaired if this pathway was disrupted.

We present HD cells recorded from the postsubiculum of rats with lesions of the lateral geniculate nucleus, a key relay nucleus of the cortical visual pathway, but with an intact subcortical pathway. Rats foraged in a cylinder with two large visual cues attached to the walls at 180 degrees apart. The symmetry of the cue configuration enabled testing of detection and discrimination of different cue cards: high-contrast, patterned, and control cues. The cylinder was rotated between trials to test for landmark anchoring.

HD cells from lesion animals did not landmark anchor to any of the cue card combinations tested. These results indicate that an intact cortical visual pathway is necessary for the integration of landmark information into the HD system, and may also underlie visual information flow into other areas of the spatial navigation network. Future work may target striate and extrastriate visual cortex to test how these areas process cue-relevant information and contribute to its integration into abstract representations of space.

FAST POSTSYNAPTICALLY-GATED PLASTICITY CAN GENERATE PLACE-CELL RECEPTIVE FIELDS FROM MODULAR AND DISTORTED GRID-CELL INPUTS

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Grid cells provide a well-characterized spatial input to place cells. Recent studies have suggested that this input is especially important to place fields in the center of large arenas—consistent with the remarkable ability of grid patterns to cover open spaces of arbitrary sizes. We previously described a spiking model of place-field formation based on Hebbian plasticity and integration of grid inputs simulated over real animals' trajectories. The momentary firing rate of grid inputs to place cells determined the direction of synaptic weight changes, which were gated postsynaptically by the place cell activation—consistent with later experimental observations that intrinsic excitability is correlated with a cell's propensity to form a place field. Very high learning rates were necessary for place fields to form, sometimes causing their abrupt emergence, also consistent with experimental observations. A wealth of new data, however, motivates the revision of some of the original input assumptions. (1) Grid orientation and scale are co-modular, unlike the more uniform and independent parameter distributions originally assumed. (2) Grids can undergo distortions such as compression and shearing. (3) Peak firing rates can vary across different vertices. In new simulations, adding these properties to the model inputs did not compromise its ability to produce spatially selective place fields. Place fields also emerged in simulations with trajectories recorded in larger (1.4x1.4m) arenas where more grid scales can be expressed, but more fields tended to be produced per cell, consistent with experimental observations. Thus, the principles derived from the original simulations—that place fields can form autonomously from grid cell inputs via a fast, postynaptically gated, Hebbian plasticity rule—hold up to more recent data that contradict some of the assumptions of the original simulations, demonstrating the generality of these principles across various test conditions.

UNRAVELLING THE ROLE OF THE RETROSPLENIAL BIDIRECTIONAL CELLS IN LANDMARK PROCESSING – NEUROANATOMY TO BEHAVIOUR

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For efficient navigation, a subject must be able to disambiguate similar local environments and locate themselves globally. To do so, a neural substrate that conjunctively encodes both local and global environment is likely to exist. The discovery of bidirectional (BD) cells in a symmetrical, visually-rotated two-compartment box (Jacob et al., 2017) suggests that such conjunctive encoding might exist in the head direction (HD) system. In that study, a subpopulation of directional cells in dysgranular retrosplenial cortex (dRSC) was found to be more sensitive to local visual cues.

We hypothesize that the BD system may exist as an anatomically separate system to the HD system, receiving a different pattern of inputs and supporting the use of local (as contrasted with global) compass information. To test this, we employed two parallel approaches: a neuroanatomical approach to find out the differences in inputs to dRSC and granular RSC (gRSC), and a behavioural assay to demonstrate the use of local compartmental information in rats.

Neuroanatomically, in retrograde tracing studies we observed differences in projections to the different RSC sub-regions, with gRSC (and by extension, only HD cells) receiving significantly more inputs from ADN and dorsal subiculum. Thus, gRSC may receive more bottom-up vestibular-weighted and context-related directional information. Preliminary observations suggest that there may also be a segregation in the inputs from anteroventral thalamus to the different RSC sub-regions. Behaviourally, we developed an object-location-odour task in which rats were found to be able to utilize context (odours) to detect a spatial displacement (location change) in the visually rotated two-compartment box. With these findings, future work can now be directed to dissecting the neural circuit underlying the BD system by selectively inactivating the relevant projections and examining the rats' ability to use its local compass to resolve spatial ambiguity.

EGOCENTRIC REPRESENTATION OF ENVIRONMENTAL BOUNDARIES IN THE STRIATUM.

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Movement through space is a basic behavior of all animals. Sensory information about the world and the movements executed are both represented within an egocentric reference frame, one that is centered on the agent. An animal sees something to its left and executes movements in a given direction relative to itself based on that information, such as walking straight ahead (of itself) or turning (away from) its left. Despite the fact that sensory information and behavioral output are represented within an egocentric reference frame, an extensive allocentric, world-centered, spatial representation is maintained within the hippocampal formation that is utilized for navigating to distant goals. In order for the allocentric translation vectors generated by the hippocampal formation to be acted upon they must first be transformed into an egocentric reference frame. The hippocampal formation is known to mediate allocentric navigation strategies, with several allocentric spatial cell types having been identified including grid, border, head direction and place cells. An alternative, egocentric, navigation system is localized within the striatum, yet little is known about how spatial information is represented within an egocentric reference frame. We implanted rats with hyperdrives targeting the medial portion of the striatum and recorded single units while they foraged in a large open field. A novel spatial cell type was identified that represents the boundaries of the environment within an egocentric reference frame that we have termed egocentric boundary cells (EBCs). Egocentric boundary cells fire when an animal is heading with a specific orientation and distance to any of the boundaries of the environment. Across the population of EBCs the presence of boundaries at a range of angles around the animal are coded. Unlike the allocentric spatial representation in the hippocampal formation that remaps across environments, EBCs maintain a stable egocentric representation of boundary locations relative to the animal across multiple familiar, as well as novel, environments. Overall, the medial striatum contains navigation related cells including EBCs that may be part of a larger egocentric spatial representation involved in implementing allocentric translation vectors generated by the hippocampal formation.

SPATIAL CORRELATES OF THE RETROSPLENIAL CORTEX DURING FREE EXPLORATION

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The retrosplenial cortex (RSC) is an association area that is highly interconnected with sensory and motor processing regions as well as structures including the hippocampal formation (HPC), entorhinal cortices (EC), and anterothalamic nuclei (ATN) that are known to represent an animal's position or heading direction with respect to the external environment. Given this anatomy, it is perhaps no surprise that neural ensembles of the RSC encode numerous variables relevant to spatial navigation, including: position within a well-known route, position or heading within a global and/or local environment, and the current or upcoming actions of the animal. Investigations of the HPC, EC, and ATN have often focused on spatial responses observed while the animal freely explores an open arena. In contrast, RSC spatial representations have, with a few exceptions, been primarily examined in linear environments while the animal performs track running tasks. Given that RSC serves as both an input and output hub for the broader neural spatial circuitry, it is important to register RSC spatial responses in the two-dimensional (2D) environment with respect to place cells, grid cells, and head-direction cells of the HPC, EC, and ATN. In the current work, we sought to further characterize RSC spatial representations during free exploration. To do so, we performed in vivo electrophysiological recordings while rats explored familiar and novel arenas that had varying shapes or visual cue configurations. Consistent with previous work, we observed both allocentric and egocentric spatial representations within the region during open field exploration. We report that individual RSC neurons can exhibit complex 2D spatial correlates that are reliable across sessions and can anchor to either local or distal cues. RSC neurons also exhibited linear and non-linear speed related firing as well as other self-motion correlates. Finally, a sub-population of RSC neurons exhibited activity that was tuned to the egocentric relationship of the animal with respect to environmental boundaries. Collectively, these results identify multiple features of RSC spatial mapping in 2D environments that may have interesting implications for the formation or anchoring of spatial correlates in regions reciprocally connected with the region.

IS ERROR ACCUMULATION IN GRID CELLS COHERENT WITH HEAD-DIRECTION DRIFT IN ABSENCE OF VISUAL LANDMARKS?

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Grid cells of the medial entorhinal cortex (MEC) provide an accurate estimate of the position of an animal. Computational models indicate that grid cells can be generated by a continuous attractor network in which grid cells are arranged according to their grid phase. Within the network, the position of the animal is represented by a localized bump of activity. When an animal moves, the activity bump moves within the network to keep track of the position of the animal, a process referred to as path integration. Path integration is thought to depend on the activity of head-direction (HD) cells and speed cells, which provide information about heading and running speed, respectively. However, there is still no definitive evidence that HD cells convey this directional information to grid cells because the interaction between these two cell types have not been studied extensively.

In this project, we aim to provide evidence that grid cells integrate directional information from head-direction cells. We performed simultaneous recordings of head-direction cells and grid cells in normal lighting conditions and in complete darkness. We found that during dark periods, the preferred direction of HD cells and grid cell orientation drift over time. We are currently testing different algorithms to extract directional information from the activity of pairs of grid cells. Ultimately, we want to determine whether the drift in the preferred directions of HD cells and that in grid cell orientations are coherent.

THE ROLE OF THALAMIC RETICULAR NUCLEUS IN PROCESSING OF THE HEAD-DIRECTION SIGNAL

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Head-direction (HD) cells serve as the brain's internal 'compass' and each of them is tuned to the specific direction the animal is facing, independently of its location and ongoing behavior. Recurrent inhibition is hypothesised to play an important role in controlling the network dynamics of the HD system and it may select subsets of neurons coding for the same direction. Thalamic reticular nucleus (TRN) provides inhibitory input to thalamic neurons and it may take part in shaping the HD signal in the anterodorsal thalamic nucleus (AD). Still, connectivity and functional importance of the AD-TRN circuit remain elusive.

We performed anatomical characterisation of the reciprocal TRN-AD circuit and used a combination of high-density single unit recordings and optogenetic interrogation in freely moving mice in order to assess its functional importance. Using viral-genetic tract tracing in VGAT-Cre mice, we observed that TRN sends a dense projection to AD, and that density of TRN projection is higher than in the neighbouring thalamic nuclei. Furthermore, injection of a retrograde fluorescent tracer into TRN produced ubiquitous labelling in AD, showing that vast majority of AD neurons project to back to TRN. Preliminary electrophysiological-optogenetic analysis of this reciprocal connectivity indicates that TRN inhibits thalamic HD cells: Optogenetic stimulation of TRN leads to inhibition of HD cells in AD at short latency.

Further experiments using selective optogenetic inactivation of AD-TRN and TRN-AD projections will determine whether thalamic inhibition plays a role in shaping the network activity and directional tuning of thalamic HD cells.

CODING OF SPATIAL VARIABLES IN THE HIPPOCAMPUS OF FREELY FORAGING MACAQUE

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The hippocampal formation (HF) is essential for spatial contextual learning and memory in both humans and animals. While the response properties of hippocampal neurons have been extensively characterized, mostly in rodents, how the HF encodes spatially relevant variables in freely moving primates remains little known. Using wireless neural logger, we recorded single unit activity and local field potentials (LFPs) with chronically implanted, movable tetrodes in the hippocampus of a rhesus macaque freely foraging for randomly scattered food pellets in a circular arena. The LFPs exhibited characteristic sharp-wave ripples (peak power at ~110-120 Hz) across a limited depth while no prominent theta-band oscillations (5-12 Hz) were observed during locomotion. To study the coding properties of hippocampal neurons, we fit multiple, linear-nonlinear Poisson models to the spiking activity of each neuron by focusing on the navigational variables position, head direction, and moving speed. Preliminary analysis indicates that a subset of neurons (~25%) encoded at least one of the 3 variables or a combination of them. We are currently investigating what other behavioral or internal variables could further improve model performance.

MODELING EGOCENTRIC BEARING SELECTIVITY IN THE RAT PARAHIPPOCAMPAL REGION

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Head direction cells, grid cells, and other spatially responsive neurons (including conjunctive cells) have been shown to intermingle within the postsubiculum (PoS), parasubiculum (PaS), and medial entorhinal cortex (MEC) of the rat. Population analyses across these regions reveal a rough transition from direction to position encoding, with PoS cells largely encoding head direction and MEC cells primarily encoding position information. These functional differences are in accordance with anatomical connectivity, as PoS receives projections from the head direction circuit and MEC provides dense inputs to the hippocampus where place cells are found. However, mechanisms underlying the functional transition from direction to position encoding have not been fully characterized.

We have developed a method for modeling potential aspects of this direction-position transformation by analyzing the encoding of egocentric place bearing (EPB) in parahippocampal cells. A subset of cells in the posterior parietal cortex fire in response to an animal's heading relative to a salient cue; it is therefore reasonable that cells could provide information about egocentric bearing relative to arbitrary places within an environment (i.e. egocentric place bearing), such that a navigating animal is constantly aware of how it is oriented with respect to its surroundings. The parahippocampal region, with its unique mixture of direction and position encoding, provides a potential substrate for this representation. Preliminary evidence suggests that EPB is indeed represented by parahippocampal neurons in a manner independent of allocentric head direction or position, with a general increase in EPB selectivity from PoS through PaS to MEC. Such area-specific differences could provide critical insights into fundamental mechanisms behind the transformation from direction to position encoding in the mammalian brain.

TRAVEL DIRECTION AS A FUNDAMENTAL COMPONENT OF HUMAN NAVIGATION

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Research in humans and animals has identified fundamental components of path integration, such as head direction and speed, that combine to support navigation.From first principles, however, travel direction, rather than head direction, should combine with speed and time to form a travel trajectory. Typically, head direction and travel direction are perfectly correlated, thus, how people's sense of self-motion responds to travel direction is still unclear. The goal of current study is to seek evidence from human behavioral data during linear travel that supports the hypothesis that travel direction is a fundamental signal for human navigation. We adopted an adaptation paradigm from visual neuroscience to show that navigation flexibly recalibrates in response to the environment. Participants experienced visual self-motion in a landmark-free virtual hallway. The hallway had a cardinal frame of reference marked by a sun and a moon, which were positioned over the far front and back end of the hallway, respectively. During the 60-second adaptation phase, participants first experienced travel toward the sun as the global travel direction. Critically, we included occasional turns to change the local facing direction while maintaining the constant global travel direction, thereby decoupling heading and travel directions. During the 10-second test phase, participants experienced back-

and-forth movement toward the sun and the moon. Participants were then asked to judge whether their movement during test was more toward the sun or more toward the moon. Visual adaptation of travel direction would be evidenced by a shift in the proportion of reported "sun" directions compared to the actual proportion of travel in the sun direction. Preliminary results suggest that people's behavioral response to linear travel direction flexibly recalibrates during visual adaptation.

A NEURAL SIMULATION OF HIPPOCAMPAL AND STRIATAL CONTRIBUTIONS TO LEARNING

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When solving spatial tasks, animals follow distinct navigational strategies. Previous work has shown that these strategies depend on a distinct set of brain regions. Allocentric place learning is dependent on the hippocampus, whereas the striatum underlies an egocentric response learning. We have implemented a simulation of these hippocampal and striatal contributions to spatial navigation. The model consists of a network of rate-coded neurons, with different learning rules governing the different brain areas. The striatum learns associations between sensory inputs and actions through a model-free reinforcement learning strategy relying on reward prediction errors. The hippocampus uses place cells to implement a model-based form of learning. To test our model, we used it to solve a variety of spatial tasks such as the Morris Water Maze, a double Y-maze and a multi-compartment environment. Our model explains a variety of behavioural findings in both healthy and hippocampal lesioned animals. In addition, we propose how this hippocampal representation could support multi-step planning using place cells that fire differentially for different trajectories.

THE EFFECT OF BODY-BASED CUES ON HUMAN NEURAL REPRESENTATIONS FOR SPACE FOLLOWING ACTIVE NAVIGATION

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Body-based cues, which include vestibular, proprioceptive, and somatosensory input, are hypothesized to play an important role in the neural basis of spatial representations formed during navigation. Alternatively, it may be that navigation-related spatial representations are largely modality independent, and thus body-based input, particularly during retrieval, may be less relevant. Due to technological limitations, however, little is known about the influence of body-based cues on neural representations of space in humans. Here, participants navigated three cities under different levels of body-based cues using novel immersive virtual reality devices: 1) impoverished condition: rotations and translations via joystick, 2) limited condition: rotations via body rotations and translations via joystick, 3) immersed condition: rotations via body rotations and translations via an omnidirectional treadmill. Participants were trained to criterion on a judgment of relative directions (JRD) pointing task on all three cities prior to fMRI scanning. During scanning, all participants performed better than chance on the JRD task for all three cities. Analyses of whole-brain activation and functional connectivity revealed no significant differences during the JRD task for the three levels of immersive encoding, suggesting little influence of body-based cues on retrieval of spatially relevant information during the JRD task. As a positive control, both the activation and functional connectivity analyses revealed significant differences between the JRD task and active baseline and rest conditions, which included brain areas previously implicated in navigation, such as the hippocampus, retrosplenial cortex, parahippocampal cortex, and precuneus. Together, our findings suggest that the absence of body-based cues does not significantly alter spatial representations relevant to navigation, supporting the idea that such representations are largely modality independent during retrieval.

DISSOCIATION OF FRONTAL-MIDLINE DELTA-THETA AND POSTERIOR ALPHA OSCILLATIONS: A MOBILE EEG STUDY

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Numerous reports have demonstrated low-frequency oscillations during navigation using invasive recordings in the hippocampus of both rats and human patients. Given evidence, in some cases, of low-frequency synchronization between midline cortex and hippocampus, it is also possible that low-frequency movement-related oscillations manifest in healthy human neocortex. However, this possibility remains largely unexplored, in part due to the difficulties of coupling free ambulation and effective scalp EEG recordings. In the recent study (Liang, Starrett & Ekstrom, Psychophysiology, in press), participants freely ambulated on an omnidirectional treadmill and explored an immersive virtual reality city rendered on a head-mounted display while undergoing simultaneous wireless scalp EEG recordings. We found that frontal-midline (FM) delta-theta (2-7.21Hz) oscillations increased during movement compared to standing-still periods, consistent with a role in active navigation. Our study thus provides novel evidence that FM delta-theta oscillations arise, in part, from real-world ambulation. In a second study, we next investigated the specificity of these oscillations to spatial navigation. The navigation related hypothesis would suggest that theta oscillations are specific to spatial navigation while the memory-related hypothesis would suggest theta oscillations represent a more general signal to both space and time, as is relevant to the task. In this second study, participants navigated a plus maze with one teleporter and one target store in each arm. They visited a sequence of stores interleaved with teleporters, with the teleporters providing a means of manipulating visual and ambulatory input that otherwise provide strong cues for movement. In spatial blocks, participants employed the distance traveled to determine which target store to visit, with time held constant, while in temporal blocks, participants used the amount of time spent in the teleporter to determine which target to visit, with distance held constant. Movement speed was balanced across all conditions. We recorded wireless scalp EEG using the same setup on an omnidirectional treadmill in the first study, while participants explored the plus maze containing teleporters. Analyses will specifically investigate whether movement-related frontal-midline theta oscillations 1) persist during teleportation, as suggested by a prior intracranial study using recordings in the hippocampus 2) are reduced or similar to what is observed during active body-based movement in other sections of the environments 3) code both spatial distance and temporal intervals, or are specific to space.

ROUTE LEARNING AND AGEING: ARE OLDER ADULTS REALLY WORSE NAVIGATORS?

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Older adults experience difficulties in several landmark based route learning tasks when compared to younger adults. In typical route learning paradigms, all participants are given the same exposure to the environment or route before their route knowledge is assessed. However, given a general age related slowing of cognitive processing, it is not surprising that, under these conditions, older adults learn less about the environment than young adults. We present a series of experiments to investigate whether impaired route knowledge in older adults actually reflects a specific spatial deficit or simply reflects a reduction in learning rate. In the first two route learning experiments, young and old participants either received the same amount of training (Experiment 1) or were trained until they could correctly recall at least 90% of the route (Experiment 2). In Experiment 1 we see the expected age-related differences in associative cue knowledge and knowledge for the sequence in which landmarks were encountered. When we control for learning in Experiment 2, we do find that old participants take longer to learn the route than younger participants, but the performance difference on the associative cue task is abolished. The only difference remaining between age groups relates to participants' knowledge about the sequence in which landmarks were encountered. Experiment 3 investigates the role of sequence knowledge in route learning and the related difficulties faced by older adults.

VENTRAL-DORSAL FUNCTIONAL CONTRIBUTION OF THE POSTERIOR CINGULATE CORTEX IN HUMAN SPATIAL ORIENTATION: A META-ANALYSIS.

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Many functional Magnetic Resonance Imaging (fMRI) studies investigating the role of the retrosplenial cortex in human spatial orientation and orientation often report increased neural activities that are localized outside of the conventional borders of retrosplenial cortex proper. This may suggest that the larger and anatomically heterogeneous region of the posterior cingulate cortex may be ascribed different functions in human spatial orientation and navigation. To test this hypothesis, we performed a meta-analysis of fMRI studies investigating spatial orientation and navigation. In all examined studies, we found that ventral portions of the posterior cingulate cortex were more likely involved in passive viewing of scenes, or navigation and spatial computation, all leading to an encoding process of spatial properties; conversely, dorsal portions of the posterior cingulate cortex were more likely to be involved by cognitive demands to recall spatial information in order to navigate to non-visible locations. The greatly varying resting-state functional connectivity profiles of these ventral and dorsal posterior cingulate regions support the conclusion that these regions are indeed contributing to different functional properties of the complex phenomenon of orientation and navigation.

CORTICAL REPRESENTATIONS OF THE NATURAL STATISTICS OF OBJECTS IN CONTEXT

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Many objects have a natural place in the world-a location or context where they can typically be found. For example, tea kettles are often found in kitchens and fire hydrants on city sidewalks. This type of contextual knowledge can help a navigator identify where it is in the world ("I'm in the kitchen") and what other objects it might encounter. A key issue for characterizing how contextual knowledge is represented in the human brain is understanding the statistical structure of object-and-scene co-occurrence in the natural environment. Here we used a technique adapted from computational linguistics to identify the latent statistical structure of object co-occurrence in a large set of natural scenes. This quantitative model generates a set of multidimensional embeddings that capture information about the contexts in which objects typically occur. We used these embeddings in an fMRI experiment to examine the cortical representation of contextual knowledge during natural object perception. In the scanner, subjects viewed a large set of objects, shown individually with no scene background. Using voxelwise encoding models, we identified linear mappings between the contextual embeddings of objects and their associated cortical responses, and we assessed whether these models could predict the fMRI responses to a held-out set of object categories. Our preliminary findings suggest that high-level visual cortex routinely encodes contextual associations when viewing individual, isolated objects, even when this information is not present in the immediate perceptual scene. These representations were most prominent in scene-selective regions, which have previously been implicated in the processing of spatial environments and navigational landmarks. These findings suggest that a key function of scene-selective cortex is to link the local perceptual scene with statistical representations of object co-occurrence in the natural environment.

AGE-RELATED CHANGES IN THE PROCESSES UNDERLYING OBJECT LOCATION MEMORY

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Successful navigation requires the ability to memorise and recognise the locations of objects from the same and different viewpoints. While past studies have shown age-related deficits in object location memory tasks, the source of these deficits remains unclear. In this study we have used a novel paradigm to further investigate the effects of cognitive ageing on object-location memory and on spatial perspective taking. The paradigm required participants to view arrays of 6 identical objects placed in the middle of a rectangular virtual room and then report at test whether something has changed. The image of the room presented at test could be from the same perspective as the one studied during encoding or involved a perspective shift of 45° or 135°. In half of the trials the object locations remained unchanged, whilst the spatial relationship between the objects was manipulated in the remaining trials. Preliminary signal detection analysis shows that the introduction of a 45° perspective shift leads to a substantial decrease in performance in older adults, with little additional effect from increasing the perspective shift to 135°. In contrast, performance of younger adults drops in a more linear fashion with increasing perspective shifts. Finally, the current data shows that older adults performed worse than younger participants across conditions in which object location was manipulated. This is discussed with reference to different spatial coding strategies in object location memory between younger and older participants

SINGLE-NEURON CODING OF CURRENT AND MOTIVATIONALLY RELEVANT LOCATIONS IN THE HUMAN MEDIAL TEMPORAL LOBE

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The hippocampus and surrounding medial temporal lobe (MTL) are essential for spatial memory and navigation, with an extensive rodent literature characterizing cell types involved in spatial coding. There is growing evidence that spatially selective cells code for goal locations in addition to current location. To investigate these representations in the human brain we are recording single-neuron data from patients with intractable epilepsy while they play Treasure Hunt, a video-game–like task that measures people's ability to remember links between objects and locations. I find that a significant proportion of MTL neurons show spatial modulation during each of the spatial task phases (navigation, encoding, and recall). Furthermore, during navigation I find that 7% of the MTL neurons are modulated by current location, and 11.5% are modulated by current goal location. During object-location encoding I find that the firing rate mainly reflects whether there is something to encode and not subsequent memory performance. This provides evidence that a significant proportion of human MTL neurons code for motivationally relevant locations in addition to current location during goal-directed spatial navigation.

CALCIUM IMAGING OF LATERAL SEPTUM GABAERGIC NEURONS IN FREELY BEHAVING MICE

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The lateral septum (LS) is the main subcortical target of the hippocampal formation, receiving strong projections from the pyramidal neurons of CA3, CA1 and subiculum neurons. A large body of evidence has underlined the role of the hippocampus in constructing a detailed internal spatial representation of the environment. However, there is little evidence on how this hippocampal spatial map is processed in downstream regions such as the LS for goal directed navigation. The LS consists of a large heterogenous population GABAergic cells. Spatially tuned cells have been previously reported in the LS (Zhou et al., 1999; Leutgeb and Mizumori, 2002; Takamura et al., 2006), yet how their firing characteristics relate to hippocampal inputs remains unknown. Using cutting edge viral tracing techniques and calcium imaging with miniaturized fluorescence microscopy, we characterized the spatial firing properties of cells in the LS based upon their anatomical connections and hypothesized functional relationship with the hippocampal formation and medial septum. For this, we recorded activity of pathway defined GABAergic LS subpopulations using both open field and goal directed navigation tasks.

ROLE OF MEDIAL SEPTUM PARVALBUMIN NEURONS IN SUPPORTING HIPPOCAMPAL PREDICTIVE CODING IN NORMAL AND AD CONDITIONS

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The exact role of the hippocampus in spatial learning and memory is still not fully understood. Earlier work and the discovery of place cells has comforted the existence of a cognitive map that relies on distance and direction codes that arise from entorhinal cortex grid cells. Several lines of research support the role of the hippocampus in predictive coding, both online during exploration through phase precession (firing of place cells ahead of their place fields) and offline, during sharp-wave ripples (preplay of trajectories to be explored). More recent models propose that the hippocampus codes for representations that maximize future reward by performing predictions (Stachenfeld et al., 2017). Importantly, hippocampal sequences can only be reliably observed in environment involving a memory task (Pastalkova et al., 2008) and medial septum pharmacological inactivations are associated with perturbed place cells offline, but not online processing (Wang et al., 2014). Importantly, place fields persist (Koenig et al., 2011) and can emerge in new environments (Brandon et al., 2014) under pharmacological medial septum inactivations that are associated with reduced hippocampal theta oscillations and grid fields abolition. However, since these experiments were not performed in an environment that involved a memory task, it is difficult to conclude on the impact of decreased theta on hippocampal coding. We propose that hippocampal theta rhythms that are supported specifically by medial septum parvalbumin interneurons contribute to offline predictions of the future behaviourally relevant locations to be explored. We combined chronic recordings of large CA1 hippocampal cell assemblies in mice performing in a spatial working memory task that involved enriched multimodal sensory cues. Because of the neurochemical complexity of the medial septum, we combined our calcium imaging recordings with targeted optogenetic modulation of medial septum parvalbumin cells to control theta rhythms. We performed calcium imaging in an APP mouse model in similar tasks to verify the relationship between CA1 predictive coding and spatial working memory performances.

A CELL CLASS THAT RELAYS SELF-MOTION INFORMATION TO AN ANGULAR INTEGRATION CIRCUIT IN DROSOPHILA

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Like many animals, fruit flies integrate their own locomotor movements to keep track of their angular orientation in the absence of external sensory cues. How is this computation achieved? Several cell classes important for building the fly's sense of heading were recently shown to innervate a central-brain structure called the protocerebral bridge. Here we report on the physiology of a new cell class that innervates the protocerebral bridge and seems to relay angular velocity signals to the heading circuit. These cells show calcium signals that correlate with the fly's angular velocity while the animal walks in the dark, but preliminary evidence suggests that these cells do not respond to rotational optic flow (a different cue that can update the fly's heading signal). Initial perturbational evidence suggests that disrupting these cells' synaptic output degrades the ability of the downstream heading system to update its heading estimate. Finally, in addition to signaling angular velocity, these cells' calcium signals also correlate linearly with the fly's forward walking velocity. Future work will determine how these cells contribute toward updating the flies' angular heading estimate and how forward velocity tuning in these cells interacts with their angular velocity signaling to influence their computational role in the circuit.

A NEURAL COMPARISON OF CURRENT AND DESIRED HEADING FOR CONTROL OF LOCOMOTOR STEERING IN DROSOPHILA

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The ability to maintain a desired heading direction is a basic component of many navigational tasks. Neurons sensitive to an animal's heading were first described in rats and, more recently, heading cells were also discovered in Drosophila. Specifically, a group of neurons innervating a donut-shaped structure, called the ellipsoid body, track the fly's angular heading through a sustained bump of calcium activity that travels around the donut. How do flies use this heading signal to guide behaviour? We found that wildtype flies walking in a simple virtual environment will maintain a fixed heading direction for several minutes, with the specific angle chosen to walk along varying across flies. Moreover, normal synaptic function in the heading neurons of the ellipsoid body is required for flies to properly execute such persistently oriented locomotion. Specifically, flies in which synaptic release in heading neurons is impaired do not make proper corrective turns towards their angular goal direction. Our results suggest that flies compare their current heading, as estimated by their heading neuron activity, with a target or goal heading direction, to control locomotor steering.

LOCAL MODIFICATION OF THE GRID CELL FIRING PATTERN IN A GOAL-DIRECTED NAVIGATION TASK

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Entorhinal grid cells are spatially selective neurons whose firing fields form a regular triangular pattern across an environment. This activity is thought to form an Euclidean map-like representation of the rat's location and orientation based on movement-related information. So far, grid cell firing has never been analyzed as rats are engaged in a goal directed navigation behavior. In this study, we recorded grid cells while rats performed a goal-directed navigation task in a circular arena polarized by a visual cue card. In this task, animals learnt to reach and stay for two seconds in an unmarked area, in order to receive sugar pellets that are randomly scattered on the floor. Animals performed the task in successive light, dark, and light sessions. Our aim was to determine if the presence of a spatial goal influences grid cell activity both in the presence and absence of external landmarks. Results showed that grid cell firing pattern is modified around the goal zone. In particular, field spacing expanded in the vicinity of the goal. Furthermore, we observed that the grid maps of all grid cells recorded during successive days had the same orientation in each single rat. Finally, grid cell spatial selectivity and regularity strongly decreased in darkness. This decrease was associated with altered performance in the task. That firing patterns can be distorted and locally modified in certain zones of the environment in a goal-directed navigation task suggests that motivational salience influences the grid cell spatial representation.

VARIANT RESPONSES OF RETROSPLENIAL BI-DIRECTIONAL CELLS IN A CUE-RICH ENVIRONMENT

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A classic limbic head direction (HD) cell fires whenever the rat is facing a particular direction and stays inactive in other directions. The recent discovery of bi-directional (BD) cells in rat retrosplenial cortex (RSC) reveals a dominance of intra-maze visual landmarks in directional signal processing. A BD cell fires selectively when the rat heads two opposing directions in a symmetrical box, which consists of two connected identical compartments, each scented with a unique odour and attached a directionally reversed cue card. Most BD cells reserved a BD firing pattern showing reversed firing peaks in single enclosures. However, it is unclear what primarily drives the behaviours of BD cells to be different from HD cells, and whether their distinct responses emerge specifically from the symmetrical configuration. We hypothesised that if the directionality of BD cells is principally driven by visual inputs, then they may show unidirectional tuning or maintain a BD pattern to global landmarks even in an asymmetric space. Alternatively, BD cells may lose tuning due to changes of visual cues and/or configuration. In addition to the symmetrical box, where BD cells were identified, we recorded RSC directional cells in a circular arena with rich distal cues before and after the box sessions. We found an intermixed responses of BD cells in the arena - some lost directional selectivity, whereas some showed directional tuning including a few maintained a BD pattern mostly in the last arena trial. In contrast, HD cells behaved coherently showing unidirectional firing patterns across environments, meaning that global landmarks effectively anchored HD cells, but not always BD cells. Variant responses of BD cells suggest a subtle effect of global landmarks in the current open arena, but the underlying directional signal awaits more evidence. Future experiments may test the effectiveness of landmark as directional anchor of BD cells with controlled cue type or availability.

HUMAN PERCEPTION OF SELF-LOCATION

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Place-selective cells have been identified in humans (Ekstrom et al., 2003), and complementary research on non-human primates (Hori et al., 2005) and rodents (Muller & Kubie, 1987) suggest that predictions about place responsive activity in human behavior warrant investigation. The current study was based on the finding (Lenck-Santini et al., 2005) that rodent place cells partially remap after spatial environmental change (rotating objects relative to enclosure) but are unaffected by non-spatial change (object substitution). Two experiments evaluated human perceived self-location in response to spatial and non-spatial change in a virtual environment (VE). Participants studied object locations in a learning VE with three orienting cues: two landmark objects and a blue stripe on the wall of the surrounding circular room. Participants then performed judgments of relative direction in which they imagined various perspectives using the learned object locations. This task was performed in a test VE that was unchanged from the learning VE, or in which the orienting cues were changed spatially (objects rotated relative to wall stripe) or non-spatially (object substitution). Perceived self-location was inferred from the presence/absence of a sensorimotor alignment effect (SAE), indicated by facilitation for imagined perspectives aligned with the body at retrieval. The presence of the SAE indicates the participant believes he/she is located in the learning VE. Contrary to predictions, the SAE was present in all test VEs, even the spatial-change VE. We proposed a methodological issue whereby participants ignored the blue stripe and therefore were unaffected by the spatial change. In the second experiment, relative salience of the landmark objects and wall stripe were equated. Current data indicate that perceived self-location in this experiment is disrupted by spatial change, as predicted by rodent place cell remapping.

VISION-BASED MODEL OF PRIMATE SPATIAL COGNITION: COORDINATE TRANSFORMATIONS, LIMITED VISUAL FIELD AND REORIENTATION

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Primate spatial orientation is a complex multisensory process heavily dependent on sensory inputs integrated and modulated in temporal and spatial domains. Even though rodent studies suggest a basic model of primate spatial orientation, several issues remain to be addressed. First, while extensive experimental evidence suggest that egocentric-allocentric coordinate transformations occur in the parietal cortex through the mechanism of gain modulation, it is still unclear how gain-modulated visual receptive fields are linked to location-sensitive firing in the hippocampal formation. Second, primates have a much smaller visual field in contrast to rodents. Whether basic learning algorithms, proposed to sustain place field learning in the rodent, can lead to coherent spatial representations under such a constraint remains an open question. Finally, both rodent and primate data suggest a segregation between geometric and landmark cues during vision-based reorientation, neural mechanisms of which remain poorly understood. To address these issues, we developed a neural network model of visual information processing for spatial learning that links parietal gain fields with spatial orientation functions, suggests a crucial role of visual short-term memory for spatial learning with a limited visual field, and provides an insight into geometry processing in the brain.

DO RATS AND HUMANS USE A PREDICTIVE MAP TO NAVIGATE STOCHASTIC ENVIRONMENTS?

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The mammalian brain has developed a remarkable capacity to flexibly navigate dynamic environments, exploiting shortcuts and taking efficient detours when needed. Past research has focused on three generally separate approaches: studying rats in mazes, humans in virtual reality and reinforcement learning (RL) algorithms in simulated worlds. Here we present a novel experimental framework allowing direct comparison between rats, humans and artificial RL agents as they navigate to a hidden goal in an open arena while negotiating dynamically shifting canyons that obstruct movement. Initial analysis reveals that rats and human display many similarities in their behaviour: demonstrating an impressive ability adapt to blocked paths and also common errors involving failures to suppress previously rewarded routes that are no longer effective. Preliminary analysis revealed that the trajectories of both species are most similar to the simulated trajectories of RL agents employing a successor representation their environment, providing support for the view that the neural systems for navigation use a predictive map of the environment to facilitate flexible behaviour.

CHARACTERIZING HEALTHY MEMORY AND EXECUTIVE FUNCTIONS THROUGH NAVIGATION TO DETECT COGNITIVE OUTLIERS AT THE INDIVIDUAL LEVEL

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Complex navigation involves not only motor and perceptual abilities but also memory and executive functions. Our challenge is to use a navigation task to evaluate both episodic memory and executive functions at the individual level, while disentangling their respective contributions.

The Starmaze is a virtual environment in which participants have to learn how to find their way. Along with this environment, we developed a number of parameters intended to qualitatively and quantitatively characterize the navigation behavior (strategy and performance) at each learning stage of the task. A dedicated software has been developed to automatize the computation of those parameters.

To characterize the functions contributing to the navigation performance and strategies, and associate them with specific navigation parameters, we had 40 volunteers undergo our navigation tasks on one hand and neuropsychological tests validated with respect to specific cognitive functions on the other hand.

By analyzing the navigation parameters and neuropsychological results altogether, we plan to cluster the navigation parameters into groups of co-varying performances associated with specific functions.

With this clustering, we will be able to determine the most relevant navigation parameters for assessing each function.

In parallel, we are gathering reference data to characterize the distribution of each relevant navigation parameter across the healthy population. With this reference database defining a Health record of memory and executive functions, we will be able to situate the navigation skills of any individual with respect to a control population (paired for age, sex…). We will illustrate how this paves the way for individual assessment with data from ASD patients.

CEREBELLUM, PLACE CELLS AND SEQUENCE BEHAVIOR

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Our ability to optimize navigation in a known environment requires the use of a reliable internal representation of the external world. The hippocampus contains specialized pyramidal neurons called place cells that fire at specific locations and provide dynamic information about self-location relative to the environment. Yet, converging evidences indicate that, during navigation, hippocampal pyramidal cells might also code for sequence, time or even goals, depending on the associated behavior. Our previous work indicates that cerebellar activity influences hippocampal spatial representation during free exploration of a familiar place. Whether it also participates in other aspects of hippocampal coding underlying navigation remains to be unveiled. In the current study, we designed a new behavioral task allowing to record hippocampal pyramidal cell activity as well as hippocampal and cerebellar LFP during both foraging and goal-directed behavior. Using an electrical stimulation of the medial forebrain bundle as reward, we showed that WT and L7-PCKI mice rapidly learn to alternate between direct paths to the goal and foraging behavior in the rest of the arena. However, while most WT spontaneously developed a reproducible complex sequence behavior to maximize the number of reward during foraging, this behavior was hardly observed in the mutant mice. In this context, hippocampal coding was strikingly different between WT and L7-PKCI mice. Indeed, WT pyramidal cells revealed loose spatial properties as illustrated by the higher number of cells with multiple place fields, the increase in out-of-field firing rate and the lower spatial information context compared to L7-PKCI mice. In addition, L7-PKCI mice express a higher proportion of hippocampal place cells coding for the goal location. Finally, analyses of oscillatory activity between hippocampal and cerebellar LFP revealed a lower coherence in the theta band in L7-PKCI mice compared to WT. These results strengthen the existence of a cerebellum influence on hippocampal activity.

THE DENTATE GYRUS ENCODE CONJUNCTION OF OBJECT AND SPATIAL INFORMATION VIA COMPETITIVE LEARNING

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The dentate gyrus is hypothesized to operate as a competitive network in which sparse-orthogonal representations emerge progressively during learning, yet physiological evidence are missing. We record over 27 days putative granule (GC) and mossy (MC) cells, identified by spike features and optogenetic, as mice run repetitively through a sequence of objects fixed on a treadmill belt. GCs initially encode specific object locations or distance intervals, suggesting excitation from single object or grid cell inputs, and progressively develop discrete context-specific or multiple non-specific place fields. MCs display numerous broad fields and strong firing rate increases in object locations that persists throughout learning. We show that a competitive network model incorporating hebbian learning reproduces GC transformations, predicts gradual integration of object and grid cell information, and requires modulation of inhibition by MCs to control object representations. Hence, GC competitive network progressively encodes conjunctions of object and spatial information and MCs regulate the information represented by GCs.

RAPID INCREASE IN NAVIGATIONAL PERFORMANCE AND HIPPOCAMPAL NEURAL ACTIVATION DURING A VIRTUAL WATER MAZE TASK

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The Morris Water Maze is a widely-used behavioral test of spatial learning, memory and navigation, yet the neural basis of this behavior is not well characterized. We have recently developed a virtual water maze task in which rats can run more than 100 trials in a single session [1], which allows measurement of within-session changes in behavior and the underlying neural dynamics. Surprisingly, we find relatively little allocentric spatial selectivity in pyramidal units in dorsal CA1, the traditional “Place Cells.” Instead, neural activity is tuned to other navigationally-relevant egocentric parameters, e.g. distance traveled, heading direction, linear speed, and angular speed [2]. Here, we investigate within-session changes in behavioral performance and neural activity. Extensive studies have shown that hippocampal activity is altered with experience, with a significant increase in the number of active neurons [3] and their firing rates [4,5] within the first few trials on a simple task, even in a familiar environment [3,4,5]. We find that during the virtual water maze, performance improved rapidly within the first 5-10 trials each day, even though rats were well-trained on the task. The mean firing rate of CA1 pyramidal neurons and the total number of neurons active also increased and behavioral performance was positively correlated with firing rate and tuning to egocentric parameters. Thus, experience-based changes in the egocentric neural activity are correlated with experience-based improvements in behavior. These experience-based changes may be driven by similar mechanisms of synaptic plasticity [4,5] demonstrated in earlier studies on linear tracks [3, 4, 5], thus linking behavioral learning with hippocampal activity and cellular mechanisms of plasticity.

1. JD Cushman et al. PLoS One (2013). 2. JJ Moore et al. SfN Abstract #263.03 (2016). 3. MR Mehta, BL McNaughton, NIPS (1997). 4. MR Mehta et al., PNAS (1997). 5. MR Mehta et al., Neuron (2000)

SINGLE-UNIT ACTIVITY FLEXIBLY MODULATED BY BOTH SPACE AND MEMORY IN THE HUMAN MEDIAL TEMPORAL LOBE

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The structures of the medial temporal lobe (MTL) have consistently been linked to spatial cognition and memory processes across species, including humans. However, the manner in which these structures participate in episodic memory retrieval as well as representation of spatial location is unclear. Recording from neurosurgical patients with depth electrodes in the MTL, we sought to untangle the spatial and mnemonic modulation of neural activity as subjects performed a memory task in a virtual environment. As has previously been reported we observed stable and consistent spatial firing indicative of place cell activity in the MTL while subjects moved through the environment. We also observed place-modulated cells that were flexibly active during maintenance and retrieval of object-location memories, as well as place-modulated cells whose spatial firing patterns differed between successful and unsuccessful memory trials. This is the first evidence of a conjunctive influence of space and memory retrieval on single unit activity, as well as the first evidence in humans for flexible spatial representations at the level of single cells. This serves as direct evidence that the MTL is involved in representing spatial location with reference to internal retrieval processes. These findings reveal the extent to which the brain's spatial framework may be modulated by episodic memory processes.

LATERALIZED HIPPOCAMPAL OSCILLATIONS UNDERLIE DISTINCT ASPECTS OF HUMAN SPATIAL MEMORY AND NAVIGATION

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The hippocampus plays a vital role in various aspects of cognition including both memory encoding and spatial navigation. To understand the electrophysiology of how the hippocampus supports these processes, we directly recorded intracranial electroencephalographic activity from 46 neurosurgical patients as they performed a spatial memory task. We measured signals from multiple brain regions, including both left and right hippocampus, and we used spectral analysis to identify signals related to memory encoding and navigation. In the left but not right hippocampus, the amplitude of oscillations in the 1-3 Hz "low theta" band increased when viewing subsequently remembered object-location pairs relative to those that were subsequently forgotten. In contrast, in the right but not left hippocampus, low-theta activity increased during periods of navigation. The frequencies of these hippocampal signals were slower than task-

related signals in the neocortex. These results suggest that the human brain includes multiple lateralized oscillatory networks that support different aspects of cognition.

CHARACTERIZING GRID-LIKE ACTIVITY PATTERNS IN HUMANS USING 7T FMRI

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When people think about 2D spaces, fMRI activity patterns corresponding to grid, place and head-direction cells can be seen, but characterizing these patterns, e.g. measuring gradients in grid-cell scale, is challenging. However, inhomogeneities in grid orientation and phase across grid cell populations could be leveraged to detect gradients in grid scales at the population level. We developed a novel 2D spatial autocorrelation analysis at the population level, using a representational similarity analysis approach. Using simulated data, we found that our method can detect hexagonal symmetry as a function of location in 2D space, across different grid scales. This pattern was specific to populations of grid cells, but not control noisy data. We next asked if such fine biases in the preferred grid phase across the population of grid cells could also be captured between different MRI voxels while people navigate virtual environments in a 7T scanner. We trained human participants to learn a spatial environment with high precision, and scanned their brains with sub-millimeter fMRI. We are currently analyzing these datasets with our method, and have been able to begin to characterize place-like codes in the human hippocampus.

COMPARING VIBROTACTILE SMARTPHONE INTERFACES FOR SUPPORTING NONVISUAL NAVIGATION OF VIRTUAL ENVIRONMENTS

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Exploring virtual spaces using vibration and audio cues via touchscreen-based smartphone interfaces, called a vibro-audio map (VAM), has proven effective for conveying and learning spatial information without vision. This study investigated the use of the VAM for navigation of 3-leg indoor routes rendered using two different frames of reference. In the North-Up interface, information was rendered with a fixed display where the top indicated a cardinal north orientation. In the Forward-Up interface, information was rendered so the top of the display consistently represented the participant's forward walking direction. In the learning phase, blindfolded-sighted participants explored the phone's touchscreen by using a single finger to trace the corridor layout, with hallways represented as the region between two parallel vibrating lines (i.e., representing walls). In both conditions, different audio cues were used to indicate the start and end positions, intersections, and wall collisions. In the testing phase, participants were positioned at the route's starting point in a virtual environment (VE), and instructed to physically walk the route just learned from the VAM and to verbally indicate when they believed they had reached the route's terminus. Statistically significant results were found for the North-Up interface, where participants performed at higher levels of task completion accuracy with lower task learning times compared to participants using the Forward-Up interface. Findings have implications for development of haptic interfaces supporting spatial learning and non-visual navigation. Broader applications of this work will also inform the design of new navigation displays for eyes-free applications (e.g., driving, emergency response, etc.) and use by blind and visually impaired navigators.

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A MULTIMODAL THERMOGRAPHIC INTERFACE TO AID NONVISUAL NAVIGATION

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Thermographic imaging has been used for years to aid individuals with navigation and spatial learning tasks in complete darkness, fog, smoke, and other situationally blind scenarios. These interfaces work by visually displaying heat signature information. This study explores the efficacy of heat sensing to support nonvisual navigation and spatial learning using vibration and audio via smartphone interfaces.

Twenty blindfolded-sighted participants used a Samsung Galaxy S6 smartphone with a Flir One thermal imaging camera to complete three navigation and spatial learning tasks. Ten participants used a 'Touch interface', which allowed them to point the camera while concurrently exploring thermal information presented on the touchscreen. Audio/vibration output was triggered based on the thermal representations under the user's finger. A low pitch tone and no vibration indicated no heat detection. A higher tone and pulsing vibration signaled a heat signature. Faces detected within a heat signature were specified by a higher tone and a faster pulse. The other ten participants used a 'Point interface', which had the same cues but instead of touching the screen, the center of the camera's field of view was used for triggering output.

Each participant completed three simulated tasks: finding an empty seat in a row of five chairs, finding an empty seat in an aisle with three inward facing chairs on either side, and finding a person facing forward in a row of five chairs. For each task, participants practiced, explored from a stationary position, and navigated to their target. They carried the device with them for the entirety of the task. Accuracy and completion time were recorded.

While there were no significant differences between interface modes for stationary scanning, results indicated superior navigation performance when using the 'Point interface'. Our findings support the efficacy of using heat sensing for nonvisual navigation tasks in small indoor environments.

EVERYDAY TAXI DRIVERS: DO GIFTED NAVIGATORS HAVE LARGER HIPPOCAMPI?

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Cognitive mapping – learning distance and direction relations between locations as opposed to stimulus-response associations for places – is supported by the hippocampus (O'Keefe & Nadel, 1978). Taxi drivers who undergo extensive training about the layout of and routes through London have enlarged hippocampi compared to bus drivers (Maguire, Woollett, & Spiers, 2006), presumably as a result of their training (Woollett & Maguire, 2011). But do these gross anatomical differences correlate with navigation ability in non-experts? On the one hand, individual differences in navigation ability are large in normal samples (Weisberg et al., 2014). On the other hand, experts who undergo extensive training may differ from people simply at the upper end of a normal distribution. Here, we used a desktop virtual environment to assess navigation ability in undergraduate students. Participants learned the names and locations of eight buildings. Learning was assessed with an onsite pointing task: participants were positioned at each of the eight buildings, then had to point directly at all other buildings. Structural MRI scans were collected in a separate session. We used a planned sequential analysis (Lakens, 2014), collecting 30 participants, analyzing the data, then expanding the sample by 20 participants three times (maximum N=90) if results were equivocal. After 70 participants, we find a small correlation between overall hippocampal volume and pointing accuracy, $r(70) = .20$, $p = .10$. Data collection will continue to 90, but, if this result holds, studies of experts may have limited implications for hippocampal structure-function relations to account for normal variability.

TOWARDS AN EARLY DIAGNOSIS OF ALZHEIMER'S DISEASE USING IMMERSIVE VIRTUAL REALITY

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Alzheimer's disease (AD) is a progressive neurodegenerative condition and the leading cause of dementia. To date, all clinical trials aiming to develop a disease modifying therapy have failed primarily due to the inability to identify the disease at an early stage. The entorhinal cortex (EC) is the first region to exhibit neurodegeneration in AD. As such, detection of EC dysfunction may aid early diagnosis of AD and the stratification of individuals for future interventional therapies aimed at slowing the progression of disease. Spatially modulated EC neurons (grid and head-direction cells) are heavily implicated in navigation by path integration (PI), and the application of a PI test may therefore aid in detecting EC dysfunction in the earliest stages of AD. Hence, we sought to develop a PI task using immersive virtual reality (iVR) to test the hypothesis that PI is impaired in pre-dementia AD.

Patients with mild cognitive impairment (MCI, n = 45), age-matched (n = 30) and young controls (n=30) each completed the PI task. Where available MCI patients were further stratified as having positive (MCI+, n=11) or negative (MCI-, n=14) AD biomarkers on the basis of CSF amyloid/tau studies. The PI task consists of participants sequentially walking along an L-shaped outbound path before being asked to return to their starting location. Importantly, the virtual environments are devoid of local cues to minimise the opportunity for landmark-based navigation strategies. Consistent with our hypothesis, MCI patients exhibit significantly larger errors than young and age-matched control participants. In addition, MCI+ patients exhibit significantly larger errors than MCI- patients and both control groups. Moreover, the PI task exhibits high classification accuracy and superior diagnostic sensitivity and specificity compared to best-in-class neuropsychological tests for delineating MCI+ from MCI-.

INCIDENTAL SPATIAL LEARNING THROUGH MODIFIED NAVIGATION INSTRUCTIONS

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Navigation assistance systems support navigating especially in multi-tasking situations like car driving. With an increasing use of assistance systems, however, less information about the spatial surrounding is processed and orienting abilities decrease. Here, we present a new approach that aims at preventing orienting loss by incidentally triggering spatial learning during use of navigation assistance by including landmark information in navigation instructions.

First results revealed that navigation instructions providing landmark information improve incidental spatial learning in a driving simulator setup (Gramann et al., 2017). Participants drove a predefined route through an unknown virtual city using either modified or standard navigation instructions. Immediately afterwards participants with modified navigation instructions demonstrated better landmark recognition for different landmark types (navigation relevant, irrelevant, and novel). Wunderlich and Gramann (2018, submitted) were able to replicate the effect even after three weeks between navigation and retrieval. Event-related brain activity during the recognition task revealed an increased late positive complex independent of landmark type likely reflecting more retrievable information after using modified navigation assistance in general. As kinesthetic and proprioceptive information are important for spatial knowledge acquisition, a third study investigated pedestrians navigating through Berlin. Recognition performance after two weeks was again significantly higher for modified navigation instructions and accompanying event-related brain activity presented significant differences between instruction conditions.

In conclusion, including landmark information in auditory navigation instructions is a promising step towards navigation assistance systems that incidentally train the users' spatial abilities without increasing mental load. Future work will address the underlying structural and neural changes.

DIFFERENCES IN THETA MODULATION BETWEEN GRANULAR AND DYSGRANULAR RETROSPLENIAL CORTEX IN RODENTS

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Theta modulation helps synchronize the firing of extended hippocampal system neurons, improving information passing among distal brain regions implicated in spatial processing. The retrosplenial cortex (RSC) occupies a key cortical position within this navigation network as it represents a convergent point for two functional circuits. Due to the dense connectivity of the granular RSC (gRSC) with limbic areas involved in spatial cognition and displaying clear theta oscillations, gRSC is thought to be important for spatial learning based on internally-generated, and mnemonic information. In contrast, the dysgranular RSC (dRSC) receives important visuospatial information and is linked to visual landmark processing, consistent with the presence of head direction cells guided by landmarks (Jacob et al. 2017). In this study, we tested whether these anatomical and functional differences are reflected in the firing of non-directional RSC cells, while rats explored two spatial contexts with distinct visual and olfactory properties. Most cells in gRSC were theta-rhythmic, although there was no difference between frequency or power of theta oscillations recorded in gRSC and dRSC extra-cellular space. For single spikes, gRSC theta-rhythmic cells displayed stronger theta modulation, and a more consistent phase preference for the descending phase of theta oscillations compared to dRSC, showing a clear dissociation between gRSC and dRSC theta-like neuronal activity and theta oscillations. Consistent with previous studies, these oscillations might be derived from a common hippocampal source and modulate the activity of some RSC cells. However, only gRSC cells are suggested to generate theta rhythmic firing locally and independently from the hippocampus. Differences in theta modulation indicate possible neuronal mechanisms underlying the unique contribution of gRSC and dRSC to spatial processes. Overall, these findings contribute to the characterization of the two RSC subregions as parts of distinct mnemonic and visuospatial circuits, whose interaction enables spatial learning when animals change environments.

AGING AND COGNITIVE MAP DECAY: EFFECTIVENESS OF COMPENSATORY AUGMENTATIONS

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The normal and healthy aging process is accompanied with natural cognitive and physical changes which one must adapt to during everyday tasks. One of which, navigation, is crucial to independence for older adults. This work focused on the characterization of decay in cognitive maps, an important mental structure utilized for navigation. Beyond decay, the work also tested the effectiveness of compensatory augmentations, spatial aids designed to slow cognitive map decay. Two studies were conducted using free-exploration of indoor computer-based virtual environments as a means of developing cognitive maps. The first study had older adults (60-80 years) and younger adult controls (20-40 years) learn and maintain cognitive maps over time (days and weeks after learning). The second study focused solely on older adults with the introduction of two types of compensatory augmentations. One augmentation was designed to enhance the online learning process by allowing increased visual access to landmarks and the other augmentation strengthened the offline maintenance process utilizing a modified memory reconsolidation technique. In both experiments, testing involved map sketching and pointing tasks at multiple temporal testing intervals (immediately after learning followed by 1 day, 1 week, and 2 weeks after learning). Results of the first experiment showed clear age group differences in the magnitude and function of cognitive map decay with older adults experiencing greater (logarithmic) loss of cognitive map accuracy over time as compared to younger adults. The second experiment found that the compensatory augmentations were successful at delaying/reversing the decay process for older adults. The present work furthers fundamental understanding of navigation and aging, while simultaneously presenting promising results for the usage of spatial navigational aids with older adult populations.

ENVIRONMENTAL DEFORMATIONS DYNAMICALLY SHIFT THE COGNITIVE MAP

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Environmental deformations induce stereotyped distortions in the time-averaged activity of grid and place cells. Here we (i) demonstrate that many of these distortions can emerge from border cell-grid cell interactions and (ii) report evidence for previously unrecognized dynamics in rodent cellular responses and human spatial behavior resulting from these interactions. We first implemented a computational model in which input from border cells resets the spatial phase of grid cells at boundaries, thus maintaining the learned relationship between grid phase and these boundaries, and grid cell input resets place field locations accordingly. This model reproduced several experimentally observed deformation phenomena, including scale-dependent and local distortions in time-averaged grid fields as well as stretched, duplicated, and fractured place fields. This model further generated a striking new prediction: when neural responses are analyzed in terms of the most recently contacted boundary, one should observe history-dependent ‘shifts’ in grid phase. We reanalyzed two classic grid rescaling datasets and found clear evidence of this phase shift phenomenon. Next, we tested whether similar boundary-tethered shifts could be observed in human spatial memory. We taught participants the locations of objects within square virtual reality environments (desktop and immersive VR), and then asked them to replace these objects in stretched or compressed versions of this environment. In agreement with our model predictions, we observed shifts in the replaced locations of objects during deformation trials that were dependent on the most recently contacted boundary. Together, these results provide convergent evidence that cognitive maps in rodents and humans are dynamically shifted by displaced boundaries after environmental deformations.

OSCILLATORY DYNAMICS IN THE LIMBIC THALAMO-CORTICAL NETWORK REVEAL SUBCORTICAL INFORMATION FLOW TO AND FROM THE HIPPOCAMPAL FORMATION

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The thalamus relays sensory signals to the cortex, but also between cortical areas. These networks exhibit a wide range of oscillatory dynamics, modulated by various factors such as brain states and attentional recruitment. These interactions arise from a combination of feed-forward (thalamo-cortical) and feedback (cortico-thalamic) controls. The sensory and motor components of these networks, involving the posterior thalamus, have been widely studied in

vitro as well as in vivo models. In contrast, the anterior part of the thalamus is a key part of the limbic system: it receives subthalamic inputs from the mammillary bodies, and is reciprocally connected with the hippocampal formation and the midline cortex. These thalamo-cortical networks are essential for navigation and memory formation, among other limbic-related functions, yet they have only been poorly characterized in vivo so far. To further our understanding of these networks, we collected thalamo-hippocampal and thalamo-cortical neuronal ensembles and Local Field Potentials (LFP) during freely moving behavior and sleep. We show that thalamic nuclei of the anterior thalamus, including the antero-dorsal (AD), antero-ventral (AV), and antero-medial (AM), can be discriminated on the basis of their influence on, or

entrainment by hippocampal and cortical activity. In particular, thalamic neurons were differentially modulated during non-REM sleep by the thalamo-cortical slow waves (the fluctuation between DOWN and UP states) and the hippocampal sharp-waves ripples (SWRs). The onset of UP states in AD precedes UP states in neighboring nuclei by up to 100ms. The late-onset neurons in AV and AM were strongly responsive to SWRs and were generally highly modulated by theta oscillations during wakefulness and REM sleep. These results suggest that AD neurons, which transmit a signal related to head-direction to cortical and hippocampal areas, may play a key role in activating downstream targets. In contrast, other anterior thalamic nuclei are mainly driven by cortical and hippocampal feedback and may play a key role in transmitting hippocampal outputs to other cortical areas.

EGOCENTRIC BOUNDARY CELL REPRESENTATION IN THE MOUSE DORSAL MEDIAL STRIATUM

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The hippocampal formation is composed of several cell types that represent the environment within an allocentric reference frame, such as place, head direction, and grid cells. These cells are known to be critical for spatial navigation and contextual representation. However, during spatial navigation the sensory stream collected is transmitted to the brain relative to the movement of the organism, within an egocentric frame that requires transformation to an allocentric frame for hippocampal storage. Conversely, upon memory recall, the contextual memory must be reconverted to an egocentric frame for navigation in the familiar environment. To begin understanding this process, identification of how and where an egocentric frame is represented in the brain is essential. Recently striatal cells have been recorded that are tuned to egocentric spatial representation of environmental boundaries. These egocentric boundary cells (EBCs) are stable across novel and familiar environments and respond to boundaries at a fixed distance and consistent orientation. However, some characterizations of EBCs are difficult to address with single unit recordings but can be overcome with calcium imaging. Here we used miniature microendoscopes to visualize neuronal calcium transients in the dorsal medial striatum of mice. With this technique large numbers of cells were recorded that allow for assessment of functional topography in the striatum as well as identification of temporally structured activity within neuronal ensembles. Moreover, calcium imaging permits cellular registration, which enables analyses of the generalizability of EBC tuning across time and environments. With this technique we further characterize egocentric representations and investigate the spatial localization of functional EBC clusters in the striatum.

GRID CELL DYSFUNCTION IN THE MEDIAL ENTORHINAL CORTEX CORRELATES WITH PATH INTEGRATION DEFICITS IN A MOUSE MODEL OF ALZHEIMER'S DISEASE

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Alzheimer’s disease (AD) is a neurodegenerative disease characterized by spatial memory impairments in the form of disorientation and difficulty navigating. One potential circuit-level mechanistic explanation for these symptoms is a disruption of spatial coding in the brain's navigation system that consists of grid cells, head-direction cells, and border cells in the medial entorhinal cortex (MEC). Here, we employed in-vivo electrophysiological recordings in the freely behaving transgenic J20 mouse model of AD, which expresses an onset of beta-amyloid (AB) plaques in the MEC at four months of age. We demonstrate that grid cells are disrupted in aged J20 animals (months 5-7). Network-level impairments of non-classified cells in the MEC are detectable in young J20 animals (months 2-4), preceding the formation of plaques. To corroborate our physiological findings, we aimed to better characterize the nature of spatial memory impairment seen in AD and to propose a function for the MEC in navigation and memory. J20 mice were tested in a path integration food-foraging task in darkness where they must integrate self-motion cues such as heading direction and movement speed to continuously update their perceived location in space. Without allocentric visual cues, this task provides an opportunity to characterize the classic navigational deficits seen in AD patients as well as the role of specific MEC cell types in navigation. Our preliminary data show that aged J20 mice demonstrate impaired path integration behaviour which correlates to the observed physiological dysfunction. Overall, our results suggest that grid cells in the MEC are important targets for future therapies to restore spatial cognitive function in human AD patients.

INVESTIGATION OF THE HEAD DIRECTION SIGNAL IN THE ANTERODORSAL THALAMIC NUCLEUS USING MINIATURIZED MICROSCOPES IN BEHAVING MICE

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Head direction (HD) cells are some of the most abundant spatially tuned neurons in the brain. These cells are found in a series of regions starting in the brainstem and extending through the hypothalamus, thalamus, and up into the cortex areas that govern navigation and spatial memory. One area of interest is the Anterodorsal Thalamic nucleus (ADN), which contains a high concentration of HD cells (60%). One major obstacle to obtaining data from this region, especially in mice, is its small size (a spherical nuclei with a 0.3mm diameter). Thus, previously reported data has rarely shown recordings of more than 10 HD cells simultaneously. Here, we show calcium imaging of more than 50 HD cells at once and during behaviour using miniaturized microscopes (Miniscopes). To reach the ADN, we implanted 0.5mm-diameter GRIN relay lenses, in mice that were injected, beforehand, with a non-specific adeno-associated virus (AAV) to express GCaMP6f, in the target region, which reduced damage to the brain tissue to a minimum. Calcium transients allowed us to identify HD cells by means of a weighted averaging of the fluorescence changes in different angle bins as well as spike inference algorithms. Our recordings show a stable preferred firing direction of HD cells for more than two months. The reliability of HD cell firing was assessed by the correlation of the fluorescence signal with the recreated stimulus signal. Interestingly, our data shows a possible clustering of the HD cells with regards to their preferred firing directions and a potential topographical representation of the animal's head direction in the ADN. This preliminary finding needs to be further investigated. This technique provides the opportunity to in vivo imaging of a substantial population of HD neurons and, apart from revealing the physical arrangement of these cells, it will allow us to analyze the network dynamics of the HD system in such a way that would have been impossible otherwise.

EFFECTS OF EARLY EXPERIENCE ON SPATIAL REPRESENTATION OF LARGE-SCALE ENVIRONMENTS IN THE BAT HIPPOCAMPUS

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The proper function of brain circuits depends both on processes that require normal experience, and on processes which are independent of experience. The long-term effects of altered sensory experience on the brain have been extensively studied, but very little is known about the long-term physiological effects of abstract, cognitive experiences. The hippocampus offers an excellent substrate for addressing this question, because this high-level brain region is very far removed from the sensory periphery, and it contains abstract representations of space – yet, despite their abstractness, these spatial codes are amenable to detailed quantification. A number of studies have examined the normal development of spatial representations in the hippocampal formation of rat pups, during ontogeny; however, it is unknown how alterations in early experience affect spatial representation in the adult hippocampus – and in particular, the representation of naturalistic environments. We are addressing this question by investigating adult spatial representation of a very large environment in the hippocampus of laboratory-born bats, which were never exposed to large-scale environments (larger than a few meters) – and compare it to wild-born adult bats, which were exposed to very large spatial scales when they were flying outdoors. The main difference between these two groups of bats is in a very abstract parameter – the spatial scale of the environment that they experienced – whereas the sensory and motor experiences are normal for both groups of bats. We are using a miniature wireless electrophysiology system to record place cells in hippocampal area CA1 of laboratory-born bats that are flying in a very long 200-m tunnel, in comparison to wild-caught adult bats performing the same task in the same tunnel. Here we will present preliminary neuronal recordings that aim to elucidate how hippocampal representations are shaped by abstract features of early experience.

SOCIAL PLACE-CELLS IN THE BAT HIPPOCAMPUS

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Social animals need to know the spatial position of conspecifics, for purposes of social interactions and group navigation. However, it is unknown how the position of others is represented in the brain. Here, we addressed this question by studying Egyptian fruit bats (Rousettus aegyptiacus) – highly social mammals that excel in observational-learning and in navigation. We designed a spatial observational-learning task where animals were trained in pairs: In each trial, one bat ('observer') had to observe and remember the flight-trajectory of the other bat ('demonstrator'). After a short delay, the observer had to imitate the demonstrator's flight to receive a reward – which required the observer to pay close attention to the demonstrator's position. We recorded hippocampal dorsal-CA1 neurons from the observer bat using a miniaturized wireless electrophysiology system that allowed recording of individual neurons in freely flying bats. A neuronal subpopulation represented the position of the other bat, in allocentric coordinates. About half of these "social place-cells" represented also the observer's own position—that is, were place cells. The representation of the demonstrator bat did not reflect self-movement or trajectory planning by the observer. Some neurons represented also the position of inanimate moving objects; however, their representation differed from the representation of the demonstrator bat. This suggests a role for hippocampal CA1 neurons in social-spatial cognition.

SPATIAL NAVIGATION BEYOND EPISODIC MEMORY

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INTRODUCTION: Spatial navigation is impaired in various neurological disorders and is one of the first cognitive functions to decline in Alzheimer's disease. Currently, assessments available in clinical settings only vaguely resemble real-life difficulties and fail to incorporate essential aspects of this cognitive function. Paradigms applied in experimental settings are more advanced, often including virtual three-dimensional (3D) environments, however they frequently apply free exploration and episodic memory tasks, both potential confounders. Thus, methods are needed which minimise the demand on spatial memory and executive functions in order to investigate their involvement in navigation.

METHODS: A paradigm is presented which does not rely on free exploration or episodic memory tasks, but nevertheless incorporates core elements of spatial navigation such as mental rotation and the synchronisation of egocentric and allocentric perspectives. The naturalistic, 3D stimuli used in this novel task were created using the open-source graphics software Blender and are inspired by real-life deficits of patients with navigational impairments. In the current study, the paradigm is used to assess spatial navigation abilities in patients with mild cognitive impairment (MCI) and healthy older adults.

RESULTS: The conceptualisation of the task as well as test score distributions and correlations with demographic data and performance on visuo-spatial and memory tests are presented for patients with MCI and healthy participants with and without subjective difficulties in spatial navigation.

DISCUSSION: This paradigm can potentially provide a feasible and ecologically valid approach for differentially assessing spatial navigation beyond episodic memory abilities. Since the task does not require head motion or the use of a controller, it is highly promising for various clinical and experimental settings, specifically in older participants and patients without gaming experience.

STEP-LIKE MOVEMENT OF PLACE-CELL SEQUENCES: EVIDENCE FOR DISCRETE ATTRACTOR DYNAMICS, OR A DECODING ARTEFACT?

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The sequential reactivation of place cells during sharp wave/ripple episodes (SWRs), occurring during immobility, is widely viewed as a memory-related process. However, the mechanistic origin of these sequences remains unclear. A recent study has analysed the ensemble dynamics of hippocampal place cells based on large-scale recordings (Pfeiffer and Foster, 2015). The decoded trajectories of "off-line" place-cell sequences showed a pattern of step-like movement: The step sizes of these trajectories were correlated with the phase of slow-gamma oscillations, such that large steps occurred at phases of low population activity, and vice versa. The authors interpreted their finding as evidence for autoassociative (i.e., discrete attractor) dynamics. However, two recent simulation models (Jahnke et al., 2015; Gönner, Vitay and Hamker, 2017) have shown that the generation of discrete, step-like bursts of oscillatory sequential activity does not require discrete attractor dynamics. This discrepancy prompted us to examine the statistical properties of step size estimates. While we confirmed that the individual estimates of sequence movement in x- and y-direction are unbiased, we noted that computing step sizes based on the Euclidean distance induces a systematic positive estimation bias controlled by spike count. Theoretically, the vector length of two independent, zero-mean Gaussian-distributed random estimators follows a Rayleigh distribution, which is non-negative and right-skewed, with an expected value which depends on the sample size (n) used to estimate the x and y components, with a factor of 1/sqrt(n).

Under the null hypothesis of a smoothly varying representation of location, with a spike count modulated by oscillations, this analysis creates a systematic bias whose magnitude is correlated to oscillation phase. We propose an alternative, unbiased statistical analysis which may help to determine whether step-like movement of place-cell sequences is a true effect.

UP IS UP AND NORTH IS NORTH: HUMANS' 3D HEADING REPRESENTATION

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Previous neuroscience studies using rats and bats suggest that the represented azimuth direction on vertical and inverted surfaces is an extension of the azimuth direction on the ground (Finkelstein et al., 2015; Taube, Wang, Kim, & Frohardt, 2013). The current study investigated how humans represent their heading on vertical and inverted surfaces (wall and ceiling). In immersive virtual reality environments, participants first learned a layout of objects on the ground. In testing phases, they navigated to testing surfaces, walls or the ceiling, and re-placed the objects on that surface. Applying a least-sum-of-error method to the response locations, we calculated the relations between the directions on the testing surface (i.e., up on the wall and north on the ceiling) and the direction of north on the ground. The results showed that for majority of participants, the represented heading of UP on two opposite walls were consistent; for majority of participants who could distinguish between the directions of north and south on the ceiling, the represented heading of NORTH on the ceiling was consistent with that on the ground. These results indicate that on behavioral level, humans' represented azimuth direction on vertical and inverted surfaces is not an extension of the azimuth direction on the ground. These results imply that humans represent their heading in a full 3D coordinate system rather than an azimuth-pitch coordinate system.

DEVELOPING GLOBAL AND LOCAL COGNITIVE MAPS THROUGH PATH INTEGRATION

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This study investigated whether people can develop a global representation of local environments through path integration. Participants learned objects' locations in two misaligned rectangular rooms in an immersive virtual environment. After learning, they adopted a local view in one room and judged directions of objects within the room; the views in two consecutive trials were from different rooms and locally or globally consistent (priming task). Participants were either teleported (Experiment 1) or they locomoted between the rooms through an open environment (Experiments 2, 3) or a hallway to minimize the piloting cues (Experiments 4, 5). In Experiments 3 and 4, participants learned directions of five buildings before locomoting within and between the two rooms. In testing, after the priming task, they pointed to the buildings while adopting local views inside the rooms (across-boundary pointing task). The participants' estimated global headings were calculated from their responses to the buildings. The results showed that there was only a local priming effect when participants did not learn the buildings. When participants learned the buildings and then locomoted between the rooms through the hallway, there was only a global priming effect; whereas with richer piloting cues during locomotion, there were both local and global priming effects. Consistent with the global priming effect, the mean of participants' estimated global headings was accurate. These results suggest that people can develop a global cognitive map of two local environments through path integration. In addition, prior global representation may be important to integrating local spaces into a global map; both the global and local representations can be separately developed to multiscale cognitive maps, although this may require significant cognitive resources.

Blitz Session Talks - Abstracts iNAV 2018

Jacob Bellmund

Distorting the metric of spatial memory

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Entorhinal grid cells are characterized by spatially periodic patterns of activity and have been suggested to provide a metric of space. However, environmental geometry distorts grid-cell firing patterns in highly polarized trapezoidal compared to less polarized square environments. Here, we address the question whether human spatial cognition is influenced by these distortions of grid-cell firing patterns. Participants navigated a trapezoidal and a square arena using immersive virtual reality while learning the positions of objects. Positional memory was degraded in the trapezoid compared to the square. Following the distortions of grid-cell firing patterns in rodents, this effect was more pronounced in the narrow compared to the broad part of the trapezoid. Further, identical distances between object pairs were estimated to be different between the two parts of the trapezoid. These findings suggest that distortions of grid-cell firing patterns impact cognitive functions beyond spatial navigation.

Michael Peer

Spatial representation at different scales along the parahippocampal-retrosplenial axis

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Recent years have seen great advances in uncovering the principles of spatial representation in the brain. However, most studies focused on a specific spatial scale (e.g. room, virtual city), while the difference between representations of different scales remains unclear. Here we directly compared allocentric distance estimations across a range of spatial scales to characterize the brain systems involved in their representations. Subjects supplied a list of real-world familiar environments of different sizes – rooms, buildings, neighborhoods, cities, countries and continents. In each environment, subjects listed names of eight objects or buildings. Subjects then performed an allocentric distance comparison task between the objects/buildings under fMRI scanning. Brain activity was compared between blocks of questions in different spatial scales, using standard and tuning-curve GLM regressors and multi-voxel pattern analyses. Our analyses revealed that distance judgments at the room level activated a large network of regions in the parietal and temporal lobes. In contrast, activity at larger scales was centered at the parahippocampal and retrosplenial cortices, with a gradient of activity for increasing scale; the parahippocampal place area (PPA) was most active for comparisons at the smallest scales (room, building), and activity shifted toward the retrosplenial cortex for larger and larger scales. Overall, our findings demonstrate that spatial scale is an important parameter to consider when investigating spatial representations and interpreting past experimental results. Furthermore, the finding that the retrosplenial/posterior-cingulate region is more active in larger environments fits its suggested role in creating schematic graph-like cognitive maps, and may explain this region's involvement in other tasks that require graph-like mapping of knowledge in other cognitive domains.

Dieter Vandereist

Sonar-based mapping in bats: data, models and robots

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Echolocating bats have excellent spatial memory and are able to navigate to salient locations using solely bio-sonar. Compared to vision, bio-sonar has a small field of view, a slow update rate, and low resolution. This makes assembling a cognitive map of the environment using only sonar readings challenging. Drawing on data characterizing the sensory input available to bats, computational models, and robotic studies, we present a hypothesis explaining how bats assemble acoustic snapshots into navigable topological maps of the environment. This hypothesis hinges on two fundamental propositions. First, we propose that bats recognize places by remembering their echo signature - rather than their 3D layout. Second, we propose that bats' tendency to use stable and environment-derived flight corridors (i.e., preferred pathways for bats flying through the environment) significantly facilitates map formation. Importantly, our proposal allows bats to construct a global map of their flight paths through the environment without ever reconstructing the three-dimensional layout of the local environment from the received echo signals.

Jiayan Zhao

Walking and learning in a large-scale mediated space: Impacts of viewpoint transition and body-based cues on spatial learning in virtual reality

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Immersive technologies, including VR, are entering mainstream fostered by substantial investments of industry leaders. While many problems such as motion tracking have been successfully addressed, the potential mismatch between the spatial extent of the virtual and actual physical space remains a challenge. This makes it necessary to creatively think about locomotion in virtual environments (VEs). One of the most prominent forms of locomotion that systems such as HTC Vive or Oculus Rift offer is teleportation. Teleportation, in contrast to continuous locomotion, has the advantage of mitigating cybersickness in users wearing a head-mounted display. There is substantial research on effects of locomotion on spatial learning, but few studies exist that evaluate how teleportation, a discrete form of locomotion, may affect how we mentally represent a spatial environment. In experiment 1, we focused on different system setups and compared the spatial task performance of 179 participants navigating in a large-scale VE using a desktop computer or an immersive VR (iVR) setup. In experiment 2, we investigated the effects of viewpoint transition and body-based cues on spatial learning for the same VE. The results show that, in large-scale VEs, continuous locomotion is able to enhance spatial learning while the advantage of body-based cues is suspicious which may be weakened by underdeveloped iVR systems.

Joshua Julian

Grid realignment predicts human contextual memory

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To guide spatial behaviour successfully, the brain must retrieve memories that are appropriately associated with different navigational contexts. Grid cells in the entorhinal cortex (EC) may serve an important role in this function. Between navigational contexts, grid cells alter their firing patterns, a process known as grid realignment. However, the relationship between grid realignment and contextual memory is unclear. One possibility is that grid realignment is driven purely by changes to perceptual cues. Alternatively, grid realignment may reflect memory for navigational context per se that goes beyond sensory processing. To test the relationship between grid realignment and contextual memory, human participants learned the locations of target objects in two virtual reality arenas (Context A and B) distinguished by the shape of their boundaries (one square, one circle) and their distal orientational cues. Following training, participants underwent fMRI scanning while object location memory was tested in Contexts A and B, as well as in a third ambiguous half-square half-circle arena (Context AB). By comparing the recalled target object locations in Context AB to the correct target locations in Context A versus B, we could estimate which contextual memory (Context A or B) was reinstated in Context AB on a trial-by-trial basis. Preliminary results showed greater changes in the human EC fMRI grid-like signal across Contexts A and B than across different trials within the same context, consistent with contextual grid realignment in humans. Critically, we also found that the EC grid-like signal predicted contextual memory retrieval in Context AB on a trial-to-trial basis. Together, these results provide the first evidence for grid cell involvement in contextual memory independent of sensory processing.

Jean-Bastein Bott

Imaging of medial septal glutamatergic neurons during freely behaving navigation in mice in a dry version of the Star-Maze task

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Recent evidence suggests that medial septum (MS) glutamatergic neurons through their projections to hippocampus may code for ongoing locomotion velocity. Since these results were obtained in head-fixed mice running on a treadmill, the role of MS glutamatergic cells in more complex behavior such as navigation and memory remains unexplored.

Using miniscope calcium imaging, we characterized the spontaneous activity of identified glutamatergic neurons during various tasks in freely behaving mice. MS glutamatergic neurons form heterogeneous sub-populations of cells that are active in relation to specific behaviors. Moreover, in freely moving mice completing a goal-directed navigation task in a dry version of the Star-Maze task, MS glutamate neurons do not code for locomotion per se but rather for the spatial destination of both future and ongoing trajectories. Interestingly, optogenetic silencing of MS glutamatergic neurons before the onset of navigation impaired the precision of the navigation and memory performance without affecting the locomotion speed of the animals suggesting an essential role in spatial navigation planning.

These results suggest that medial septum glutamatergic subpopulations contribute differentially to hippocampal-dependent spatial memory. One particular subpopulation appeared indispensable for goal-directed navigation.

Daniel-Robert Chebat

The Neural Correlates of Navigation via a Simplistic Sensory Substitution Device

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Spatial navigation in the absence of vision has been investigated from a variety of approaches that have progressed our understanding of spatial knowledge acquisition by the blind, including their abilities, strategies, and corresponding mental representations. Human navigation is believed to rely on visual brain areas such as the PPA or OPA. Our previous work demonstrated the recruitment of primary visual areas in congenitally blind (CB) individuals, but not in sighted blindfolded or in late blind (LB) individuals , which may enable them to use sensory substitution devices (SSDs) efficiently. Using a combination of functional and anatomical neuroimaging techniques, our recent work has demonstrated the impact of amodal cortical processing in guiding spatial learning. The comparisons of performances between congenitally blind people and sighted people using sensory substitution devices in perceptual and sensory-motor tasks uncovered the striking ability of the brain to rewire itself during perceptual learning and to learn to interpret novel sensory information even during adulthood, not just on congenitally blind individuals, but late blind and even sighted individuals as well. In a series of experiments we demonstrate that regions that were typically considered “visual” scene selective regions can be recruited through sensory substitution during a navigation task in both congenitally blind and sighted blindfolded counterparts. We argue that scene selective regions and the navigation network in general performs modality-independent spatial computations that does not require visual input to perform spatial tasks.

Debbie Kelly

Age affects spatial working memory in pigeons

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Spatial memory involves the ability to retain and use environmental cues to find and return to places of previous reinforcement. Tests of spatial reference memory typically involve searching in stable spatial locations, whereas tests of spatial working memory include an additional complexity of navigating dynamically changing environments, or searching for a changing goal location within a static environment. Two visual cues important to many animals during spatial tasks are featural cues (e.g. colour, texture) and geometric cues (e.g. distance, direction). Previous studies have shown age-related decline in the use of these cues during tests of spatial reference memory. Less research, however, has investigated whether aging results in cue-specific decline in abilities during spatial working memory tasks. We trained adult and aged pigeons to search for a food reward in the corners of a rectangular arena with distinctive featural cues in each corner. The rewarded corner was stable within a daily session, but changed between sessions. Our results show both adult and aged pigeons had marked difficulties in learning the task. Aged pigeons tended to perseverate on the featural cues, whereas adult pigeons primarily perseverated on the geometric cues.

Tobias Navarro Schröder

Electrophysiological markers of grid cell population activity across species

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Grid cells located in the human and rodent entorhinal cortex are a critical component of the brain's spatial coding system. During virtual-reality (VR) navigation tasks with humans, the fMRI BOLD signal in the entorhinal cortex exhibits hexadirectional modulations that may reflect population activity of grid cells. However, it remains unknown whether and how grid cell population activity specifically gives rise to this hexadirectional hemodynamic fMRI signal. Here we address this issue in two steps. First, we employed a human VR navigation experiment using magnetoencephalography (MEG) and found hexadirectional signal modulations in the high-gamma band (90 Hz ±30 Hz) , source-localised to the medial temporal lobe. Next, we conducted analyses to test the relationship between grid cell activity and local field potential (LFP) recordings in freely moving rats. We found hexadirectional modulations in the same frequency band as in the human MEG navigation experiment. The orientation of this hexadirectional LFP modulation was aligned to the orientation of the hexagonally symmetric firing patterns of single grid cells. Together, these findings describe new ways to measure grid cell population activity and their non-invasive source localisation using MEG. Crucially, we link grid cell activity to measures of population activity in rats and humans, thereby elucidating the physiological basis of non-invasive grid cell population measures previously revealed with fMRI. Since grid cell function is affected early in Alzheimer 's disease, understanding how to measure their activity with non-invasive methods is of high clinical relevance.

Alexander Boone

Do task instructions matter? Individual differences in navigation strategy in virtual environments

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Mary Hegarty, University of California, Santa Barbara

Individual differences in navigation strategy in the Dual Solution Paradigm (DSP) show that some people prefer to take learned routes, while others more readily take shortcuts (Marchette et al., 2011; Boone et al., in revision). In this task, the instructions are vague ("navigate to the goal"). Thus it is unclear whether those who travel by learned routes do so because they have not formed a cognitive map and therefore cannot take shortcuts, or whether they do so because they assume that the task implies taking the learned route. Here, we begin to untangle the dis/association between cognitive mapping ability and strategy in VR navigation.

In two experiments, participants first learned a route through a virtual environment and then navigated to goals under different instructions ("go to the goal" vs. "take the shortest path to the goal"). In Experiment 1, participants first performed the standard DSP task in which they learned a route and were asked to navigate to goals. In the second environment, participants were instructed to navigate to goals by the shortest path. Participants shifted from following primarily learned routes in the first task to taking more shortcuts in the second task. A limitation of this experiment was that task order was confounded.

In Experiment 2, one group (N = 40) performed the DSP with standard instructions twice and another group (N = 40) was given shortcut instructions twice. While navigation became more efficient over time regardless of condition, the shortcut group was significantly more efficient. Men and women were more efficient when told to take the shortest route, but men were more likely to take shortcuts in both conditions.

This work indicates that use of learned route in the DSP does not necessarily imply that a person cannot take a shortcut. Sex difference in navigation strategy on this task may in part reflect difference in ability to construct a cognitive map.

Lukas Hejtmánek

Enriched body-based cues and transfer to real-world environments

Lukáš Hejtmánek, Michael Starrett, Arne D. Ekstrom

“Transfer” refers to the extent to which knowledge in one situation can augment learning in a comparable but not identical situation. Past studies using desktop virtual reality have provided mixed findings regarding the transfer of knowledge from desktop virtual reality to real-world environments, suggesting in some cases only limited efficacy of knowledge gained from in desktop VR to learning in the same real world environment. One issue widely acknowledged issue with desktop VR, however, is that it lacks vestibular and other proprioceptive input (termed “body-based input”) which in turn may limit the ability of participants to apply representations learned in one situation to the next. Here, we investigate whether knowledge gained in highly immersed virtual reality involving body-based input and free ambulation can increase subsequent transfer to the same real-world environment. To address this issue, we built a virtual model of Center of Neuroscience at UC Davis and used commercial bluetooth beacons to track participants movements in the building. This allowed us to run the same task both in the virtual environment with body-based input (using an omnidirectional treadmill with a headmounted display) and in the real world. The participant’s goal was to find and remember 6 offices around the building over the course of 36 trials. The study involved 5 different conditions, immersed VR to real-world, desktop VR to real-world, immersed VR to immersed VR, real-world to real-world, and real world to immersed VR. We collected data from 20 participants in each condition. Dependent measures involved errors in goal visits, pointing accuracy to different goal locations, path accuracy, and map drawing performance. Our preliminary findings suggest that while immersed VR initially took more time to learn, transfer rates were high to real world environments, and nearly comparable to navigating the same environment first in the real world. Our findings suggest that navigating virtual environments involving a more complete range of body-based input can enhance transfer to real world environments, suggesting the critical importance of body-based cues to this process.

Louis Kang

A geometric attractor mechanism for the self-organization of entorhinal grid modules

Louis Kang, University of California, Berkeley
Vijay Balasubramanian, University of Pennsylvania

The grid system of the mammalian medial entorhinal cortex (mEC) exhibits striking modularity. Rat grid cell recordings reveal that spatial grid scales cluster around discrete values separated by constant ratios reported in the range 1.3--1.8. Although this modular organization has been shown to be a robust and efficient encoding of spatial location, its origin is unknown. We present the first proposed mechanism through which geometric sequences of grid scales arise naturally. A series of continuous attractor networks along the longitudinal mEC axis that would otherwise generate a smooth distribution of grid scales forms modules separated by discrete jumps in scale when excitatory connections are introduced. Moreover, constant scale ratios between successive modules arise through robust geometric relationships between commensurate triangular grids, whose lattice constants are separated by $\sqrt{3} \approx 1.7$ or other ratios, or between grids containing local lattice modulations called discommensurations. These relationships persist in single neuron spatial rate maps due to faithful path integration and are unaffected by perturbations to model parameters. We speculate on how excitatory connections between attractor networks can be realized by the known architecture of the mEC and suggest analyses and experiments that test our model.

John Phillips

Spontaneous association of magnetic and visual landmark cues

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Background. Mice and other rodents have a well-developed magnetic compass that can play an important role in many aspects of spatial cognition and behavior including: helping to anchor navigational circuitry in the brain to familiar surroundings; underlying a turn algorithm used in systematic search during central place foraging; serving as a compass reference that increases the range and accuracy of path integration systems; helping to place multiple landmark arrays into register; and contributing to both the 'map' and 'compass' components of map-based homing ('true navigation'). This talk will present preliminary evidence from behavioral experiments using a modified 'Plus' water maze assay showing that the magnetic field can provide C57 BL/6 mice with a global reference system that can be used to organize local landmark arrays into a global map of familiar space. In these experiments, mice were placed individually on a platform in the center of the water maze for 5 min in the presence of a predetermined alignment of the magnetic field and a novel array of visual landmarks. 3 to 5 hours later, the mice were trained to orient relative the magnetic field without the visual landmarks (see Phillips et al. 2013). Tested the following day with only the visual landmarks (horizontal component of the magnetic field cancelled) they were able to use the landmark array to orient relative to the trained direction. These findings show that naïve mice spontaneously associate magnetic and visual landmark cues and, once this association has occurred, can transfer a learAned magnetic direction to the landmark array.

Paul Dudchenko

Place cell repetition

Paul Dudchenko, University of Stirling, Scotland

In mazes that have multiple, identical compartments arranged in parallel, place cells show repetition of their fields across compartments. This suggests that place cells encode local vistas defined by their shape and orientation. We have shown that 1) place field repetition is not seen in compartments facing different directions, 2) place field repetition depends on input from the head direction cell network, 3) spatial discrimination learning is easier when compartments face different directions, and 4) spatial discrimination learning is impaired following damage to the head direction cell network. Together, these results suggest that the head direction cell system works with the place cell system to allow disambiguation of similar locations.

Shachar Maidenbaum

Grid-like Hexadirectional Modulation of Theta Power in Human Entorhinal Cortex during Virtual Navigation

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Grid cells are a fundamental part of the brain's spatial system, playing an important role in tasks such as path integration and spatial memory. In rodents the activity of grid cells is thought to rely on large-scale theta oscillations in the entorhinal cortex. However while theta oscillations have been detected in the human entorhinal cortex, these signals are harder to see and more variable.

To examine the role of network oscillations and grid cells in humans, we test the hypothesis that in the human entorhinal cortex theta power exhibits a population-level signature of grid cells—hexadirectional modulation according to the person's heading. We collected intracranial electroencephagraphic (iEEG) data from neurosurgical patients performing a virtual spatial memory task, and found hexadirectional modulation of the power in the high-theta band (5-8Hz) during navigation. This pattern closely matched predictions from the rodent and fMRI literatures because it was specific to the theta band, to 6-fold symmetry and to the entorhinal cortex. Grid orientation was stable in each subject, but differed between subjects. Furthermore, hexadirectional modulation level correlated with behavior—stronger modulation predicted better spatial memory task performance.

These results are important theoretically by demonstrating a link between theta oscillations and the grid system in humans and practically by showing that detailed features of neural processing can be identified from population-level neural recordings, extending findings from noninvasive imaging.

Ipshita Zutshi

Hippocampal Neural Circuits Respond to Optogenetic Pacing of Theta Frequencies by Generating Accelerated Oscillation Frequencies

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Biological oscillations can be controlled by a small population of rhythmic pacemaker cells, or in the brain, they also can emerge from complex cellular
and circuit-level interactions. Whether and how these mechanisms are combined to give rise to oscillatory patterns that govern cognitive function are not well understood. For example, the activity of hippocampal networks is temporally coordinated by a 7- to 9-Hz local field potential (LFP) theta rhythm, yet many individual cells decouple from the LFP frequency to oscillate at frequencies 1 Hz higher. To better understand the network interactions that produce these complex oscillatory patterns, we asked whether the relative frequency difference between LFP and individual cells is retained when the LFP frequency is perturbed experimentally. We found that rhythmic optogenetic stimulation of medial septal GABAergic neurons controlled the hippocampal
LFP frequency outside of the endogenous theta range, even during behavioral states when endogenous mechanisms would otherwise have generated 7- to 9-Hz theta oscillations. While the LFP frequency matched the optogenetically induced stimulation frequency, the oscillation frequency of individual hippocampal cells remained broadly distributed, and in a subset of cells including interneurons, it was accelerated beyond the new base LFP frequency. The inputs from septal GABAergic neurons to the hippocampus, therefore, do not appear to directly control the cellular oscillation frequency but rather engage cellular and circuit mechanisms that accelerate the rhythmicity of individual cells. Thus, theta oscillations are an example of cortical oscillations that combine inputs from a subcortical pacemaker with local computations to generate complex oscillatory patterns that support cognitive functions.

Crystal Bae

Collaborative Route Planning and Navigation in a Novel Environment

Crystal Bae - University of California, Santa Barbara

This study investigates both route planning and situated navigation by pairs of people (dyads) in a wayfinding task in an unfamiliar environment. Participants collaborated on a task to both plan and execute a route between a given origin and destination point. Each dyad was video-recorded by the researcher during both the planning and navigation phases. Using this rich repository of video-recorded interaction alongside collected data on participants' navigational planning and execution, I investigate strategies of social role-taking (such as leading and following), the use of environmental cues and references, and uncertainty in wayfinding.

In this data blitz talk, I will share results from my study and invite additional feedback on further analysis and next steps. In the planning phase of this study, each dyad was given start and end points between which they had to devise and agree upon a route to take. From coded interactions of these route planning interactions, I propose explanations for successful collaborative route planning and several contributors to uncertainty in the planning phases of navigation.

Each dyad was then taken to the study site where they navigated together between those same start and end points, while being video-recorded and GPS-tracked. I will present my analysis of where and when dyads deviated from the route as previously planned, and suggest where social role-taking between the participants either inhibited or supported successful navigation. This research agenda furthers our understanding of collaboration during navigation, and additionally illuminates the impact of social roles on decision-making and interaction in a wayfinding task.

Sang Ah Lee

Spatiotemporal continuity in episodic memory: A developmental approach

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Episodic memory involves mentally replaying experiences by binding components of memory into a continuous spatiotemporal framework. For decades, we have known that spatial navigation and episodic memory share a hippocampal neural basis. Yet, it is still unclear how these processes are related. By tracking developmental changes in both abilities, this study explores the hypothesis that a privileged link between space and time provides the representational scaffold upon which episodic memory and mental simulation are constructed.

Many studies have demonstrated that children begin to develop an adult- like episodic memory only around the age of six. This developmental change has been attributed to an improvement in the capacity to bind together components of memory. The present experiments target children's ability to bind together the what and where components of memory in temporal order (when) using nonverbal methods. The results suggest that children first develop the ability to reliably bind together space and time (i.e., where + when) and then, around six years of age, successfully bind together what + where + when.

We note two important insights from these findings. First, the observation that children bind the elements of where and when earlier in development raises the hypothesis that the representation of space has a privileged status in binding over continuous time. Second, the successful binding of content (what) to the earlier-developing spatiotemporal continuity (where-when) occurs at a similar age at which children exhibit increased flexibility in their navigational spatial representations, which is also coincidental with a crucial stage in the maturation of hippocampal function. Beyond characterizing cognitive development, we hope that such behavioral tests can help provide insight into the specific cognitive impairments in clinical populations with hippocampal dysfunction. To end the talk, I will share an example from Williams Syndrome, a neurodevelopmental disorder associated with severe spatial impairment.

Silvia Viana da Silva

Genetically targeted expression of APP to CA3 subpopulation of hippocampal principal neurons leads to neuronal network dysfunction and memory impairment

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Alzheimer's disease (AD) is a neurodegenerative disorder characterized by a striking loss of episodic memory. We used transgenic mice that express human amyloid precursor protein (APP) selectively in CA3 pyramidal cells as models to investigate how amyloid beta peptide induced synaptic toxicity leads to hippocampal circuit and memory dysfunction during early phases of AD. CA3-APP mice have normal basal synaptic transmission but impaired synaptic plasticity at Schaffer collateral synapses from 2 months of age. To test for memory deficits, we performed a spatial alternation task on a figure-8 maze with either no delay or brief delays (i.e., 2 s or 10 s) at the beginning of the center arm. Introducing a delay period is known to make the task hippocampus-dependent, in contrast to the continuous version. Aged CA3-APP mice (16-19 months) show deficits in hippocampus-dependent memory while younger mice (4-6 months) display only a transient deficit during the initial days of testing, reaching control levels after 5 days of behavioral testing. To understand changes in network function that may underlie the behavioral phenotypes, we recorded neuronal activity before, during, and after the mice performed the spatial alternation task. Despite the limited expression of APP, we find extensively altered hippocampal physiology. In recordings performed in the CA1 region of aged CA3-APP mice we observed a decrease in the frequency of theta and gamma oscillations in the transgenic mice. Younger CA3-APP mice also show a decrease in theta and gamma frequencies, but less pronounced when compared with the aged CA3-APP. We further identify a transient peak in the LFP at the Beta range (15-30Hz) in the central arm, close to the point where the mice need to turn right or left. Our data thus indicate that local synaptic plasticity deficits may lead to network dysfunction, and the results strengthen the idea that memory in AD could be improved by restoring brain oscillations.

Lorenz Gönner

Step-like movement of place-cell sequences: evidence for discrete attractor dynamics, or a decoding artefact?

Lorenz Gönner, Julien Vitay, Fred H. Hamker

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The sequential reactivation of place cells during sharp wave/ripple episodes (SWRs), occurring during immobility, is widely viewed as a memory-related process. However, the mechanistic origin of these sequences remains unclear. A recent study has analysed the ensemble dynamics of hippocampal place cells based on large-scale recordings (Pfeiffer and Foster, 2015). The decoded trajectories of "off-line" place-cell sequences showed a pattern of step-like movement: The step sizes of these trajectories were correlated with the phase of slow-gamma oscillations, such that large steps occurred at phases of low population activity, and vice versa. The authors interpreted their finding as evidence for autoassociative (i.e., discrete attractor) dynamics. However, two recent simulation models (Jahnke et al., 2015; Gönner, Vitay and Hamker, 2017) have shown that the generation of discrete, step-like bursts of oscillatory sequential activity does not require discrete attractor dynamics. This discrepancy prompted us to examine the statistical properties of step size estimates. While we confirmed that the individual estimates of sequence movement in x- and y-direction are unbiased, we noted that computing step sizes based on the Euclidean distance induces a systematic positive estimation bias controlled by spike count. Theoretically, the vector length of two independent, zero-mean Gaussian-distributed random estimators follows a Rayleigh distribution, which is non-negative and right-skewed, with an expected value which depends on the sample size (n) used to estimate the x and y components, with a factor of 1/sqrt(n).
Under the null hypothesis of a smoothly varying representation of location, with a spike count modulated by oscillations, this analysis creates a systematic bias whose magnitude is correlated to oscillation phase. We propose an alternative, unbiased statistical analysis which may help to determine whether step-like movement of place-cell sequences is a true effect.

Stacy Doore

Natural-language spatial cues for learning and navigating indoor environments

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Background: Automated scene descriptions provide critical conceptual links between metric, topologic, and network spatial information. In order to present a sufficient level of spatial detail for nonvisual scene understanding and navigation tasks, conceptual and linguistic models should accommodate a user's preferred frame of reference, as well as include multimodal cues. This study focused on natural-language spatial relations used to form a cognitive representation of an indoor space.

Methods:Open response scene descriptions were collected from ten participants for two small rooms populated with a collection of office furniture. The furniture consisted of large, free-standing objects arranged in a room with standard structural elements (e.g., walls, windows, doors). Participants were instructed to provide scene descriptions for a blind person who would use the verbal descriptions to conceptualize the scenes well enough to perform a spatial task. Descriptions were analyzed to identify conceptual and syntactic linguistic patterns.

Results:Three primary conceptual spatial relations (contact, disjoint, partOf) were identified. Descriptions consisted of spatial references to the physical room structures (e.g., walls, windows, and doors) and abstract conceptual regions (e.g., center of room, left side of room). Underspecified spatial prepositions were preferred over more descriptive spatial terms and structural elements were the primary reference objects used to describe the position of objects in the room.

Conclusion:These results provide specifications for automated scene descriptions and speak to the type and structure of spatial information needed for nonvisual navigation and other spatial tasks. They also provide new insight for creating improved models of automated indoor scene descriptions by defining what constitutes a reasonable linguistic description for capturing relationships between objects and the structures that comprise the indoor space.

Yuri Agrawal

Vestibular loss is associated with impaired spatial navigation in Alzheimer's Disease

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There is increasing recognition that patients with Alzheimer's disease (AD) have heterogeneous clinical features. Some AD patients experience greater motoric and spatial impairments early in the disease course, such as impairments in gait, spatial memory, and spatial navigation. These symptoms are thought to contribute to the increased morbidity, earlier institutionalization, and shorter survival observed in patients with AD relative to cognitively-normal adults. The vestibular system is an important contributor to spatial orientation and navigation, and recent evidence suggests that AD patients have greater levels of vestibular impairment relative to age-matched controls.

In this presentation, two recent studies will be reviewed that investigated whether vestibular loss predicted impaired spatial navigation in a cohort of ~50 patients with mild cognitive impairment (MCI) or AD. First we considered a neurocognitive measure of spatial navigation ability, the Money Road Map Test (MRMT). We also considered a behavioral measure of spatial navigation skill, specifically driving difficulty. We used the cervical vestibular-evoked myogenic potential (cVEMP) as a measure of vestibular function. We observed that vestibular loss was significantly associated with a greater number of errors on the MRMT (7.7 errors for patients with unilateral vestibular loss; 6.9 errors for patients with bilateral vestibular loss), and that AD patients with bilateral vestibular loss had a 12-fold increased odds of driving impairment relative to AD patients with preserved vestibular function.

These data suggest that vestibular loss may contribute to a "spatial" subtype of MCI/AD, characterized by disproportionate deficits in spatial navigation ability.

Jascha Grübel

EVE: A framework for running virtual reality experiments in neuroscience

Jascha Grübel, Raphael P. Weibel, Christoph Hölscher and Victor R. Schinazi

Experiments in neuroscience often rely on virtual reality (VR) to investigate navigation inside the MRI scanner. While these studies are limited by the lack of locomotion and proprioceptive feedback, researchers have successfully immersed participants using passive (e.g., videos, images) or active (e.g., movement mediated by a control interface) virtual environments in order to study different aspects of their spatial memory. However, conducting VR experiments inside the MRI scanner can be cumbersome and time consuming due to issues with the hardware, software and the extraction/synchronization of data. In this talk, we will present some of the functionalities of the EVE (Experiments in Virtual Environments) framework that can facilitate the setup, implementation, and evaluation of VR experiments in neuroscience. EVE is designed to reduce repetitive and error-prone steps that often occur during the design of VR experiments. The framework is based on the popular platforms of Unity 3D and MiddleVR. This allows researchers, who do not have specialized training in computer science, to design virtual environments and connect with physical (e.g., eye tracker, electrodermal activity) and virtual sensors (e.g. location marker, collectible items) for data collection and synchronization. EVE further assists researchers by providing data management and evaluation capabilities including database support, questionnaire tools, visualization tools, and scripting for R. The framework includes a series of replay tools that researchers can use to run quick diagnostic analyses (e.g., video playback, path tracing) at the scanner or more in depth analyses at the laboratory using the custom made R package evertools. We will present some of these functionalities in the context of several experiments conducted at the Chair of Cognitive Science at ETH Zurich.

Marta Sabariego

Spatial working memory performance and intrahippocampal processing recover after mEC lesions

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Alterations in the entorhino-hippocampal loop have been suggested to underlie the memory deficits in early stages of different types of dementia, traumatic brain injury, temporal lobe epilepsy, and brain ischemia. Detection of physiological dysfunctions in these brain areas could therefore provide insight into network mechanisms that could be enhanced or regenerated. Here we used mEC-lesioned rats to understand the contribution of mEC to hippocampus-dependent memory and hippocampal physiology. In particular, mEC and sham lesioned rats were trained to perform a spatial alternation task on a figure-8 maze that included left and right return arms and a center arm. Both groups performed similarly during trials without delay, but when a delay was imposed, the mEC lesion group made significantly more errors. After further training, the behavioral performance of the mEC lesion group improved. CA1 cells in mEC lesioned rats discriminated less well between left and right maze segments than cells in control animals. Unexpectedly, CA1 cells of control and lesioned rats showed equally distinct neural coding after rats entered the maze stem from either the right or left side, which suggests that information about the trajectory was regained. We therefore asked whether CA3 is a possible source for separate neural codes for left and right trajectories, which could then be forwarded to CA1 on the stem. We found that a subpopulation of CA3 cells in mEC lesioned rats consistently distinguished between right and left sides of the maze, and CA3 inputs could thus forward information about spatial sequences to CA1 as the rat enters the stem. Taken together, spatial coding was more effectively retained in CA3 than in CA1 cells without mEC inputs, which suggests that the processing of inputs to the hippocampus from sources other than mEC can support spatial working memory and that spatial computations in a circuit without mEC projections can support the recovery of memory performance.

Marcia Becu

Age-related preference for geometric cues during real-world navigation: behavioral and neuroimaging correlates

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Healthy aging is associated with changes in the way people navigate in space. These changes have been previously characterized in terms of age-related deficits in the use of allocentric strategies. However, given that navigation strategies are conditioned by the sensory cues present in the environment, an alternative hypothesis is that navigation difficulties in aged people are associated with spatial cue processing rather than with strategic choices. By having young and old participants navigate in a real, ecological environment, we show that old adults reorient preferentially according to geometric cues, thus neglecting landmark information, whereas young adults preferentially use landmarks. Recording of both body and gaze dynamics as subjects reoriented and navigated in space allowed us to identify specific behavioral patterns associated with either landmark or geometric preference. In particular, eye movement analysis revealed that the geometry-based coding adopted by older adults manifested itself in the spatiotemporal signatures of oculomotor fixations, but not in other navigational variables, and, moreover, gaze dynamics were predictive of spatial cue preference. Also, the longer reorientation time observed in old subjects was due to the need for a repetitive sampling of visual information. In addition, preliminary data from off-line anatomical MRI scans show a negative correlation between navigation performance and gray matter integrity of scene-selective structures involved in landmark processing (PPA and RSC), whereas no correlation was found with hippocampal regions. These results extend previous findings on geometric cue preference in children and therefore suggest an inverted U-profile of landmark processing across lifespan. Given the extensive use of landmarks during spatial navigation paradigms, these results challenge the traditional view of a specific deficit for allocentric strategies in aging.

Lorene Penazzi

OLM interneurons activation during spatial navigation

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Oriens lacunosum-moleculare (OLM) cells represent a key class of GABAergic interneurons involved in controlling hippocampal network states and associated behaviors. Recent reports demonstrate that OLM cells may be active in response to specific events such as during aversive stimuli delivery (e.g. shock or air-puff) or the locomotion state of the animal. However, it is still unknown whether functionally distinct OLM interneurons may selectively be engaged during one of those events.
Our aim was to characterize OLM cell activity patterns during distinct behavioral events underlying different memory processes. To do so, we performed calcium imaging of populations of OLM interneurons in freely behaving mice using the miniscope imaging technique. Spatial memory was assessed using an alternative version of the appetitive dry Star-Maze task. In this paradigm, air-puff were delivered each time the animal visited the extremity of a non-target arm. OLM cell calcium activity was analyzed during the following behavioral events: “point choice” between arm, “avoidance” of aversive non-target arms, “puff” delivery, uptake of the sucrose-sweetened water “reward”, “locomotion” and “immobility”. We were also interested in if the activity of OLM interneurons was significantly associated with different stages of memory dynamics during navigation.
This imaging study will provide a framework about the strategic contribution of OLM interneurons to spatial reference memory.

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Clare Quirk

Effects of manipulating theta frequency on medial entorhinal cells

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Computational models for generating medial entorhinal cortex (mEC) grid cells all require a running speed signal in the form of either an oscillatory or firing rate signal. Theta oscillations are prominent in the hippocampus and in mEC and increase in frequency and amplitude with faster running speeds. It has therefore been hypothesized that theta oscillations could be the speed signal to grid cells. Previous work has demonstrated that inactivating the medial septum results in a substantial reduction of theta power and disrupts the spatial periodicity of grid cells while border, head direction, and place cells are retained. However, it remains unclear whether disrupted grid patterns selectively emerge from effects on theta oscillations or, more generally, from the decreased excitation after septal inactivation. To specifically examine the influence of theta oscillation frequencies on grid cell generations, we took advantage of the role of media septal parvalbumin-expressing GABAergic (PV) cells in generating theta oscillations and selectively expressed channelrhodopsin (ChR2) in PV cells in the medial septum. We established that rhythmic stimulation of PV cells in the medial septum could be used to reliably control the frequency of theta oscillations in freely moving mice within the endogenous theta frequency range (e.g., 8 Hz) as well as outside the normal range (e.g., 10 and 12 Hz). We then recorded mEC cells in an open field and found that shifting theta to frequencies of 8 Hz, 10 Hz, and 12 Hz had no effect on the average firing rate of principal cells but significantly lowered the firing rate of interneurons relative to their baseline firing rates. We also found that pacing theta at 8 Hz and at 10 Hz reduced the spatial precision of mEC cells. These findings are consistent with the notion that theta oscillations are essential for spatial processing in the entorhino-hippocampal circuit, but they do not reveal a direct relation between theta frequency and spatial scaling.

Erica Barhorst-Cates

Active and passive learning of real-world environments with simulated restricted field-of-view

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Spatial learning of real-world environments is impaired with severe peripheral field-of-vision (FOV) loss partially because of increased attentional demands related to monitoring safe mobility. In much prior research, the effects of FOV loss on spatial learning have been studied using passive learning paradigms, in which learners are guided along walking paths in novel, indoor environments and explicitly shown the location of targets to be remembered. In a series of studies, we compared passive learning to active learning defined in two ways: active/passive locomotion and active/passive target search. For locomotion, participants walked versus being pushed in a wheelchair with 10 degree FOV. We found similar memory for learned locations, as tested with a pointing task, between active and passive locomotion conditions in both simpler (Experiment 1) and more complex (Experiment 2) spatial learning tasks. Next, we compared active versus passive learning by requiring active search for targets along the paths with either 10 or 60 degree FOV restriction. We found no difference in memory between severe and less severe FOV in this active learning task. However, compared to previously collected data with passive spatial learning where active search was not required, the passive learning task showed better memory for learned target locations. While this counters some prior research demonstrating benefits of active learning, we argue that the detriment of active learning could be explained by the increased cognitive demands induced by adding on additional cognitive challenges to the spatial learning task with severe FOV restriction. Taken together, these results suggest that active locomotion does not affect spatial learning performance in passive learning tasks with restricted FOV, but active search may actually be detrimental to performance. A within-subjects comparison of active and passive learning is ongoing.

Corine Holmes

Sequential memory, spatial integration, and observer movement: A new perspective on spatial memory

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Spatial integration is inherently linked to precise sequential memory. As we move within our natural environments, we experience the space around us as discrete episodes that must be integrated to form a unified, cohesive cognitive map. Thus, to form an accurate global representation, we must know the order in which we viewed each discrete spatial episode, as well as the direction traveled between them. In the current set of studies, we show that sequential memory for temporal order and direction is integral to spatial integration. Furthermore, compared to array rotation, we show that observer movement around a segmented spatial array – both passive and active - enhances sequential memory, and thus spatial integration, showing that sequential memory is paramount to large-scale spatial navigation. In addition, despite the fact that subsequent viewpoints are most often assimilated into that of the first experienced, observer movement yields more flexible spatial memory, such that the global representation is more accurately reconstructed from a variety of perspectives. Together, these studies advance the field of spatial memory, highlighting the importance of sequential memory - and the forces that enhance it - to spatial navigation.