# Final Progress Report for Research Projects Funded by Health Research Grants

Instructions: Please complete all of the items as instructed. Do not delete instructions. Do not leave any items blank; responses must be provided for all items. If your response to an item is "None", please specify "None" as your response. "Not applicable" is not an acceptable response for any of the items. There is no limit to the length of your response to any question. Responses should be single-spaced, no smaller than 12-point type. The report **must be completed using MS Word**. Submitted reports must be Word documents; they should not be converted to pdf format. Questions? Contact Health Research Program staff at 717-783-2548.

1. **Grantee Institution:** Carnegie Mellon University

2. **Reporting Period (start and end date of grant award period):** 1/1/2009-12/31/2011

3. **Grant Contact Person (First Name, M.I., Last Name, Degrees):** Jim Osborn, MS

4. **Grant Contact Person's Telephone Number:** 412-268-6553

5. **Grant SAP Number:** 4100047627

6. **Project Number and Title of Research Project:** Research Project 3: Memory-Based Neural Activity in the Hippocampus

7. **Start and End Date of Research Project:** 1/1/09 – 12/31/11

8. **Name of Principal Investigator for the Research Project:** David S. Touretzky

9. **Research Project Expenses**.

   9(A) Please provide the amount of health research grant funds spent on this project for the entire duration of the grant, including any interest earned that was spent:

   $ 100,894

   9(B) Provide the last names (include first initial if multiple individuals with the same last name are listed) of **all** persons who worked on this research project and were supported with health research funds. Include position titles (Principal Investigator, Graduate Assistant, Post-doctoral Fellow, etc.), percent of effort on project and total health research funds expended for the position. For multiple year projects, if percent of effort varied from year to year, report in the % of Effort column the effort by year 1, 2, 3, etc. of the project (x% Yr 1; z% Yr 2-3).

| Last Name | Position Title | % of Effort on Project | Cost |
|---|---|---|---|
| Touretzky | Research Professor | 20% | $67,330 |
| | | | |
| | | | |
| | | | |
| | | | |
| | | | |
| | | | |

9(C) Provide the names of **all** persons who worked on this research project, but who *were not* supported with health research funds. Include position titles (Research Assistant, Administrative Assistant, etc.) and percent of effort on project. For multiple year projects, if percent of effort varied from year to year, report in the % of Effort column the effort by year 1, 2, 3, etc. of the project (x% Yr 1; z% Yr 2-3).

| Last Name | Position Title | % of Effort on Project |
|---|---|---|
| Gupta | Research Assistant | 100% |
| | | |
| | | |
| | | |
| | | |

9(D) Provide a list of **all** scientific equipment purchased as part of this research grant, a short description of the value (benefit) derived by the institution from this equipment, and the cost of the equipment.

| Type of Scientific Equipment | Value Derived | Cost |
|---|---|---|
| None | | |
| | | |
| | | |
| | | |
| | | |

**10. Co-funding of Research Project during Health Research Grant Award Period.** Did this research project receive funding from any other source during the project period when it was supported by the health research grant?

Yes___X_____ No_____

If yes, please indicate the source and amount of other funds: (1) NSF IGERT fellowship to Anoopum Gupta: $40,500 direct costs per year in 2009 and 2010; (2) NIH F30 NRSA training grant to support Anoopum Gupta, July 2010 through June 2015,: $231,900.

**11. Leveraging of Additional Funds**

11(A) As a result of the health research funds provided for this research project, were you able to apply for and/or obtain funding from other sources to continue or expand the research?

Yes____X____ No_____

If yes, please list the applications submitted (column A), the funding agency (National Institutes of Health—NIH, or other source in column B), the month and year when the application was submitted (column C), and the amount of funds requested (column D). If you have received a notice that the grant will be funded, please indicate the amount of funds to be awarded (column E). If the grant was not funded, insert "not funded" in column E.

Do not include funding from your own institution or from CURE (tobacco settlement funds). Do not include grants submitted prior to the start date of the grant as shown in Question 2. If you list grants submitted within 1-6 months of the start date of this grant, add a statement below the table indicating how the data/results from this project were used to secure that grant.

| A. Title of research project on grant application | B. Funding agency (check those that apply) | C. Month and Year Submitted | D. Amount of funds requested: | E. Amount of funds to be awarded: |
|---|---|---|---|---|
| Anoopum Gupta: Cognitive Maps and Novel Behavioral Sequences in the Hippocampus (NIH F30 training grant) | ☒NIH<br>☐ Other federal (specify:_____ _____)<br>☐ Nonfederal source (specify: _____) | December 2009 | $231,900 | $231,900 |
| | ☐NIH<br>☐ Other federal (specify:_____ _____)<br>☐ Nonfederal source (specify: _____) | | $ | $ |
| | ☐NIH<br>☐ Other federal (specify:_____ _____)<br>☐ Nonfederal source (specify: _____) | | $ | $ |

11(B) Are you planning to apply for additional funding in the future to continue or expand the research?

Yes_____ No____X_____

If yes, please describe your plans:

**12. Future of Research Project.** What are the future plans for this research project?

Anoopum Gupta has completed his PhD and returned to medical school for the last two years of his training as an MD. He may work with the PI, David Touretzky, on some additional analyses of the data he has collected as time permits.

**13. New Investigator Training and Development**. Did students participate in project supported internships or graduate or post-graduate training for at least one semester or one summer?

Yes____X_____ No_____

If yes, how many students? Please specify in the tables below:

| | Undergraduate | Masters | Pre-doc | Post-doc |
|---|---|---|---|---|
| Male | | | 1 | |
| Female | | | | |
| Unknown | | | | |
| **Total** | | | **1** | |

| | Undergraduate | Masters | Pre-doc | Post-doc |
|---|---|---|---|---|
| Hispanic | | | | |
| Non-Hispanic | | | 1 | |
| Unknown | | | | |
| **Total** | | | **1** | |

| | Undergraduate | Masters | Pre-doc | Post-doc |
|---|---|---|---|---|
| White | | | | |
| Black | | | | |
| Asian | | | 1 | |
| Other | | | | |
| Unknown | | | | |
| **Total** | | | **1** | |

**14. Recruitment of Out-of–State Researchers**. Did you bring researchers into Pennsylvania to carry out this research project?

Yes_____ No____X_____

If yes, please list the name and degree of each researcher and his/her previous affiliation:

**15. Impact on Research Capacity and Quality**. Did the health research project enhance the quality and/or capacity of research at your institution?

Yes_____ No____X_____

If yes, describe how improvements in infrastructure, the addition of new investigators, and other resources have led to more and better research.

**16. Collaboration, business and community involvement.**

16(A) Did the health research funds lead to collaboration with research partners outside of your institution (e.g., entire university, entire hospital system)?

Yes____X____ No_____

If yes, please describe the collaborations:

The project included a collaboration with Professor A. David Redish of the Department of Neuroscience of the University of Minnesota.

16(B) Did the research project result in commercial development of any research products?

Yes_____ No____X_____

If yes, please describe commercial development activities that resulted from the research project:

16(C) Did the research lead to new involvement with the community?

Yes_____ No____X_____

If yes, please describe involvement with community groups that resulted from the research project:

**17. Progress in Achieving Research Goals, Objectives and Aims.**

List the project goals, objectives and specific aims (as contained in the grant application's strategic plan). Summarize the progress made in achieving these goals, objectives and aims for the period that the project was funded (i.e., from project start date through end date). Indicate whether or not each goal/objective/aim was achieved; if something was not achieved, note the reasons why. Describe the methods used. If changes were made to the research goals/objectives/aims, methods, design or timeline since the original grant application was submitted, please describe the changes. Provide detailed results of the project. Include evidence of the data that was generated and analyzed, and provide tables, graphs, and figures of the data. List published abstracts, poster presentations and scientific meeting presentations at the end of the summary of progress; peer-reviewed publications should be listed under item 20.

This response should be a DETAILED report of the methods and findings. It is not sufficient to state that the work was completed. Insufficient information may result in an unfavorable performance review, which may jeopardize future funding. If research findings are pending publication you must still include enough detail for the expert peer reviewers to evaluate the progress during the course of the project.

Health research grants funded under the Tobacco Settlement Act will be evaluated via a performance review by an expert panel of researchers and clinicians who will assess project work using this Final Progress Report, all project Annual Reports and the project's strategic plan. After the final performance review of each project is complete, approximately 12-16 months after the end of the grant, this Final Progress Report, as well as the Final Performance Review Report containing the comments of the expert review panel, and the grantee's written response to the Final Performance Review Report, will be posted on the CURE Web site.

**There is no limit to the length of your response. Responses must be single-spaced below, no smaller than 12-point type. If you cut and paste text from a publication, be sure symbols print properly, e.g., the Greek symbol for alpha (α) and beta (ß) should not print as boxes (□) and include the appropriate citation(s). DO NOT DELETE THESE INSTRUCTIONS.**

Understanding how cognitive processes arise from neural tissue involves, in part, determining the computational roles played by various brain structures. The hippocampus is one of the major structures of the brain, receiving inputs from much of the cortex and from several important subcortical areas, such as the basal ganglia and amygdala. It is believed to be important for both memory formation and spatial representation. In the rodent, hippocampal pyramidal cells have compact spatial firing fields, called "place fields," suggesting that the hippocampus might be specialized for encoding the rodent's location on a "cognitive map".

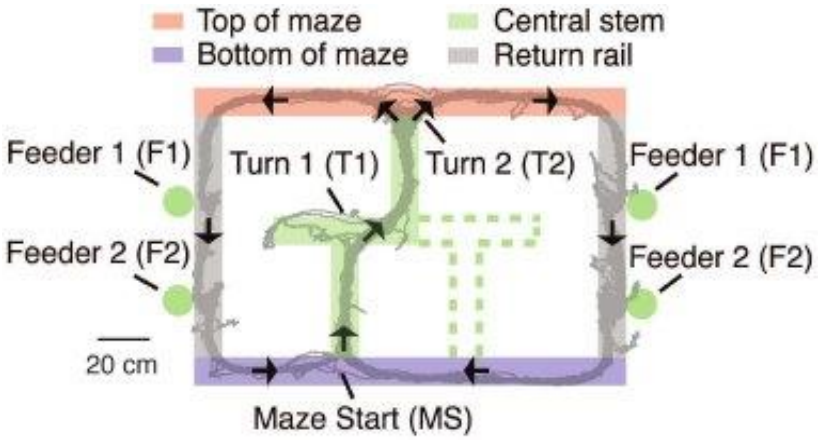
Recent experiments have shown that the hippocampus encodes more than just the animal's current location. Under some circumstances, the hippocampus "replays" a trajectory the animal recently experienced by rapidly reactivating place cells during a "sharp wave" that occurs when the animal is stationary and the hippocampus is in an EEG state called LIA (Low-amplitude Irregular Activity). A slower type of replay can occur when the animal is paused but attentive and the hippocampus is exhibiting theta rhythm. In a process called "vicarious trial and error",

which can occur when the animal pauses at a choice point in a T-maze, the hippocampus can "play" a trajectory corresponding to travel down one of the two maze arms. The goal of this project was to study these trajectory events in order to arrive at a better understanding of hippocampal information processing.

Two approaches were used. Specific Aim 1 was to apply statistical analysis techniques to multiunit recording data (obtained from experiments performed in collaboration with the Redish laboratory at the University of Minnesota) to reconstruct and characterize trajectories. Specific Aim 2 was to develop computational models to try to replicate and thus explain the experimental data. Attractor-based neural network models have been used to explain many aspects of hippocampal function and proved useful for modeling these trajectory phenomena.

**Result 1: Hippocampal replay can produce trajectories the animal never actually experienced in real life.**

We analyzed data from an experiment Anoopum Gupta conducted while visiting the Redish lab. In this experiment, rats ran laps through an elevated T-maze (see figure below) and earned food rewards on the return arms if they turned in the correct direction at the T intersection. While the rat is running, the hippocampus exhibits theta oscillations (7-10 Hz) and hippocampal place cell activity generally encodes the rat's present position on the maze. But when the rat pauses, either to consume a food reward, to contemplate which way to turn, or for some other reason, its hippocampus enters a different mode known as LIA (Large-amplitude Irregular Activity), punctuated by sharp waves. During these sharp waves, place cells replay sequences of activity corresponding to portions of trajectories through the maze. However, the sequences are replayed at several times real time, and they may be played in either forward or backward order.




The experiment yielded several interesting results. First, replay was not limited to temporally recent events. Some of the sequences replayed corresponded to portions of the maze the rat had last visited more than 10 minutes ago. Second, the selection of sequences to replay was not random. If the rat was currently performing a task where it had to always turn left at the T-intersection, it was more likely to replay trajectories from the right side of the maze (which it had visited during a previous task) than if it was performing a task where it had to alternate between left and right turns. This suggests the rat mentally rehearses past trajectories if it cannot re-experience them during normal behavior. The third and most significant result was that the rat

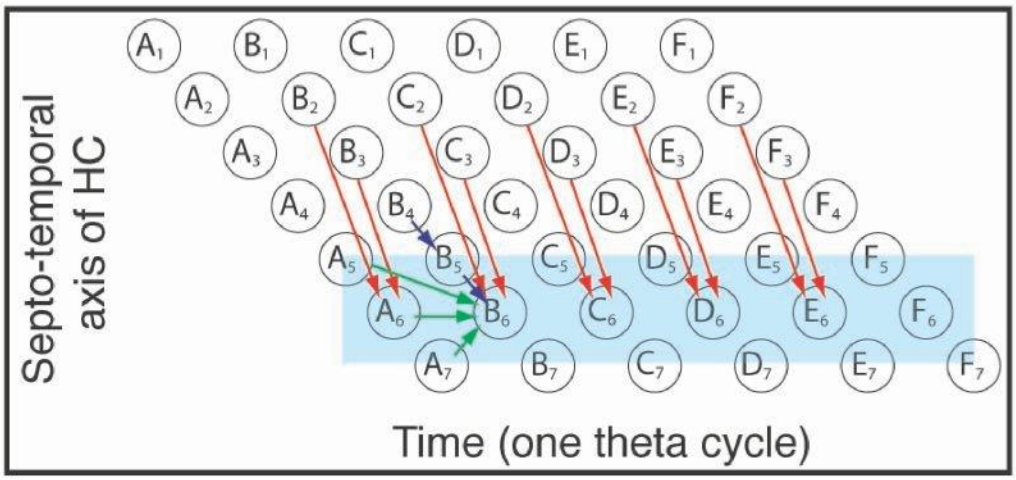
occasionally exhibited novel “shortcut” sequences that were consistent with the structure of the maze, but which it had never traversed in real life, such as proceeding up the right return rail, across the top of the maze, and down the left return rail. This result suggests that replay events may help to consolidate the rat’s experiences into a more general “cognitive map” that reflects the true spatial structure of the environment, including potential routes not yet attempted.

These results were published in a 2010 article in Neuron.

**Result 2: An attractor model of replay can produce forward, backward, and shortcut trajectories.**

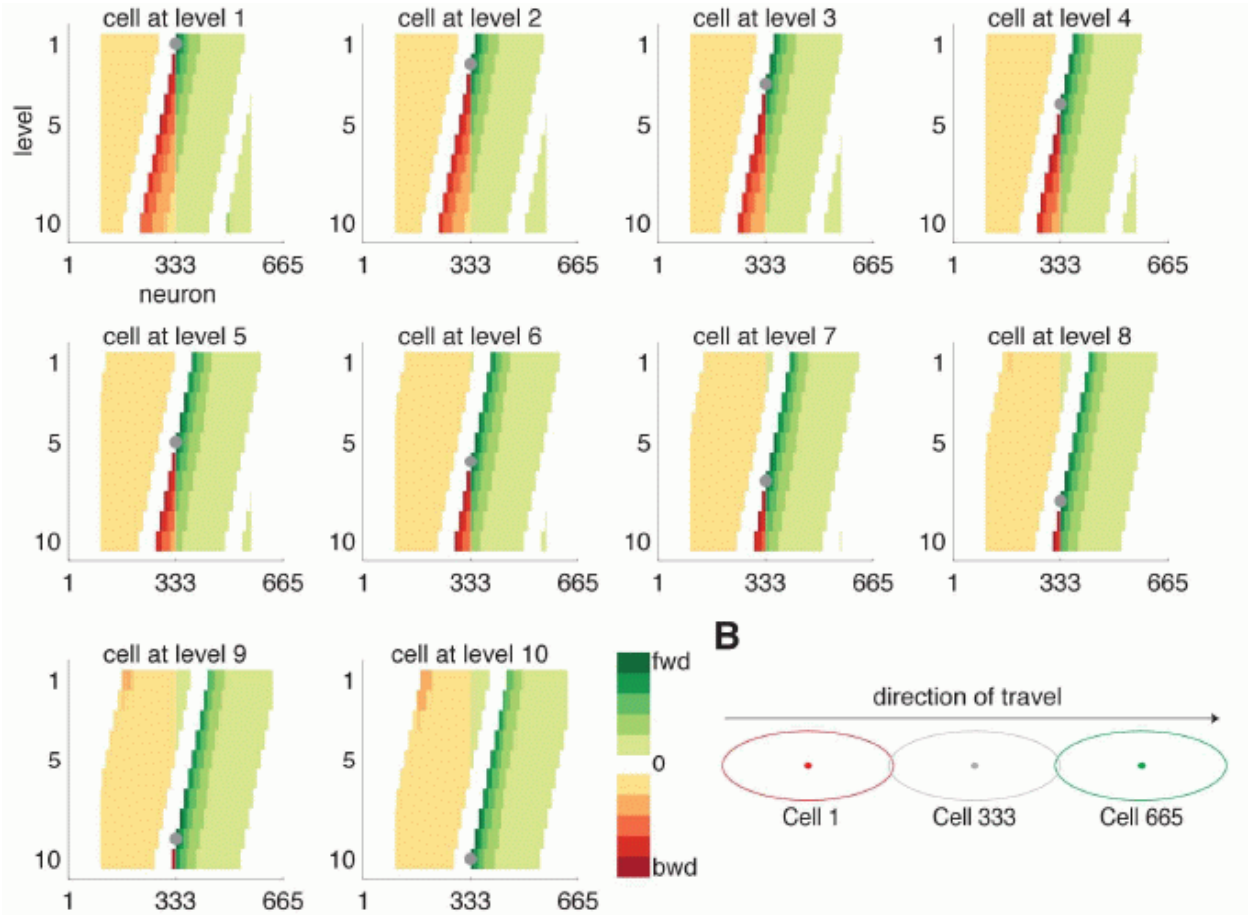
Analysis of sharp wave activity patterns reveals neural firing sequences representing trajectories the rat has experienced (forward replay). But there are also sequences corresponding to the reverse of these trajectories (backward replay). Sequences are assumed to result from a chain of synaptic connections, e.g., observing the sequence A-B-C would suggest that there is an excitatory connection from neuron A to neuron B, and a similar connection from neuron B to neuron C. The synaptic learning rule for potentiating a synapse from A to B requires that neuron A fire before neuron B. Since the rat only experiences the trajectory in forward order, how could the brain learn the connections from C to B and from B to A that would allow it to replay the sequence in reverse order?

Our proposed solution to this puzzle was to exploit the recently reported theta rhythm phase gradient along the longitudinal (septo-temporal) axis of the hippocampus (Lubenov and Siapas, Nature, 2009). While cells at all levels are firing in forward sequence as the rat experiences a trajectory, the firing of more temporal cells can be delayed by as much as 120 ms relative to cells at the dorsal pole. Since pyramidal cells in hippocampal area CA3 have wide-ranging projections, it is possible for dorsal cells representing B to acquire excitatory projections to more temporal cells representing A, as shown in the figure below (see red connection from $B_2$ to $A_6$). Forward connections can be learned at the same time (e.g., green connection from $A_6$ to $B_6$).




We developed a computer simulation of hippocampal learning that includes the theta rhythm phase gradient and longitudinal connections, and verified that both forward and backward

connections are learned when the model experiences only forward trajectories. The figure below shows the learned connection strengths between a representative cell at each of 10 septo-temporal levels and all other cells in model. Color distinguishes forward from backward connections. Connections in both directions are evident at all levels.




We then developed a separate model of hippocampal sharp wave replay, and showed that if the connection weights followed the pattern constructed by the first model, sequences could be replayed in either forward or backward order, and shortcut sequences could occur that looked very much like what had been observed experimentally.

We submitted a journal paper describing this result, but comments from reviewers led us to reevaluate the model. We had assumed that backward sequences could not be learned at a single hippocampal layer, only across layers, but this is predicated on the belief that synaptic learning could only occur within a theta cycle, not across theta cycles. Some theories of hippocampal function assign different roles to different portions of the theta cycle (storage in one portion, retrieval in another), and our assumption was motivated by such theories, but the theories are unproven.

In response to reviewer comments, we examined what the model could do if learning were permitted to occur across theta cycles. In that case, ordinary spike timing-dependent plasticity would allow connections to form in the backward direction in a single layer as the animal

progressed through a sequence, e.g., during the theta sequence A-B-C-D-E it could learn E-A and E-B connections; then during B-C-D-E-F it could learn F-B and F-C connections, and so on. Our revised simulations showed that these connections were sufficient to produce backward replay.

In light of these new simulations, our modeling work suggests two possible mechanisms for hippocampal replay. If learning can in fact occur across theta cycles, then ordinary synaptic plasticity combined with attractor dynamics and a brief refractory period can produce both forward and backward replay. If learning cannot occur across theta cycles, then the phase gradient that exists across the hippocampus can be exploited to learn the connections necessary for backward replay, but the fact that these connections are only formed across different levels of the hippocampus, not within a single level, poses some problems for our replay mechanism, as was acknowledged in our original manuscript.

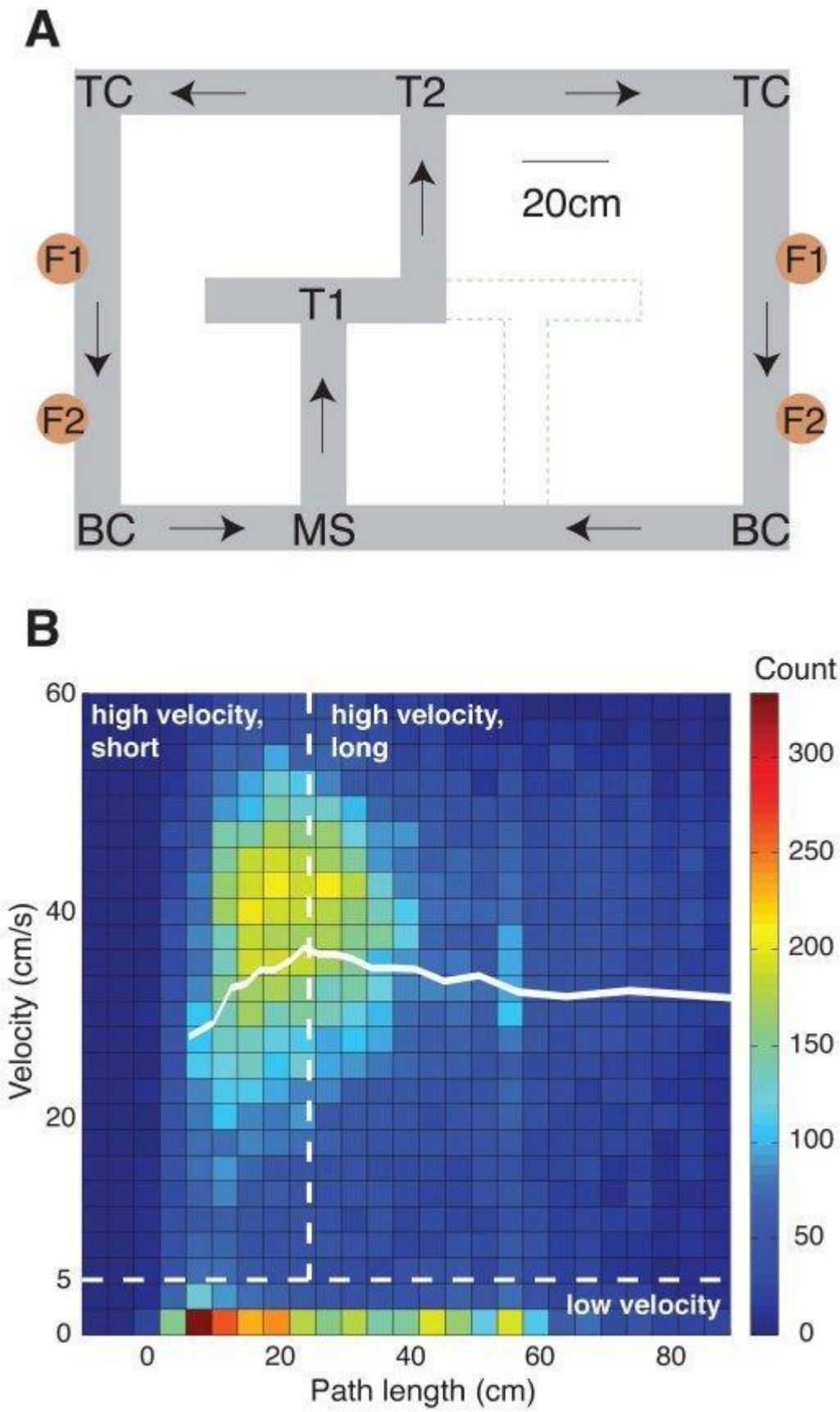
We have not produced a new manuscript to address these issues, choosing instead to devote our remaining time for this project to examining another aspect of hippocampal sequences.

**Result 3: Hippocampal theta sequences exhibit segmentation of spatial experience.**

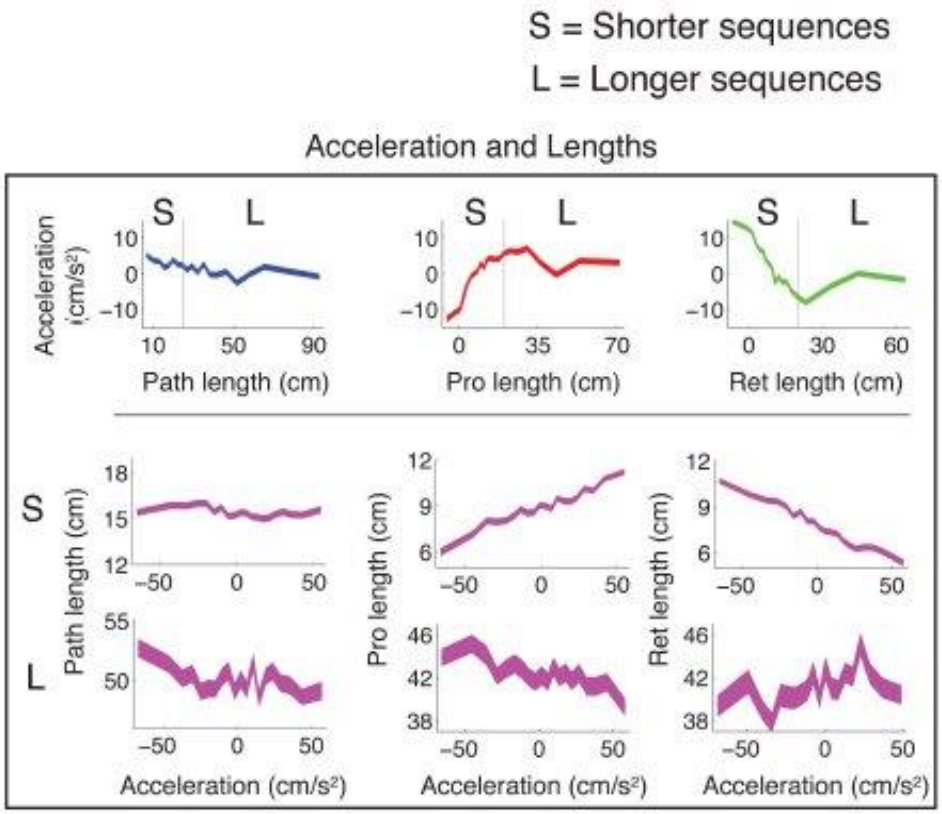
This result concerns the structure of sequences observed during theta cycle activity, rather than the faster sharp wave replay sequences described in Result 1.

Theta cycle activity begins with the firing of place cells whose fields are centered slightly behind the rat's current position, and ends with cells whose place field centers are slightly ahead of it. Thus, the pattern of activity within a theta cycle sweeps along a segment of the path the rat is traveling.

Analyzing data collected in the Redish lab on the same two-T maze described earlier, we found that as velocity increased, short theta sequences represented longer paths in the environment (see figure below). Long theta sequences seemed to be of a different nature; they occurred only at higher velocities but their lengths did not correlate with velocity.


A
TC
T2
TC
20cm
F1
F1
T1
F2
F2
BC
MS
BC
B
Count
high velocity, short
high velocity, long
low velocity
Velocity (cm/s)
Path length (cm)
60
40
20
5
0
0
20
40
60
80
300
250
200
150
100
50
0

A second important observation was that when the animal was accelerating, the prospective (Pro) portion of paths included more space ahead of the animal; when it was decelerating, the retrospective (Ret) portion of paths included more space behind the animal (see figure below). Furthermore, as path length increased, there were linear increases in both theta period and number of gamma cycles per theta cycle (graphs not shown).

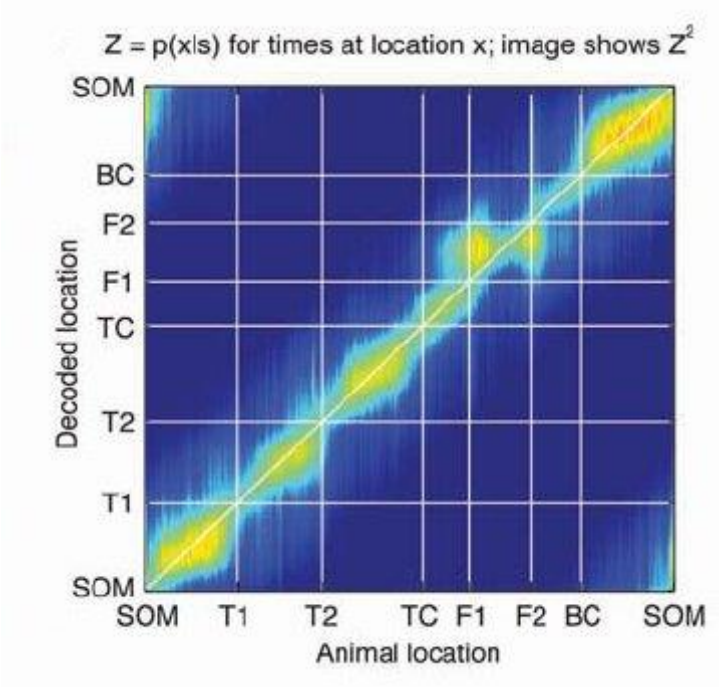



Relationship between acceleration and path length. “Path” refers to total path length, “Pro” to prospective length (paths from the rat’s current position extending forward), and “Ret” to retrospective length (from the start of the sequence to the rat’s current position). The top row shows acceleration as a function of Path, Pro and Ret length. The next two rows show path length as a function of acceleration, plotted separately for short and long paths. For short paths, Pro length increases with acceleration, whereas Ret length decreases with acceleration.

Finally, we observed that neural activity represented the environment in segments, corresponding with physical landmarks such as the corners, turn points, and feeder cups. Since the animals tended to accelerate as they left a landmark and decelerate as they approached the next one, they produced an alternating pattern of prospective and retrospective paths, resulting in a distribution of activity sequences that preferentially represented the segments between landmarks. We suggest that this can be regarded as the animal segmenting the environment into logical

"chunks". These chunks could help the animal organize its memory and enable a more abstract encoding of the structure of the task it was performing.

The figure below dramatically illustrates the segmentation of the environment evident in the distribution of theta sequences. The landmarks are the start of the maze (SOM), turns 1 and 2 (T1 and T2), feeder cups 1 and 2 (F1 and F2), and the top and bottom corners of the maze (TC and BC; see earlier figure.). If theta sequences were uniformly distributed, then they would often extend backward behind the last encountered landmark, or forward beyond the next landmark the animal was due to encounter. But this was not the case. Theta sequences tended to extend less further back as the animal left a landmark, and less further forward as it approached a landmark, leaving the sequence largely bounded *between* the landmarks immediately behind and immediately ahead of the rat. To visualize this, we computed a cross-correlation matrix comparing the animal's actual and decoded locations. During a theta sequence, the hippocampal representation will sweep along some trajectory, and this corresponds to a vertical movement through the figure. The rat's actual position at the time of the sweep determines the horizontal coordinate of that movement, and the white lines mark the landmark locations. As is evident from the figure, theta sequences were bounded by the white lines and rarely crossed them.




A paper describing these results was submitted to Nature Neuroscience in January 2012. In response to reviewer comments, we made substantial revisions and conducted some new analyses. The revised version was submitted in February 2012 and we are awaiting the next round of reviews.

**18. Extent of Clinical Activities Initiated and Completed**. Items 18(A) and 18(B) should be completed for all research projects. If the project was restricted to secondary analysis of clinical data or data analysis of clinical research, then responses to 18(A) and 18(B) should be "No."

18(A) Did you initiate a study that involved the testing of treatment, prevention or diagnostic procedures on human subjects?

_____Yes
__X___No

18(B) Did you complete a study that involved the testing of treatment, prevention or diagnostic procedures on human subjects?

_____Yes
__X___No

**If "Yes" to either 18(A) or 18(B), items 18(C) – (F) must also be completed.** (Do NOT complete 18(C-F) if 18(A) and 18(B) are both "No.")

18(C) How many hospital and health care professionals were involved in the research project?

_____Number of hospital and health care professionals involved in the research project

18(D) How many subjects were included in the study compared to targeted goals?

_____Number of subjects originally targeted to be included in the study
_____Number of subjects enrolled in the study

**Note**: Studies that fall dramatically short on recruitment are encouraged to provide the details of their recruitment efforts in Item 17, Progress in Achieving Research Goals, Objectives and Aims. For example, the number of eligible subjects approached, the number that refused to participate and the reasons for refusal. Without this information it is difficult to discern whether eligibility criteria were too restrictive or the study simply did not appeal to subjects.

18(E) How many subjects were enrolled in the study by gender, ethnicity and race?

Gender:
_____Males
_____Females
_____Unknown

Ethnicity:
_____Latinos or Hispanics
_____Not Latinos or Hispanics
_____Unknown

Race:
_____American Indian or Alaska Native
_____Asian

_____Blacks or African American
_____Native Hawaiian or Other Pacific Islander
_____White
_____Other, specify:_____
_____Unknown

18(F) Where was the research study conducted? (List the county where the research study was conducted. If the treatment, prevention and diagnostic tests were offered in more than one county, list all of the counties where the research study was conducted.)

**19. Human Embryonic Stem Cell Research.** Item 19(A) should be completed for all research projects. If the research project involved human embryonic stem cells, items 19(B) and 19(C) must also be completed.

19(A) Did this project involve, in any capacity, human embryonic stem cells?
_____Yes
__X___ No

19(B) Were these stem cell lines NIH-approved lines that were derived outside of Pennsylvania?
_____Yes
_____ No

19(C) Please describe how this project involved human embryonic stem cells:

**20. Articles Submitted to Peer-Reviewed Publications**.

20(A) Identify all publications that resulted from the research performed during the funding period and that have been submitted to peer-reviewed publications. Do not list journal abstracts or presentations at professional meetings; abstract and meeting presentations should be listed at the end of item 17. **Include only those publications that acknowledge the Pennsylvania Department of Health as a funding source** (as required in the grant agreement). List the title of the journal article, the authors, the name of the peer-reviewed publication, the month and year when it was submitted, and the status of publication (submitted for publication, accepted for publication or published.). Submit an electronic copy of each publication or paper submitted for publication, listed in the table, in a PDF version 5.0.5 (or greater) format, 1,200 dpi. Filenames for each publication should include the number of the research project, the last name of the PI, the number of the publication and an abbreviated research project title. For example, if you submit two publications for PI Smith for the "Cognition and MRI in Older Adults" research project (Project 1), and two publications for PI Zhang for the "Lung Cancer" research project (Project 3), the filenames should be:

Project 1 – Smith – Publication 1 – Cognition and MRI

Project 1 – Smith – Publication 2 – Cognition and MRI
Project 3 – Zhang – Publication 1 – Lung Cancer
Project 3 – Zhang – Publication 2 – Lung Cancer

If the publication is not available electronically, provide 5 paper copies of the publication.

**Note:** The grant agreement requires that recipients acknowledge the Pennsylvania Department of Health funding in all publications. Please ensure that all publications listed acknowledge the Department of Health funding. If a publication does not acknowledge the funding from the Commonwealth, do not list the publication.

| Title of Journal Article: | Authors: | Name of Peer-reviewed Publication: | Month and Year Submitted: | Publication Status (check appropriate box below): |
|---|---|---|---|---|
| 1.Hippocampal replay is not a simple function of experience. | A. Gupta, M. A. A. van der Meer, D. S. Touretzky, A. D. Redish | Neuron | Published March, 2010 | ☐Submitted<br>☐Accepted<br>☒Published |

20(B) Based on this project, are you planning to submit articles to peer-reviewed publications in the future?

Yes_____ No____X_____

If yes, please describe your plans:

**21. Changes in Outcome, Impact and Effectiveness Attributable to the Research Project.** Describe the outcome, impact, and effectiveness of the research project by summarizing its impact on the incidence of disease, death from disease, stage of disease at time of diagnosis, or other relevant measures of outcome, impact or effectiveness of the research project. If there were no changes, insert "None"; do not use "Not applicable." Responses must be single-spaced below, and no smaller than 12-point type. DO NOT DELETE THESE INSTRUCTIONS. There is no limit to the length of your response.

None.

**22. Major Discoveries, New Drugs, and New Approaches for Prevention Diagnosis and Treatment**. Describe major discoveries, new drugs, and new approaches for prevention, diagnosis and treatment that are attributable to the completed research project. If there were

no major discoveries, drugs or approaches, insert "None"; do not use "Not applicable." Responses must be single-spaced below, and no smaller than 12-point type. DO NOT DELETE THESE INSTRUCTIONS. There is no limit to the length of your response.

One major result, highlighted in an invited commentary piece that accompanied our Neuron paper, is that the hippocampus is capable of "playing back" sequences the animal has never actually experienced in real life. This puts hippocampal replay in a new light and will likely generate further experiments in other laboratories.

**23. Inventions, Patents and Commercial Development Opportunities.**

23(A) Were any inventions, which may be patentable or otherwise protectable under Title 35 of the United States Code, conceived or first actually reduced to practice in the performance of work under this health research grant? Yes_____ No___X_____

If "Yes" to 23(A), complete items a – g below for each invention. (Do NOT complete items a - g if 23(A) is "No.")

a. Title of Invention:

b. Name of Inventor(s):

c. Technical Description of Invention (describe nature, purpose, operation and physical, chemical, biological or electrical characteristics of the invention):

d. Was a patent filed for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?
Yes_____ No____

If yes, indicate date patent was filed:

e. Was a patent issued for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?
Yes_____ No____
If yes, indicate number of patent, title and date issued:
Patent number:
Title of patent:
Date issued:

f. Were any licenses granted for the patent obtained as a result of work performed under this health research grant? Yes_____ No____

If yes, how many licenses were granted?_____

g. Were any commercial development activities taken to develop the invention into a commercial product or service for manufacture or sale? Yes___ No____

If yes, describe the commercial development activities:

23(B) Based on the results of this project, are you planning to file for any licenses or patents, or undertake any commercial development opportunities in the future?

Yes_____ No____X_____

If yes, please describe your plans:

**24. Key Investigator Qualifications.** Briefly describe the education, research interests and experience and professional commitments of the Principal Investigator and all other key investigators. In place of narrative you may insert the NIH biosketch form here; however, please limit each biosketch to 1-2 pages. *For Nonformula grants only – include information for only those key investigators whose biosketches were not included in the original grant application.*

## BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

| NAME | POSITION TITLE |
|---|---|
| Touretzky, David Stuart | Research Professor of Computer Science |
| eRA COMMONS USER NAME<br>Touretzky | |

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

| INSTITUTION AND LOCATION | DEGREE *(if applicable)* | YEAR(s) | FIELD OF STUDY |
|---|---|---|---|
| Rutgers University, New Brunswick, NJ | B.A. | 1978 | Computer Science |
| Carnegie Mellon University | M.S. | 1979 | Computer Science |
| Carnegie Mellon University | Ph.D. | 1984 | Computer Science |

### A. Positions and Honors.

**Positions and Employment**

1984-1987 Research Associate, Computer Science Department, Carnegie Mellon University
1987-1991 Research Scientist, Computer Science Department, Carnegie Mellon University
1991-2000 Senior Research Scientist, Computer Science Department, Carnegie Mellon University
2000- Research Professor (title changed from Principal Scientist in July 2003), Computer Science Department, Courtesy appointment (since 1996) in the Robotics Institute.

**Other Experience and Professional Memberships**

1976- Member, Association for Computing Machinery (ACM)
1982- Member, Association for the Advancement of Artificial Intelligence (AAAI)
1993- Member, Society for Neuroscience
1995- Board of Directors, Neural Information Processing Systems (NIPS) Foundation
1995- Co-Director, graduate training prog., Center for the Neural Basis of Cognition, Carnegie Mellon
2007- Director of Robotics Education, ARTSI Alliance (see ARTSIAlliance.org)

**Honors**

2006 Distinguished Scientist, Association for Computing Machinery

### B. Selected peer-reviewed publications (in chronological order).

(Publications selected from 39 peer-reviewed journal articles and 70 peer-reviewed conference papers)

1. Touretzky, D. S. and Hinton, G. E. (1988) A distributed connectionist production system. Cognitive Science, vol. 12, number 3, pp. 423-466.

2. Horty, J. F., Thomason, R. H., and Touretzky, D. S. (1990) A skeptical theory of inheritance in nonmonotonic semantic nets. Artificial Intelligence 42(2-3):311-348, April 1990.
3. Touretzky, D. S. (1990) BoltzCONS: Dynamic symbol structures in a connectionist network. Artificial Intelligence vol. 46, pp. 5-46.
4. Touretzky, D. S., and Wheeler, D. W. (1991) Sequence manipulation using parallel mapping networks. Neural Computation 3(1):98-109.
5. Touretzky, D. S., and Lee, P. (1992) Visualizing evaluation in applicative languages. Communications of the ACM, 35(10):49-59.
6. Touretzky, D. S., Redish, A. D., and Wan, H. S. (1993) Neural representation of space using sinusoidal arrays. Neural Computation, 5(6):869-884.
7. Gupta, P., and Touretzky, D. S. (1994) Connectionist models and linguistic theory: Investigations of stress systems in language. Cognitive Science 18(1), pp. 1-50. January, 1994.
8. Touretzky, D. S., and Pomerleau, D. A. (1994) Reconstructing physical symbol systems. Cognitive Science 18(2), pp. 345-353. April, 1994.
9. Redish, A. D., and Touretzky, D. S. (1994) The reaching task: Evidence for vector arithmetic in the motor system? Biological Cybernetics, 71(4), pp. 307-317.
10. Touretzky, D. S. and Redish, A. D. (1996) Theory of rodent navigation based on interacting representations of space. Hippocampus, 6(3):247-270.
11. Redish, A. D., Elga, A. N., and Touretzky, D. S. (1996) A coupled attractor model of the rodent head direction system. NETWORK, 7(4):671-685.
12. Redish, A. D. and Touretzky, D. S. (1997) Cognitive maps beyond the hippocampus. Hippocampus, 7(1):15-35.
13. Wheeler, D. W., and Touretzky, D. S. (1997) A parallel licensing model of normal slips and phonemic paraphasias. Brain and Language, 59(1):147-201.
14. Touretzky, D. S. and Saksida, L. M. (1997) Operant conditioning in Skinnerbots. Adaptive Behavior, 5(3/4):219-247.
15. Redish, A. D., and Touretzky, D. S. (1998) The role of the hippocampus in solving the Morris water maze. Neural Computation 10(1):73-111.
16. Saksida, L. M., Raymond, S. M., and Touretzky, D. S. (1998) Shaping robot behavior using principles from instrumental conditioning. Robotics and Autonomous Systems, 22(3/4):231-249.
17. Goodridge, J. P., and Touretzky, D. S. (2000) Modeling attractor deformation in the rodent head direction system. Journal of Neurophysiology, 83(6):3402-3410.
18. Daw, N. D., and Touretzky, D. S. (2002) Long-term reward prediction in TD models of the dopamine system. Neural Computation, 14(11), 2567-2583.
19. Touretzky, D. S., Weisman, W. E., Fuhs, M. C., Skaggs, W. E., Fenton, A. A., and Muller R. U. (2005) Deforming the hippocampal map. Hippocampus 15(1):41-55. PMID: 15390166
20. Fuhs, M. C., VanRhoads, S. R., Casale, A. E., McNaughton, B., and Touretzky, D. S. (2005) Influence of path integration vs. environmental orientation on place cell remapping between visually identical environments. Journal of Neurophysiology 94(4):2603-2616. PMID: 15958062
21. Fuhs, M. C., and Touretzky, D. S. (2006) A spin glass model of path integration in rat medial entorhinal cortex. Journal of Neuroscience 26(16):4266-4276. PMID: 1662-4947
22. Daw, N. D., Courville, A. C., and Touretzky, D. S. (2006) Representation and timing in theories of the dopamine system. Neural Computation 18(7):1637-1677.
23. Courville, A. C., Daw, N. D., and Touretzky, D. S. (2006) Bayesian theories of conditioning in a changing world. Trends in Cognitive Sciences, 10(7):294-300.
24. Touretzky, D.S., Halelamien, N.S., Tira-Thompson, E.J., Wales, J.J., and Usui K. (2007) Dual-coding representations for robot vision in Tekkotsu. Autonomous Robots 22(4):425-435.