Flexible modulation of sequence generation in the entorhinal-hippocampal system

Daniel C. MacNamee, Kimberly L. Stachenfeld, Matthew M. Botvinick and Samuel J. Gershman

Huang Nan

Peking University

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Outline

1. Background
1.1 Entorhinal-Hippocampal Circuit
1.2 Cognitive Function of EHC
1.3 Problems to address

2. Model

3. Results
3.1 Foraging in open environment
3.2 Goal-directed trajectory with Lévy jumps
3.3 Generative cycling from minimally auto-correlated sampling
3.4 Diffusive hippocampal reactivation for structure consolidation
3.5 Degraded spatio-temporal consistency from dysregulated input

4. Conclusion

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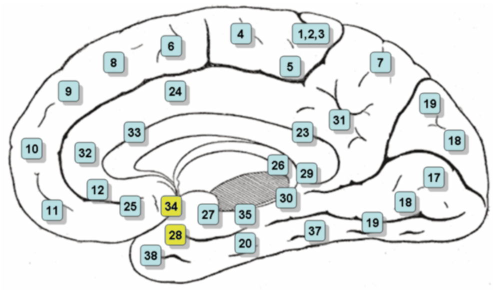
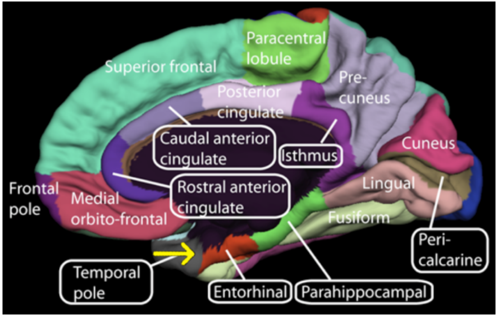
The Entorhinal Cortex

- An area of brain's allocortex
- Medial temporal lobe



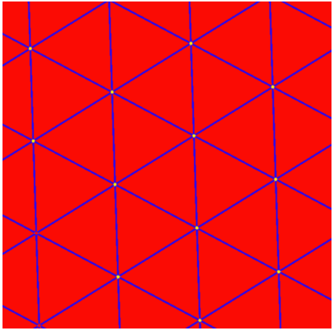
- Network hub for memory, navigation, and perception of time



Source: `https://en.wikipedia.org/wiki/Entorhinal_cortex`

Entorhinal Cortex: Grid Cells

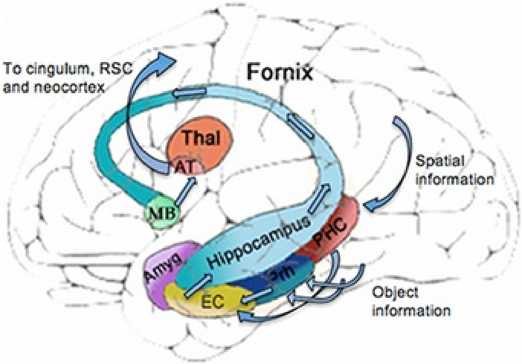
- A type of neuron within the entorhinal cortex
- Fires at regular intervals as an animal navigates an open area
- Encoding location, distance, and direction
- Found in many animals from rodents to human



Source: https://en.wikipedia.org/wiki/Grid_cell

The Hippocampus

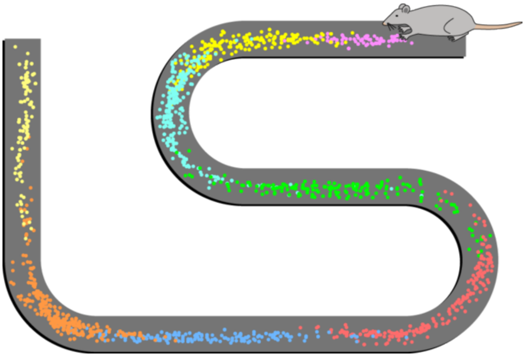
- Located in allocortex
- A part of Limbic system
- Information consolidation
    - Short-term memory
    - Long-term memory
    - Spatial memory associated with navigation



Source: `http://dx.doi.org/10.1111/nyas.12467`

Hippocampus: Place Cells

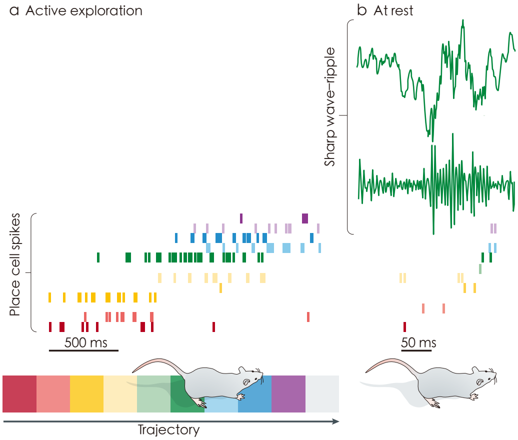
- Pyramidal neuron in the Hippocampus
- Fires when an animal enters certain place (known as place field)
- Act collectively as cognitive representation of spatial location (known as cognitive map)



Source: `https://en.wikipedia.org/wiki/Place_cell`

Previous discovery: Replay in EHC

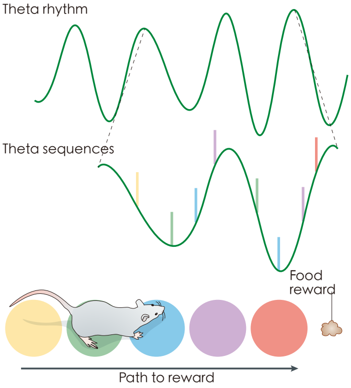
- Sequential non-local reactivation of hippocampal place codes
- Temporally compressed representation of a previously experienced trajectory
- Embedded within hippocampal sharp-wave ripples (SWRs)
- Recently observed to behave like random walk rather than keeping track of physical traversals



Source: `https://www.nature.com/articles/nrn.2016.21`

Previous discovery: Precess of Theta sequences

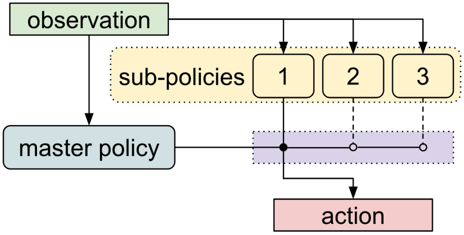
- Also sequential non-local reactivation of hippocampal place codes
- Typically phase precess through local positions
- May sweep ahead to remote locations along potential paths available



Source: `https://www.nature.com/articles/nrn.2016.21`

Problems to address

- How to reconcile these diverse forms of sequential hippocampal representation?
- How to parsimoniously realize distinct modes of such sequence generation?



Source: `https://openai.com/blog/learning-a-hierarchy/`

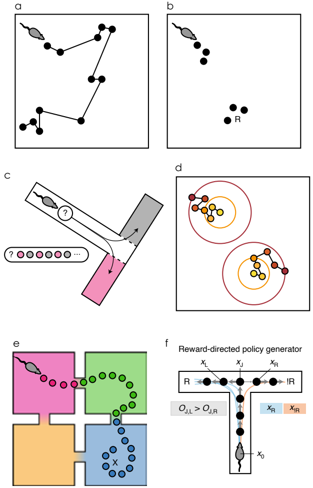


Fig 1

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Model setup

Biological model		Computational model
Hippocampus	$\mapsto$	Sequence Generator
Grid cells	$\mapsto$	Encoding infinitesimal generators
Establishing neocortical memory	$\mapsto$	Learning from experiential replay
Hypothetical spatial trajectories	$\mapsto$	Samples of possible future behavior
Distinct modes of sequence generation	$\mapsto$	Systematically modulated sampling regime

Model description

- Internal state sequence $\mathbf{x} = (x_0, x_1, \cdots, x_t)$ is sample from a probability distribution $p(\mathbf{x})$ defined over state-space $\mathcal{X}$
- State-space $\mathcal{X}$ is considered to be discrete (via discretization for continuous state-spaces) in a form of matrix-vector products
- Sequence generation is initialized with an initial distribution $p\left(x_0\right)$ at $t = 0$, denoted as $\rho_0 = p(x_0), \cdots, \rho_t = p(x_t)$
- Thus evolution of state distribution over time is characterized by its derivative $\dot{\rho} = \frac{d\rho}{dt}$
- Evolution is assumed to be time-invariant, thus determined by a master equation

$$\tau \dot{\rho} = \rho O \tag{1}$$

where O is the infinitesimal generator encoding the dynamics of the system

Model derivation

- We can analytically solve equation 1 as

$$\rho_{\Delta t} = \rho_0 e^{\frac{\Delta t}{\tau} O} \tag{2}$$

  and we term $e^{\frac{\Delta t}{\tau} O}$ as a **propagator**
- Fixing $\Delta t = 1$ we have a propagator $P_\tau = e^{\frac{1}{\tau} O}$ for per time step
- Then we view sampling as

$$x_{t+1} \approx \mathbf{1}_{x_t} P_\tau \tag{3}$$

  where $\mathbf{1}_{x_t}$ is a one-hot vector indicating state at time t

Model derivation

- It is unrealistic for neural circuit to compute the propagator P_τ directly as

$$P_\tau = \sum_{n=0}^{\infty} \frac{\left(\tau^{-1} O\right)^n}{n!} \tag{4}$$

- Propagator can be efficiently computed by eigen-decomposition of $O = G\Lambda W$

$$P_\tau = G e^{\frac{1}{\tau}\Lambda} W \tag{5}$$

where tuning the tempo τ is referred to as **spectral modulation**

- Let $s_\tau(\lambda) = e^{\frac{\lambda}{\tau}} \Rightarrow S = e^{\frac{1}{\tau}\Lambda}$, this can be written as

$$P_\tau = GSW \tag{6}$$

Model derivation

- G is the matrix of generator eigenvectors (column), referred to as **spectral components** $\phi_k = [G]_{\cdot k}$
- Each spectral component is rescaled according to time by the **power spectrum (matrix)** S
- W is simply the linear readout from the spectral representation of future state distribution ρ_{t+1} to the state space $\mathcal{X}$
- Generating sequence using spectral propagator (equation 5) is done by

$$x_{t+1} \approx \mathbf{1}_{x_t} G S W \tag{7}$$

- Spectral modulation can be achieved by applying gain control or grid rescaling to S

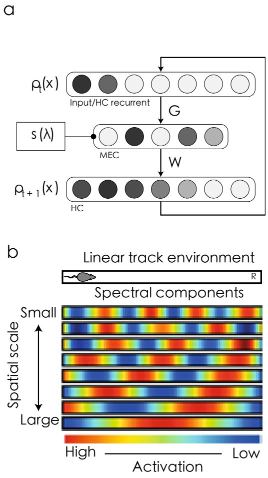

Fig 2

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Setup: Foraging in open environment

- Large open environment
- No cues for food
- Balance between efficiency and complexity

- Must search each location for food
- Serial visitations?
  (requires memory and planning)
- Random sampling?
  (requires no memory but is not efficient)
- Uncertainty-driven exploration like Gaussian Process?
  (Efficient but is much more complex)

Intuition from random walk generator

A random walk generator is in the naïve form of

$$s_\tau(\lambda) = e^{\frac{\lambda}{\tau}}$$

- $\tau \to 0$
- Samples target states at large spatial scales
- Global Reorientation
- Repeatedly traverse the environment
- Cost too much energy

- $\tau \gg 0$
- Samples target states at small spatial scales
- Local search
- Oversampling within limited area
- Take to long to fully explore

Solution: Stability control

Introducing a stability parameter α to the modulation as

$$s_{\tau,\alpha}(\lambda) = e^{\frac{|\lambda|^{\alpha}}{\tau}} \tag{8}$$

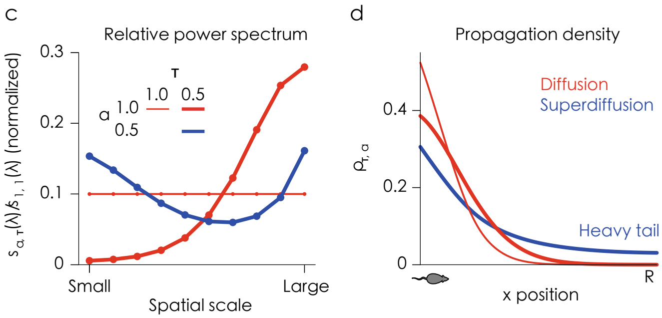


Fig 2

Result: Simulated sampling from distinct regimes

- Diffusive regime failed to fully explore the environment
- Superdiffusive regime approximately evenly explored

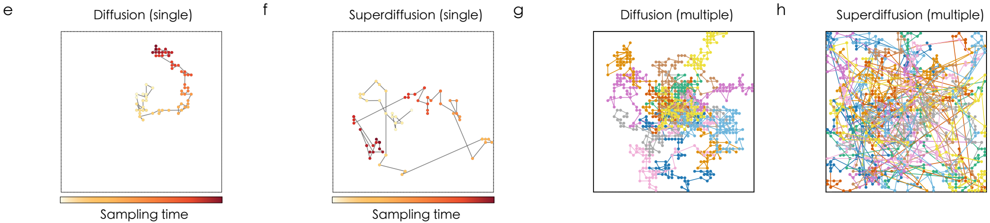


Fig 2

Result: Exploration efficiency and step size

- Diffusive regime failed to fully explore the environment
- Superdiffusive regime aprroximately evenly explored

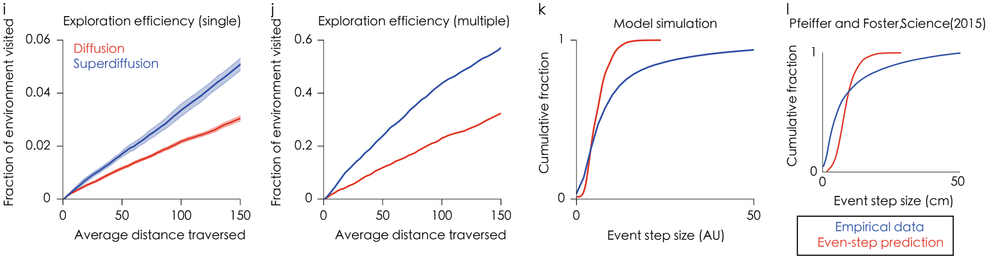


Fig 2

Setup: Goal navigation

- Open environment
- Single reward location repeatedly baited
- Need to remember the location of reward (*home*) and **plan** the trajectory to it in *away* events

Pfeiffer and Foster, *Nature* (2013)

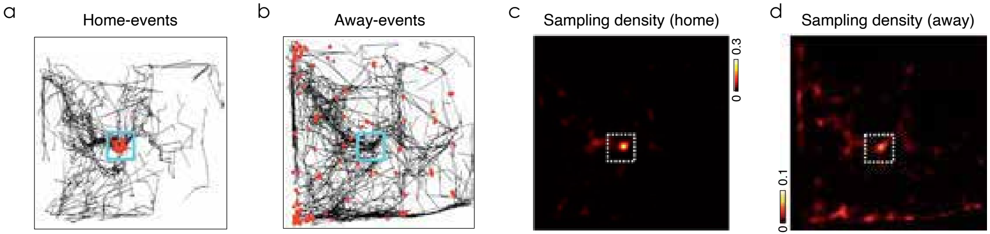


Fig 3

Solution: Motivation value

Introducing a motivation value v to the modulation as

$$O_{h\cdot} \leftarrow \frac{O_{h\cdot}}{v} \tag{9}$$

where h indexes the home state $x_h \in \mathcal{X}$
This overrepresenting of home state biased the probability transition towards home state

Result: Random walk with biased jumps

- Superdiffusive regime generated random walk trajectories with biased jumps to the rewarded location

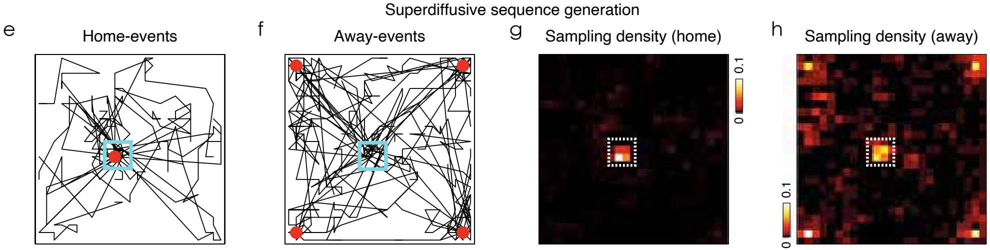


Fig 3

Result: Diffusive regime failed

- With the same generator, in diffusive regime, home is not over-represented

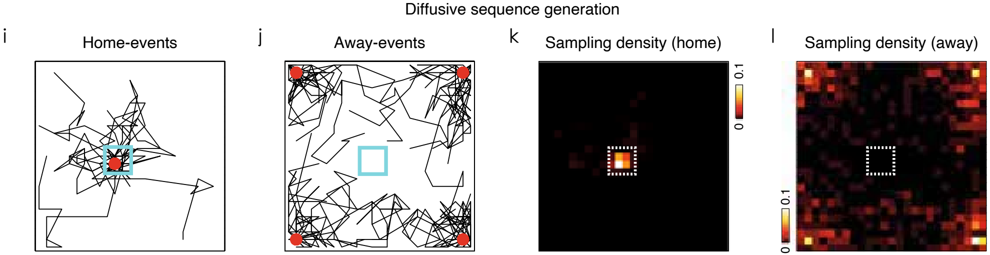


Fig 3

Result: Sampling probability comparison

- Remote activation is achieved by a localized increase in the sampling probability at home state

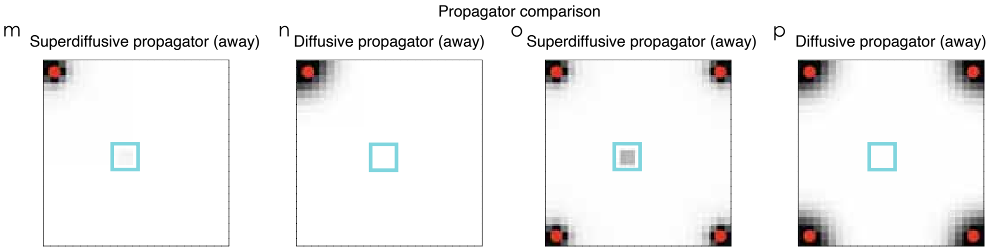


Fig 3

Setup: Goal navigation

- Circular track environment
- Multiple reward locations repeatedly baited
- Non-local, non-diffusive activation pattern of place cells were observed

Wikenheiser and Redish
Nature Neuroscience (2015)

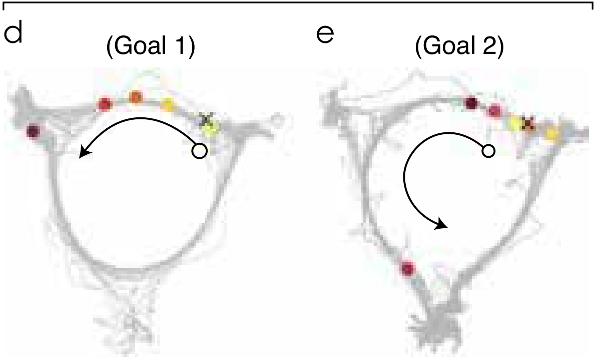


Fig 4

Result: Jumps and local roll-outs

- Superdiffusive regime had a strong tendency to jump to the reward location

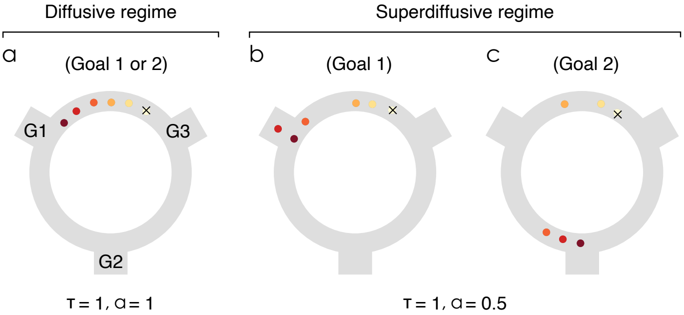


Fig 4

Result: Comparison in probability

- Remote goals are over-represented in superdiffusive propagation

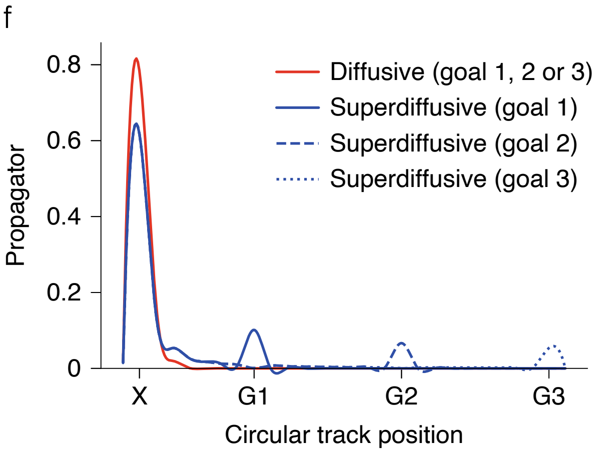


Fig 4

Result: Look-ahead distances

- Defined as distances to the furthest encoded locations
- The look-ahead distances scaled with the distances to reward at initial state
- The look-ahead distances are similar upon goal arrivals

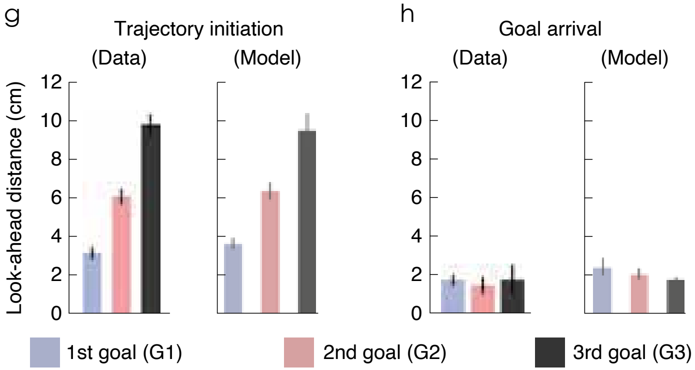


Fig 4

Setup: Binary decision

- Need to evaluate possible future trajectories
- Decisions are made at junction that may lead to reward
- Observed to be generative cycling between two possible trajectories

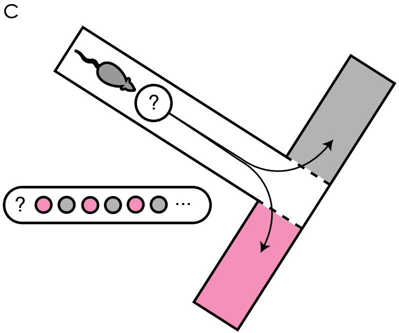


Fig 1

Intuition from Monte-Carlo sampling

- Based on sampling and retrieving rewards and computing Monte-Carlo estimates

$$\mathbb{E}\left[r\right] \approx \hat{r} = \frac{1}{N}\sum_{i=1}^{N} r(x_i) \tag{10}$$

- Sampling-Evaluating-Estimating cycle forms a Markov chain Monte Carlo (MCMC)
- Key evaluation of MCMC's quality is its sample variance $\mathbb{V}\left[\hat{r}\right]$
- A major source of $\mathbb{V}\left[\hat{r}\right]$ is generative auto-correlations

Intuition from Monte-Carlo sampling

- Technically $\mathbb{V}\left[\hat{r}\right]$ is proportional to integrated auto-correlation time Δt_{ac}

$$\Delta t_{ac} = \sum_{t=0}^{\infty} C_X(t) \tag{11}$$

- $C_X(t)$ is the auto-correlation function
- Δt_{ac} can be viewed as the average iterations needed for an independent sample
- Algorithms like Metropolis-Hastings (MH) and Gibbs sampling (GS) are designed to reduce Δt_{ac} while preserving the estimation accuracy

Solution: Minimally auto-correlated power spectrum

- Δt_{ac} of state X is demonstrated to be able to be expressed by $s_\tau(\lambda_k) := s(k)$
- Minimizing Δt_{ac} can be achieved through optimizing $s(k)$ to $s_{mac}(k)$
- $s_{mac}(k)$ should differ greatly from diffusive regime as the latter has large overlapping propagation distributions
- So $s_{mac}(k)$ should sample states that do not admit likely paths between
- Sequence generation regime would shift to $s_{mac}(k)$ when approximating junction

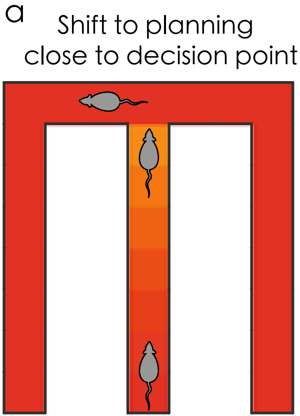


Fig 5

Result: The numerical result of $s_{mac}(k)$

- Distinct from both diffusive and super-diffusive regimes
- Counter-weighted spectral components across spatial scales
- The Heaviest negative weighting applied to large scale spectral component is referred to as the Dominant Spectral Component (DSC)

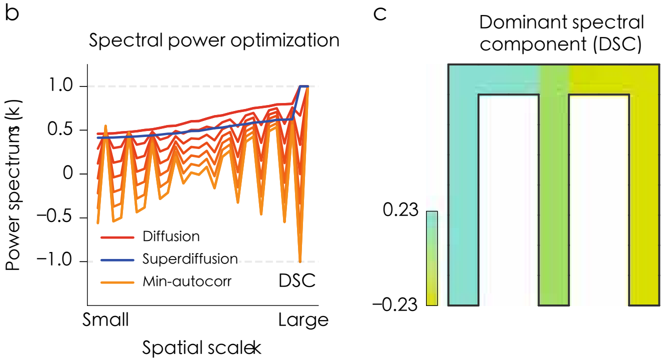


Fig 5

Result: Samples of $s_{mac}(k)$

- Similar to diffusive regime at junction
- Successively samples states from the opposing arm

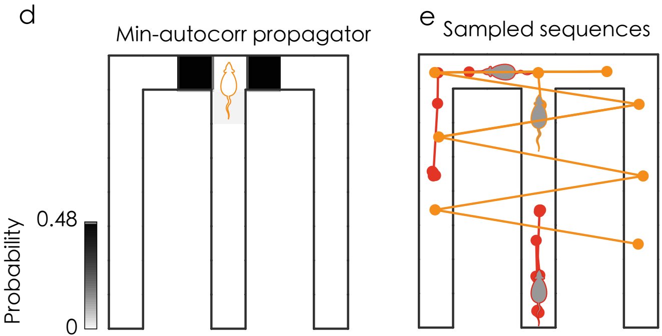


Fig 5

Result: Comparison in auto-correlation

- Lowest auto-correlation in generative cycling sequences
- $s_{mac}(k)$ leverages the hierarchical structure of the environment for efficient sampling

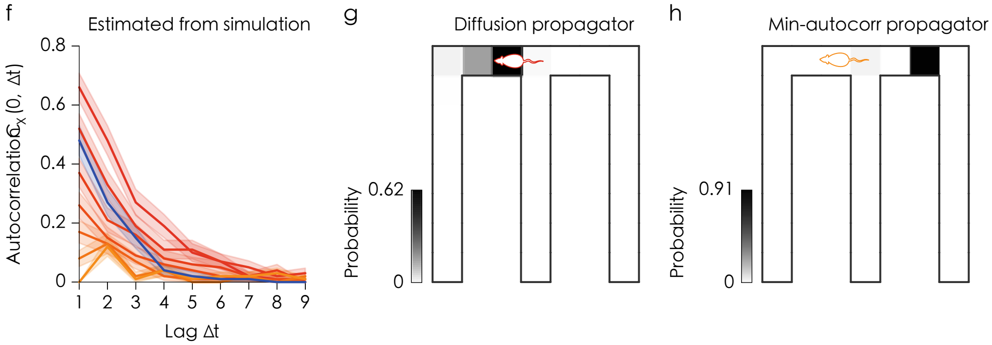
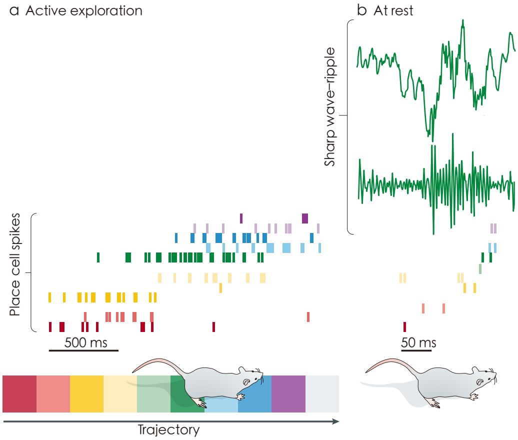


Fig 5

Setup: Memory consolidation

- Forage randomly dropped food pellets when active
- Record and decode SWRs from post-exploration (sleep SWRs; offline) and immobile pauses (wake SWRs; online)
- Distinct operational modes were identified statistically



Source: `https://www.nature.com/articles/nrn.2016.21`

Result: Mean displacement of SWRs

- Mean displacement (MD)

$$\text{MD}(t) = \langle \|x_t - x_0\| \rangle \tag{12}$$

- Linearly related to time with slope α^{-1}
- Wake SWRs are super-diffusive; sleep SWRs are diffusive

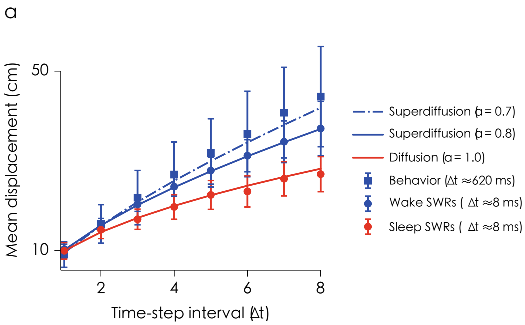


Fig 6

Result: Displacement distribution

- Empirical sleep SWRs step distribution are well-approximated by diffusive propagator

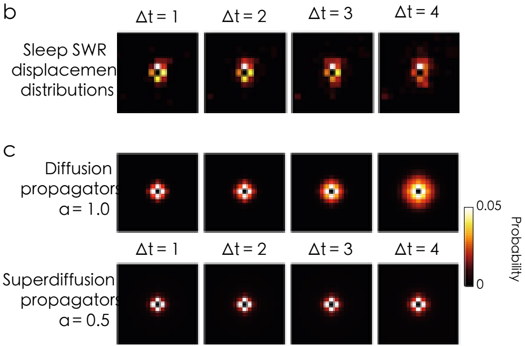


Fig 6

Setup: Learning process

- Simulated environment within a graph structure
- Target to learn the environment representation formalized as successor representation (SR)

a

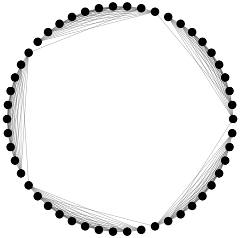


Fig 7

Result: Simulation results

- Diffusive regime results in best learned SR

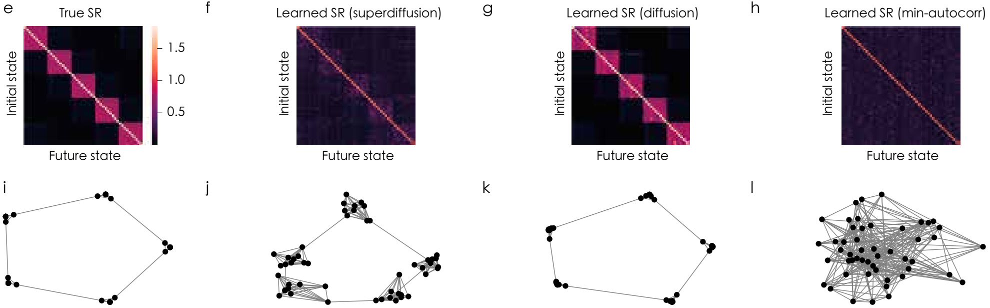


Fig 7

Result: Metrics comparison

- Diffusive regime embody fundamental spatial biases
- This also holds for directed graph structure (not shown here)

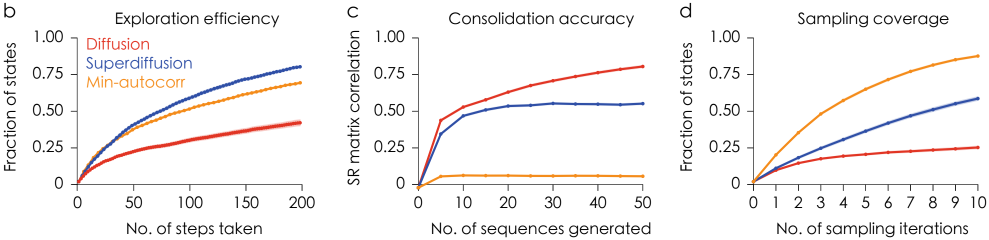


Fig 7

Setup: Turbulence

- Shifting from one regime to another requires the spectral modulation of MEC activity be coherently balanced across grid modules
- Dysregulated MEC activity may inbalance the spectral modulation thus disrupt the spatio-temporal structure of the hippocampal representations

Result: Power spectra and sequence generation

- Altering α results in seemingly minor differences in power spectra
- Sequence generated significantly differed (approximately uniform across space)

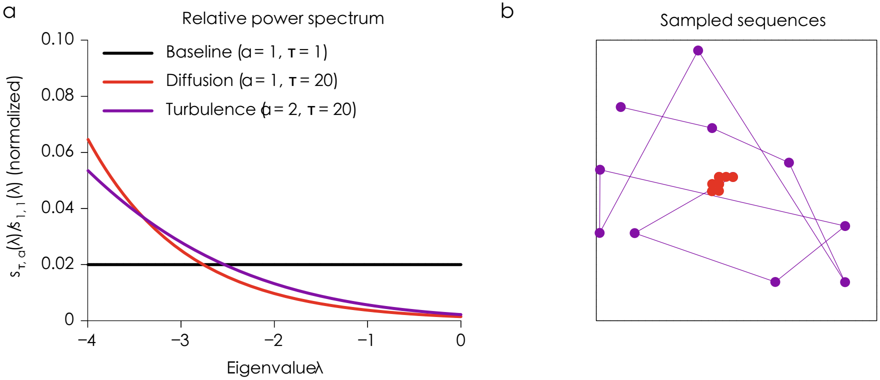
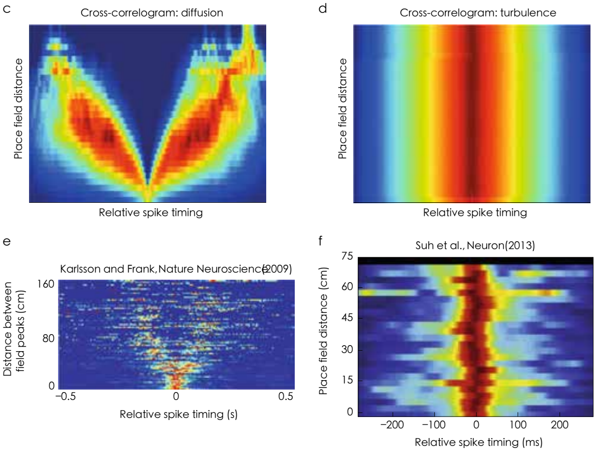


Fig 8

Result: Turbulent sequence generation

- Turbulent spectral modulation failed to preserve the cross-correlation between spatial and temporal displacement



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Highlights

- Predicted the casual relationship between the power spectrum of MEC activity and the statistical dynamics of hippocampal sequence generation
- Developed an algorithmic framework for associating and reconciling distinct dynamic modes of hippocampal sequence generation

Thanks for listening!