

# Firing rate adaptation affords place cell theta sweeps, phase precession and procession

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## Abstract

Hippocampal place cells in freely moving rodents display both theta phase precession and procession, which is thought to play important roles in cognition, but the neural mechanism for producing theta phase shift remains largely unknown. Here we show that firing rate adaptation within a continuous attractor neural network causes the neural activity bump to oscillate around the external input, resembling theta sweeps of decoded position during locomotion. These forward and backward sweeps naturally account for theta phase precession and procession of individual neurons, respectively. By tuning the adaptation strength, our model explains the difference between “bimodal cells” showing interleaved phase precession and procession, and “unimodal cells” in which phase precession predominates. Our model also explains the constant cycling of theta sweeps along different arms in a T-maze environment, the speed modulation of place cells’ firing frequency, and the continued phase shift after transient silencing of the hippocampus. We hope that this study will aid an understanding of the neural mechanism supporting theta phase coding in the brain.

### eLife assessment

This work represents an **important** contribution to computational neuroscience by providing a parsimonious model for spiking-phase precession/procession in the hippocampus. The proposed model, which relies on firing-rate adaptation, is able to capture many distinct experimental observations about phase precession/procession, such as forward and backward sweeps, as well as constant cycling of sweeps across different arms of a T-maze. The **convincing** evidence presented in support of this work relies on classical analytical and computational techniques about continuous attractor networks.

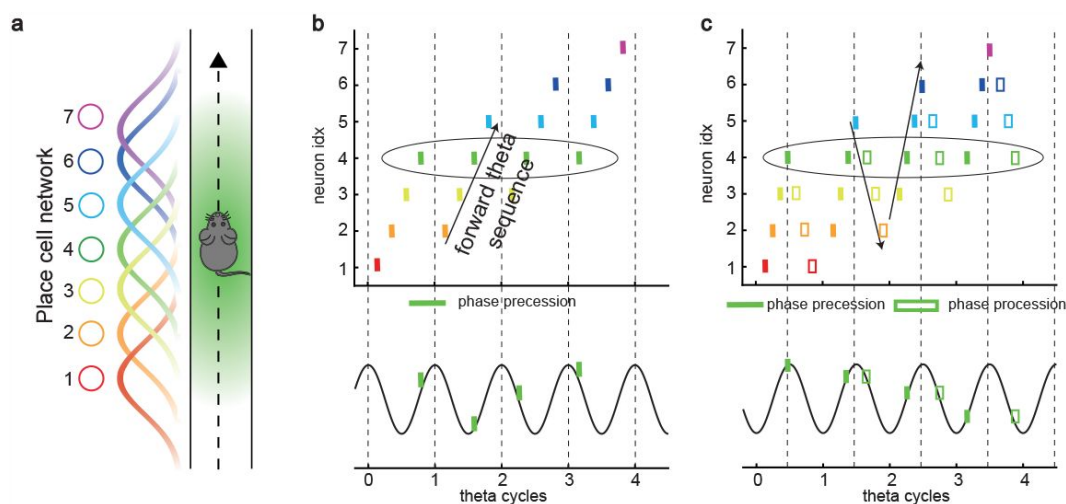
## Introduction

One of the strongest candidates for temporal coding of a cognitive variable by neural firing is the ‘theta phase precession’ shown by hippocampal place cells. As an animal runs through the firing field of a place cell, the cell fires at progressively earlier phases in successive cycles of the ongoing LFP theta oscillation, so that firing phase correlates with distance traveled ([O’Keefe and Recce, 1993](#) ; [Skaggs et al., 1996](#) ) (see also ([Schmidt et al., 2009](#) )) ([Fig. 1a&b](#) ). At the population level, phase precession of individual cells gives rise to forward theta sequences once starting phases are aligned across the population ([Feng et al., 2015](#) ), where neurons representing successive locations along the trajectory of the animal display predictable firing sequences within individual theta cycles ([Johnson and Redish, 2007](#) ). These prospective sequential experiences (looking into the future) are potentially useful for a range of cognitive faculties, e.g., planning, imagination, and decision-making ([O’Keefe and Recce, 1993](#) ; [Skaggs et al., 1996](#) ; [Hassabis et al., 2007](#) ; [Wikenheiser and Redish, 2015](#) ; [Kay et al., 2020](#) ).

Besides prospective representation, flexible behaviors also require retrospective representation of sequential experiences (looking into the past). For instance, in goal-directed behaviors, it is important to relate the reward information that might only occur at the end of a sequence of events to preceding events in the sequence ([Foster et al., 2000](#) ; [Foster and Wilson, 2006](#) ; [Diba and Buzsáki, 2007](#) ). A recent experimental study ([Wang et al., 2020](#) ) described retrospective sequences during online behaviors (also indicated by ([Skaggs et al., 1996](#) ; [Yamaguchi et al., 2002](#) )), namely, reverse theta sequences, interleaved with forward theta sequences in individual theta cycles ([Fig. 1c](#) ). Such retrospective sequences, together with the prospective sequences, may cooperate to establish higher-order associations in episodic memory ([Diba and Buzsáki, 2007](#) ; [Jaramillo and Kempter, 2017](#) ; [Pfeiffer, 2020](#) ).

While a large number of computational models of phase precession and the associated forward theta sequences have been proposed, e.g., the single cell oscillatory models ([O’Keefe and Recce, 1993](#) ; [Kamondi et al., 1998](#) ; [Harris et al., 2002](#) ; [Lengyel et al., 2003](#) ; [Losonczy et al., 2010](#) ) and recurrent activity spreading models ([Tsodyks et al., 1996](#) ; [Romani and Tsodyks, 2015](#) ), the underlying neural mechanism for interleaved forward- and reverse-ordered sequences remains largely unclear. Do reverse theta sequences share the same underlying neural mechanism as forward sequences, or do they reflect different mechanisms? If they do, what kind of neural architecture can support the emergence of both kinds of theta phase shift? Furthermore, since forward theta sequences are commonly seen, but reverse theta sequences are only seen in some circumstances ([Wang et al., 2020](#) ), are they commensurate with forward theta sequences? If not, to what degree are forward theta sequences more significant than the reverse ones?

To address these questions, we built a continuous attractor neural network (CANN) of the hippocampal place cell population ([Amari, 1977](#) ; [Tsodyks and Sejnowski, 1995](#) ; [Samsonovich and McNaughton, 1997](#) ; [Tsodyks, 1999](#) ). The CANN conveys a map of the environment in its recurrent connections that affords a single bump of activity on a topographically organized sheet of cells which can move smoothly so as to represent the location of the animal as it moves in the environment. Each neuron exhibits firing rate adaptation which destabilizes the bump attractor state. When the adaptation is strong enough, the network bump can travel spontaneously in the attractor space, which we term as the intrinsic mobility. Intriguingly, we show that, under competition between the intrinsic mobility and the extrinsic mobility caused by location-dependent sensory inputs, the network displays an oscillatory tracking state, in which the network bump sweeps back and forth around the external sensory input. This phenomenon naturally explains the theta sweeps found in the hippocampus ([Skaggs et al., 1996](#) ; [Burgess et al., 1994](#) ; [Foster and Wilson, 2007](#) ), where the decoded position sweeps around the animal’s physical position at theta frequency. More specifically, phase precession occurs when the bump



**Figure 1.**

Theta sequence and theta phase shift of place cell firing. **a**, An illustration of an animal running on a linear track. A group of place cells each represented by a different color are aligned according to their firing fields on the linear track. **b**, An illustration of the forward theta sequences of the neuron population (upper panel), and the theta phase precession of the 4th place cell (represented by the green color, lower panel). **c**, An illustration of both forward and reverse theta sequences (upper panel), and the corresponding theta phase precession and procession of the 4th place cell (lower panel). The sinusoidal trace illustrates the theta rhythm of local field potential (LFP), with individual theta cycles separated by vertical dashed lines.

propagates forward while phase precession occurs when the network bump propagates backward. Moreover, we find that neurons can exhibit either only predominant phase precession (unimodal cells) when adaptation is relatively strong, or interleaved phase precession and precession (bimodal cells) when adaptation is relatively weak.

In addition to theta phase shift, our model also successfully explains the constant cycling of theta sweeps along different upcoming arms in a T-maze environment ([Kay et al., 2020](#)), and other phenomena related to phase precession of place cells ([Geisler et al., 2007](#); [Zugaro et al., 2005](#)). We hope that this study facilitates our understanding of the neural mechanism underlying the rich dynamics of hippocampal neurons and lays the foundation for unveiling their computational functions.

## Results

### A network model of hippocampal place cells

To study the phase shift of hippocampal place cells, we focus on a one-dimensional (1D) continuous attractor neural network (CANN) (mimicking the animal moving on a linear track, see [Fig. 2a](#)), but generalization to the 2D case (mimicking the animal moving in a 2D arena) is straightforward (see Discussion for more details). Neurons in the 1D CANN can be viewed as place cells rearranged according to the locations of their firing fields on the linear track (measured during free exploration). The dynamics of the 1D CANN is written as

$$\tau \frac{dU(x, t)}{dt} = -U(x, t) + \rho \int_{-\infty}^{\infty} J(x, x') r(x', t) dx' - V(x, t) + I^{ext}(x, t), \quad (1)$$

$$r(x, t) = \frac{gU(x, t)^2}{1 + k\rho \int_{-\infty}^{\infty} U^2(x', t) dx'}, \quad (2)$$

Here  $U(x, t)$  represents the presynaptic input to the neuron located at position  $x$  on the linear track, and  $r(x, t)$  represents the corresponding firing rate constrained by global inhibition ([Hao et al., 2009](#)).  $\tau$  is the time constant,  $\rho$  the neuron density,  $k$  the global inhibition strength, and  $g$  is the gain factor. The dynamics of  $U(x, t)$  is determined by the leaky term  $-U(x, t)$ , the recurrent input from other neurons, the firing rate adaptation  $-V(x, t)$ , and the external input  $I^{ext}(x, t)$ . The recurrent connection strength  $J(x, x')$  between two neurons decays with their distance. For simplicity, we set  $J(x, x')$  to be the Gaussian form, i.e.,

$J(x, x') = J_0 / \sqrt{2\pi a} \exp[-(x - x')^2 / (2a^2)]$ , with  $J_0$  controlling the connection strength and  $a$  the range of neuronal interaction. Such connectivity gives rise to a synaptic weight matrix with the property of translation invariance. Together with the global inhibition, the translation invariant weight matrix ensures that the network can hold a continuous family of stationary states (attractors) when no external input and adaptation exist ([Tsodyks and Sejnowski, 1995](#); [Samsonovich and McNaughton, 1997](#); [McNaughton et al., 2006](#); [Wu et al., 2008](#)), where each attractor is a localized firing bump representing a single spatial location ([Fig. 2b](#)). These bump states are expressed as (see Methods. for the parameter settings and SI.2 for the detailed mathematical derivation):

$$\bar{r}(x, t) = A_r(t) \exp \left\{ -\frac{[x - z(t)]^2}{2a^2} \right\}, \quad (3)$$

where  $A_r(t)$  denotes the bump height and  $z(t)$  the bump center, i.e., the spatial location represented by the network. For convenience, we set the external input to be of the Gaussian form, which is written as  $I^{ext}(x, t) = \alpha \exp[-(x - v_{ext}t)^2 / (4a^2)]$ , with  $v_{ext}$  representing the moving speed and  $\alpha$

controlling the external input strength. Such external moving input represents location-dependent sensory inputs (i.e., corresponding to the animal's physical location) which might be conveyed via the entorhinal-hippocampal or subcortical pathways ([Van Strien et al., 2009](#)). The term  $-V(x, t)$  represents the firing rate adaptation ([Alonso and Klink, 1993](#); [Fuhrmann et al., 2002](#); [Benda and Herz, 2003](#); [Treves, 2004](#)), whose dynamics is written as

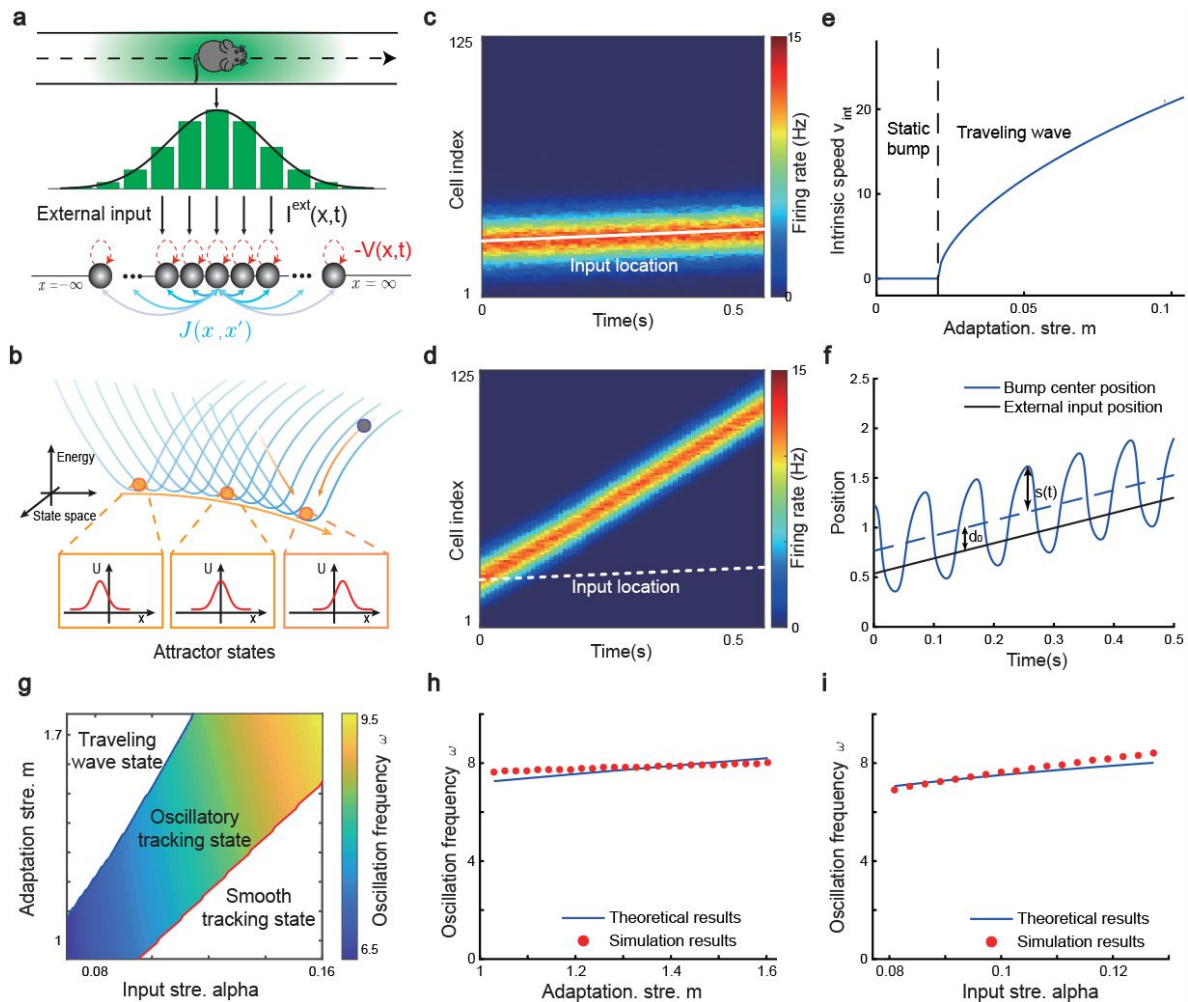
$$\tau_v \frac{dV(x, t)}{dt} = -V(x, t) + mU(x, t), \quad (4)$$

where  $m$  controls the adaptation strength, and  $\tau_v$  is the time constant. The condition  $\tau_v \gg \tau$  holds, implying that the firing rate adaptation is a much slower process compared to neuronal firing. In effect, the firing rate adaptation increases with the neuronal activity and contributes to destabilizing the active bump state, which induce rich dynamics of the network (see below).

## Oscillatory tracking of the network

Overall, the bump motion in the network is determined by two competing factors, i.e., the external input and the adaptation. The interplay between these two factors leads to the network exhibiting oscillatory tracking in an appropriate parameter regime. To elucidate the underlying mechanism clearly, we explore the effects of the external input and the adaptation on bump motion separately. First, when firing rate adaptation does not exist in the network ( $m = 0$ ), the bump tracks the external moving input smoothly (see [Fig. 2c](#)). We refer to this as the “**smooth tracking state**”, where the internal location represented in the hippocampus (the bump position) is continuously tracking the animal's physical location (the external input location). This smooth tracking property of CANNs has been widely used to model spatial navigation in the hippocampus ([Tsodyks and Sejnowski, 1995](#); [Samsonovich and McNaughton, 1997](#); [McNaughton et al., 2006](#); [Battaglia and Treves, 1998](#)). Second, when the external drive does not exist in the network ( $\alpha = 0$ ) and the adaptation strength  $m$  exceeds a threshold ( $m > \tau/\tau_v$ ), the bump moves spontaneously with a speed calculated as  $v_{int} = (2\alpha/\tau_v)\sqrt{m\tau_v/\tau - \sqrt{m\tau_v/\tau}}$  (see [Fig. 2d](#) & e and Methods. for more details). We refer to this as the “**travelling wave state**”, where the internal representation of location in the hippocampus is sequentially reactivated without external drive, resembling replay-like dynamics during a quiescent state (see Discussion for more details). This intrinsic mobility of the bump dynamics can be intuitively understood as follows. Neurons around the bump center have the highest firing rates and hence receive the strongest adaptation. Such strong adaptation destabilizes the bump stability at the current location, and hence pushes the bump away. After moving to a new location, the bump will be continuously pushed away by the firing rate adaptation at the new location. As a result, the bump keeps moving on the linear track. Similar mechanisms have been applied to explain mental exploration ([Hopfield, 2010](#)), preplay during sharp wave-ripple events in the hippocampus ([Azizi et al., 2013](#)), and the free memory recall phenomenon in the brain ([Dong et al., 2021](#)).

When both the external input and adaptation are applied to the CANN, the interplay between the extrinsic mobility (caused by the external input) and the intrinsic mobility (caused by the adaptation) will induce three different dynamical behaviors of the network (see [video 1](#) for demonstration), i.e., 1) when  $m$  is small and  $\alpha$  is large, the network displays the smooth tracking state; 2) when  $m$  is large and  $\alpha$  is small, the network displays the travelling wave state; 3) when both  $m$  and  $\alpha$  have moderate values, the network bump displays an interesting state, called the “**oscillatory tracking state**”, where the bump tracks the external moving input in an oscillatory fashion ([Fig. 2f&g](#)). Intuitively, the mechanism for oscillatory tracking can be understood as follows. Due to the intrinsic mobility of the network, the bump tends to move at its own intrinsic speed (which is faster than the external moving input, see [Fig. 2d](#)), i.e., the bump tries to escape from the external input. However, due to the strong locking effect of the external input, the bump can not run too far away from the location input, but instead, is attracted back to the location



**Figure 2.**

The network architecture and tracking dynamics. **a**, A 1D continuous attractor neural network formed by place cells. Neurons are aligned according to the locations of their firing fields on the linear track. The recurrent connection strength  $J(x, x')$  (blue arrows) between two neurons decays with their distance on the linear track. Each neuron receives an adaptation current  $-V(x, t)$  (red dashed arrows). The external input  $I^{\text{ext}}(x, t)$ , represented by a Gaussian-shaped bump, conveys location-dependent sensory inputs to the network. **b**, An illustration of the state space of the CANN. The CANN holds a family of bump attractors which form a continuous valley in the energy space. **c**, The smooth tracking state. The network bump (hot colors) smoothly tracks the external moving input (the white line). The red (blue) color represents high (low) firing rate. **d**, The travelling wave state when the CANN has strong firing rate adaptation. The network bump moves spontaneously with a speed much faster than the external moving input. **e**, The intrinsic speed of the travelling wave versus the adaptation strength. **f**, The oscillatory tracking state. The bump position sweeps around the external input (black line) with an offset  $d_0$ . **g**, The phase diagram of the tracking dynamics with respect to the adaptation strength  $m$  and the external input strength  $\alpha$ . The colored area shows the parameter regime for the oscillatory tracking state. Yellow (blue) color represents fast (slow) oscillation frequency. **h-i**, Simulated (red points) and theoretical (blue line) oscillation frequency as a function of the adaptation strength (**h**) or the external input strength (**i**).



input. Once the bump returns, it will keep moving in the opposite direction of the external input until it is pulled back by the external input again. Over time, the bump will sweep back and forth around the external moving input, displaying the oscillatory tracking behavior. It is noteworthy that the activity bump does not live within a window circumscribed by the external input bump (bouncing off the interior walls of the input during the oscillatory tracking state), but instead is continuously pulled back and forth by the external input (see Fig. S1).

Our study shows that during oscillatory tracking, the bump shape is roughly unchanged (see previous sections for the condition of shape variability), and the bump oscillation can be well represented as the bump center sweeping around the external input location. The dynamics of the bump center can be approximated as a propagating sinusoidal wave (Fig. 2f), i.e.,

$$z(t) = c_0 \sin(\omega t) + d_0 + v_{ext}t = s(t) + v_{ext}t, \quad (5)$$

where  $z(t)$  is the bump center at time  $t$  (see Eq. 3).  $s(t)$  denotes the displacement between the bump center and the external input, which oscillates at the frequency  $\omega$  with the amplitude  $c_0 > 0$  and a constant offset  $d_0 > 0$  (see Methods. for the values of these parameters and SI.3 for the detailed derivation). When the firing rate adaptation is relatively small, the bump oscillation frequency can be analytically solved to be (see also Fig. S2):

$$\omega = \sqrt{\frac{2\sqrt{\pi}\alpha ak(1+m)}{\tau\tau_v(J_0 + 2\sqrt{\pi}ak\alpha)}}. \quad (6)$$

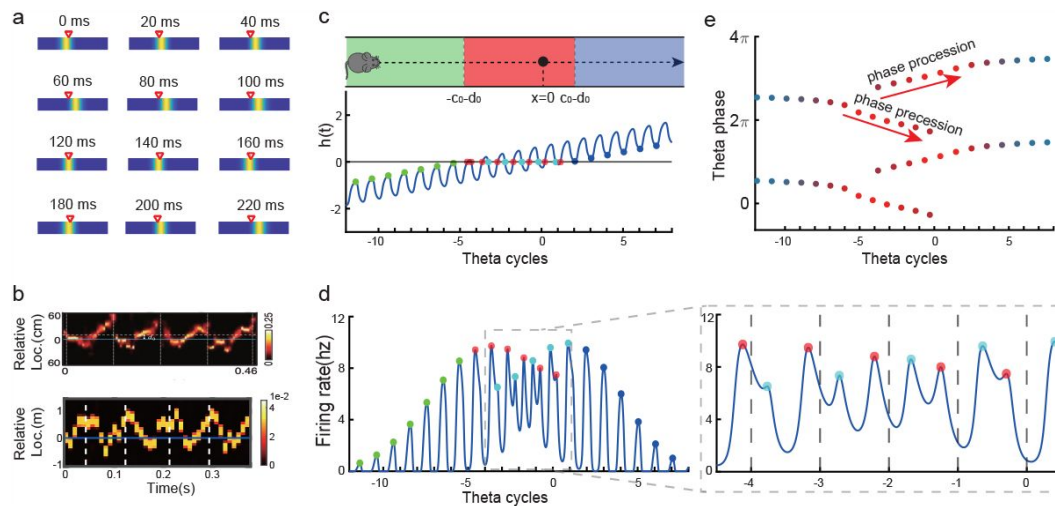
We see that the bump oscillation frequency  $\omega$  increases sublinearly with the external input strength  $\alpha$  and the adaptation strength  $m$  (Fig. 2h&i). By setting the parameters appropriately, the bump can oscillate in the theta band (6-10 Hz), thus approximating the experimentally observed theta sweeps (see below). Notably, LFP theta is not explicitly modelled in the network. However, since theta sweeps are bounded by individual LFP theta cycles in experiments, they share the same oscillation frequency as LFP theta. For convenience, we will frequently use the term LFP theta below and study firing phase shift in individual oscillation cycles.

## Oscillatory tracking accounts for both theta phase precession and procession of hippocampal place cells

In our model, the bump center and external input represent the decoded and physical positions of the animal, respectively, thus the oscillatory tracking of the bump around the external input naturally gives rise to the forward and backward theta sweeps observed empirically (Fig. 3a&b) (Wang et al., 2020). Here we show that oscillatory tracking of the bump accounts for the theta phase precession and procession of place cell firing.

Without loss of generality, we select the neuron at location  $x = 0$  as the probe neuron and examine how its firing phase changes as the external input traverses its firing field (Fig. 3c). In the absence of explicitly simulated spike times, the firing phase of a neuron in each theta cycle is measured by the moment when the neuron reaches the peak firing rate (see Methods. for modeling spike times in the CANN). Based on Eqs. 3 & 5, the firing rate of the probe neuron, denoted as  $r_0(t)$ , is expressed as

$$r_0(t) = A_r(t) \exp\left[-\frac{[0 - z(t)]^2}{2a^2}\right] = A_r(t) \exp\left[-\frac{(v_{ext}t + c_0 \sin \omega t + d_0)^2}{2a^2}\right] \equiv A_r(t) \exp\left[-\frac{h(t)^2}{2a^2}\right], \quad (7)$$



**Figure 3.**

Oscillatory tracking accounts for theta sweeps and theta phase shift. **a**, Snapshots of the bump oscillation along the linear track in one theta cycle (0 ms - 140 ms). Red triangles indicate the location of the external moving input. **b**, Decoded relative positions based on place cell population activities. Upper panel: experimental data, adapted from Wang et al. (2020). Lower panel: the relative locations of the bump center (shown by the 10 most active neurons at each timestamp) with respect to the location of the external input (horizontal line) in five theta cycles. **c**, Upper panel: the process of the animal running through the firing field of the probe neuron (large black dot) is divided into three stages: the entry stage (green), the phase shift stage (red) and the departure stage (blue). Lower panel: the displacement between the bump center and the probe neuron as the animal runs through the firing field. The horizontal line represents the location of the probe neuron, which is  $x = 0$ . **d**, The firing rates of the probe neuron as the animal runs through the firing field. Colored points indicate firing peaks. The trace of the firing rate in the phase shift stage (the dashed box) is enlarged in the sub-figure on the right hand-side, which exhibits both phase precession (red points) and procession (blue points) in successive theta cycles. **e**, The firing phase shift of the probe neuron in successive theta cycles. Red points progress to earlier phases from  $\pi/2$  to  $-\pi/2$  and blues points progress to later phases from  $\pi/2$  to  $3\pi/2$ . The color of the dots represent the peak firing rates, which is also shown in d.



where  $A_r(t)$  is the bump height, and  $h(t)$  is an oscillatory moving term denoting the displacement between the bump center and the location of the probe neuron. It is composed of a moving signal  $v_{ext}t$  and an oscillatory signal  $c_0 \sin \omega t + d_0$ , with  $c_0$  the oscillation amplitude,  $\omega$  the frequency and  $d_0$  an oscillation offset constant. It can be seen that the firing rate of the probe neuron is determined by two factors,  $A_r(t)$  and  $h(t)$ . To simplify the analysis below, we assume that the bump height  $A_r(t)$  remains unchanged during bump oscillations (for the case of time-varying bump height, see previous sections). Thus, the firing rate only depends on  $h(t)$ , which is further determined by two time-varying terms, the oscillation term  $c_0 \sin \omega t$  and the location of the external input  $v_{ext}t$ . The first term contributes to firing rate oscillations of the probe neuron, and the second term contributes to the envelope of neuronal oscillations exhibiting a waxing-and-waning profile over time, as the external input traverses the firing field (the absolute value  $|v_{ext}t|$  first decreases and then increases; see [Fig. 3d](#), also [video 2](#)). Such a waxing-and-waning profile agrees well with the experimental data ([Skaggs et al., 1996](#)). In each LFP theta cycle, the peak firing rate of the probe neuron is achieved when  $h(t)$  reaches a local minima ([Fig. 3c&d](#)). We differentiate three stages as the external input passes through the probe neuron (i.e., the animal travels through the place field of the probe neuron), i.e.,

- **the entry stage.** As the external input enters the firing field of the probe neuron (moving from left to right),  $h(t) < 0$  always holds ([Fig. 3c](#)). In this case, the peak firing rate of the probe neuron in each oscillatory cycle is achieved when  $h(t)$  reaches the maximum (i.e.,  $|h(t)|$  reaches the minimum). This corresponds to  $c_0 \sin \omega t = c_0$ , i.e.,  $\omega t = \pi/2$  ([Fig. 3e](#)). This means that the firing phase of the probe neuron at the entry stage is constant, which agrees with experimental observations ([O'Keefe and Recce, 1993](#); [Skaggs et al., 1996](#)).
- **the phase shift stage.** As the external input moves into the centre of the firing field,  $h(t) = 0$  can be achieved in each oscillatory cycle ([Fig. 3c](#)). Notably, it is achieved twice in each cycle, once as the bump sweeps over the probe neuron in the forward direction and the other as the bump sweeps over the probe neuron in the backward direction. Therefore, there are two firing peaks in each bump oscillation cycle ([Fig. 3d](#)), which are expressed as (by solving  $v_{ext}t + c_0 \sin \omega t + d_0 = 0$ ):

$$\phi_f = -\arcsin \left[ \frac{d_0 + v_{ext}t_f}{c_0} \right], \quad \phi_b = \pi + \arcsin \left[ \frac{d_0 + v_{ext}t_b}{c_0} \right], \quad (8)$$

where  $t_f$  and  $t_b$  denote the moments of peak firing in the forward and backward sweeps, respectively, and  $\phi_f$  and  $\phi_b$  the corresponding firing phases of the probe neuron. As the external input travels from  $(-c_0 - d_0)$  to  $(c_0 - d_0)$ , the firing phase  $\phi_f$  in the forward sweep decreases from  $\pi/2$  to  $-\pi/2$ , while the firing phase  $\phi_b$  in the backward sweep increases from  $\pi/2$  to  $3\pi/2$  ([Fig. 3e](#)). These give rise to the phase precession and procession phenomena, respectively, agreeing well with experimental observations ([Skaggs et al., 1996](#); [Wang et al., 2020](#); [Yamaguchi et al., 2002](#)).

- **the departure stage.** As the external input leaves the firing field,  $h(t) > 0$  always holds ([Fig. 3c](#)), and the peak firing rate of the probe neuron is achieved when  $h(t)$  reaches its minimum in each oscillatory cycle, i.e.,  $c_0 \sin(\omega t) = -c_0$  with  $\omega t = \pi/2$  ([Fig. 3e](#)). Therefore, the firing phase of the probe neuron is also constant during the departure stage

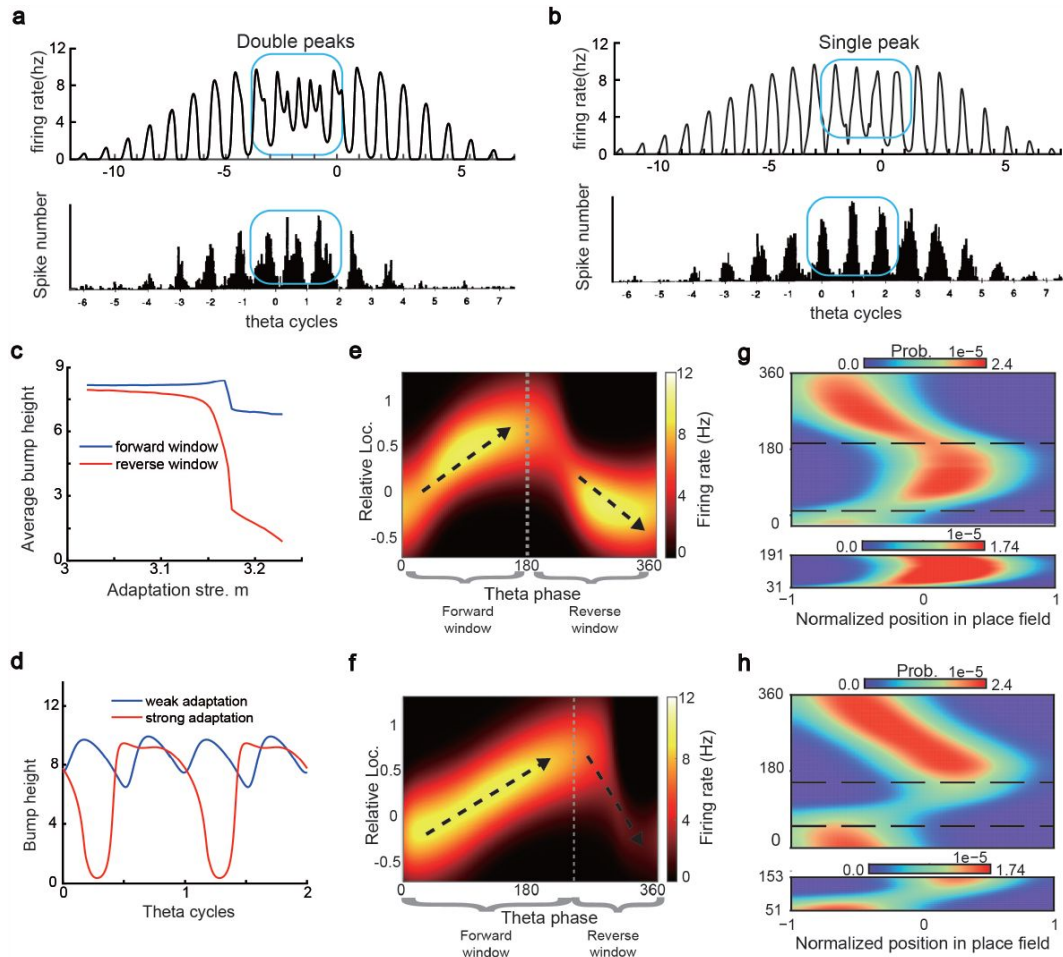
In summary, oscillatory tracking of the CANN well explains the firing phase shift of place cells when the animal traverses their firing fields. Specifically, when the animal enters the place field, the firing phase of the neuron remains constant, i.e., no phase shift occurs, which agrees with experimental observations ([O'Keefe and Recce, 1993](#); [Skaggs et al., 1996](#)). As the animal approaches the centre of the place field, the firing phase of the neuron starts to shift in two streams, one to earlier phases during the forward sweeps and the other to later phases during the backward sweeps. Finally, when the animal leaves the place field, the firing phase of the neuron stops shifting and remains constant. Over the whole process, the firing phase of a place cell is shifted by 180 degrees, which agrees with experimental observations ([O'Keefe and Recce, 1993](#); [Skaggs et al., 1996](#)).

## Different adaptation strengths account for bimodal and unimodal cells

The results above show that during oscillatory tracking, a place cell exhibits both significant phase precession and procession, which are associated with two firing peaks in a theta cycle. These neurons have been described as bimodal cells ([Wang et al., 2020](#)) ([Fig. 4a](#)). Conversely, previous experiments have primarily focused on the phase precession of place cell firing, while tending to ignore phase procession, which is a relatively weaker phenomenon ([O'Keefe and Recce, 1993](#); [Skaggs et al., 1996](#)). Place cells with negligible phase procession have been described as unimodal cells ([Fig. 4b](#)).

Here, we show that by adjusting a single parameter in the model, i.e., the adaptation strength  $m$ , neurons in the CANN can exhibit either interleaved phase precession and procession (bimodal cells) or predominant phase precession (unimodal cells). To understand this, we first recall that the firing rate adaptation is a much slower process compared to neural firing and its timescale is in the same order as the LFP theta (i.e.,  $\tau_v = 100$  ms while  $\tau = 5$  ms). This implies that when the bump sweeps over a neuron, the delayed adaptation it generates will suppress the bump height as it sweeps back to the same location. Furthermore, since the oscillatory tracking always begins with a forward sweep (as the initial sweep is triggered by the external input moving in the same direction), the suppression effects are asymmetric, that is, forward sweeps always strongly suppress backward sweeps. On the contrary, the opposite effect is much smaller, since neuronal activities in backward sweeps have already been suppressed, and they can only generate weak adaptation. Because of this asymmetric suppression, the bump height in the forward sweep is always higher than that in the backward sweep (see [Fig. 4c](#) and [Fig. S3a](#)). When the adaptation strength  $m$  is small, the suppression effect is not significant, and the attenuation of the bump height during the backward sweep is small ([Fig. 4d](#)). In such case, the firing behavior of a place cell is similar to the situation as the bump height remains unchanged as analyzed in previous sections, i.e., the neuron can generate two firing peaks in a theta cycle at the phase shift stage, manifesting the property of a bimodal cell of having both significant phase precession and procession ([Fig. 4e](#) & [g](#) and [video 2](#)). When the adaptation strength  $m$  is large, the bump height in the backward sweep attenuates dramatically (see [Fig. 4c&d](#) and the video demonstration). As a result, the firing peak of a place cell in the backward sweep becomes nearly invisible at the phase shift stage, and the neuron exhibits only predominant phase precession, manifesting the property of a unimodal cell ([Fig. 4f&h](#) and [video 3](#)).

In summary, different adaptation strengths explain the emergence of bimodal and unimodal cells. In fact, there is no sharp separation between bimodal and unimodal cells. As the firing rate adaptation gets stronger, the network bump is more attenuated during the backwards sweep, and cells with the bimodal firing property will gradually behave more like those with the unimodal firing property (see [Fig. S3b](#)). Moreover, our model confirms that even though phase procession is weak, it still exist in unimodal cells ([Fig. 4h](#) lower panel), which has been reported in previous studies ([Wang et al., 2020](#); [Yamaguchi et al., 2002](#)). This implies that phase procession is not a characteristic feature of bimodal cells, but instead, is likely a common feature of hippocampal activity, with a strength controlled by adaptation. Furthermore, the experimental data ([Fernández-Ruiz et al., 2017](#)) has indicated that there is a laminar difference between unimodal cells and bimodal cells, with bimodal cells correlating more with the firing patterns of deep CA1 neurons and unimodal cells with the firing patterns of superficial CA1 neurons. Our model suggests that this difference may come from the different adaptation strengths in the two layers.



**Figure 4.**

Different adaptation strengths account for the emergence of bimodal and unimodal cells. **a**, The firing rate trace of a typical bimodal cell in our model (upper panel) and the experiment data (lower panel, adapted from (Skaggs et al., 1996)). Blue boxes mark the phase shift stage. Note that there are two peaks in each theta cycle. **b**, The firing rate trace of a typical unimodal cell. Note that there is only one firing peak in each theta cycle. **c**, The averaged bump heights in the forward (blue curve) and backward windows (red curve) as a function of the adaptation strength  $m$ . **d**, Variation of the bump height when the adaptation strength is relatively small (blue line) or large (red line). **e-f**, Relative location of the bump center in a theta cycle when adaptation strength is relatively small (**e**) or large (**f**). Dashed line separate the forward and backward windows. **g-h**, Theta phase as a function of the normalized position of the animal in place field, averaged over all bimodal cells (**g**) or over all unimodal cells (**h**). -1 indicates that the animal just enters the place field, and 1 represents that the animal is about to leave the place field. Dashed lines separate the forward and backward windows. The lower panels in both **g** and **h** present the rescaled colormaps only in the backward window.

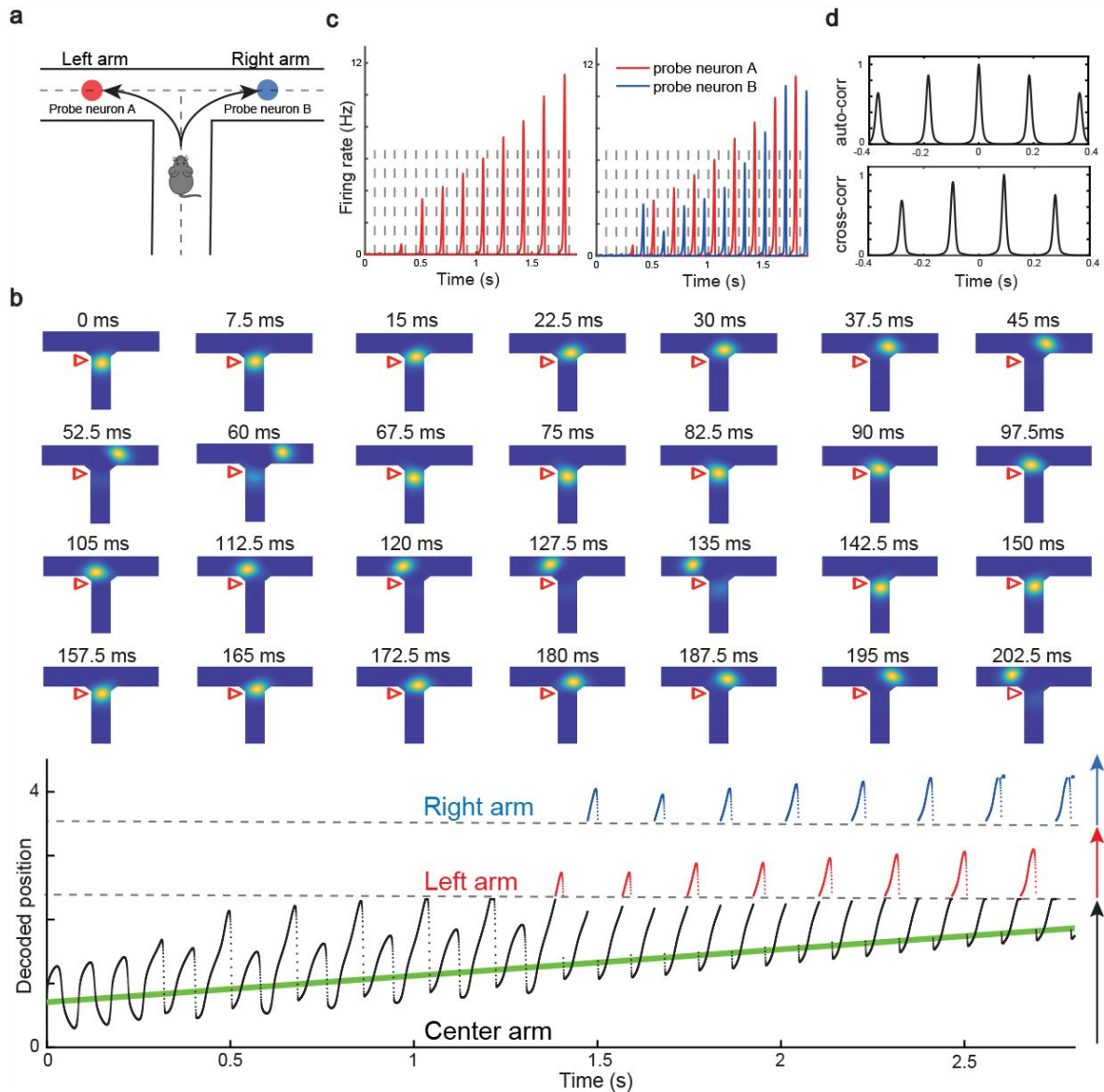
## Constant cycling of multiple future scenarios in a T-maze environment

We have shown that our model can reproduce the forward and backward theta sweeps of decoded position when the animal runs on a linear track. It is noteworthy that there is only a single hypothetical future scenario in the linear track environment, i.e., ahead of the animal's position, and hence place cells firing phase can only encode future positions in one direction. However, flexible behaviors requires the animal encoding multiple hypothetical future scenarios in a quick and constant manner, e.g., during decision-making and planning in complex environments ([Johnson and Redish, 2007](#); [Wikenheiser and Redish, 2015](#)). One recent study ([Kay et al., 2020](#)) showed constant cycling of theta sweeps in a T-maze environment (**Fig. 5a**), that is, as the animal approaches the choice point, the decoded position from hippocampal activity propagates down one of the two arms alternatively in successive LFP theta cycles. To reproduce this phenomenon, we change the structure of the CANN from a linear track shape to a T-maze shape where the neurons are aligned according to the location of their firing fields in the T-maze environment. Neurons are connected with a strength proportional to the Euclidean distance between their firing fields on the T-maze and the parameters are set such that the network is in the oscillatory tracking state (see details in Methods.). Mimicking the experimental protocol, we let the external input (the artificial animal) move from the end of the center arm to the choice point. At the beginning, when the external input is far away from the choice point, the network bump sweeps back and forth along the center arm, similar to the situation on the linear track. As the external input approaches the choice point, the network bump starts to sweep onto left and right arms alternatively in successive theta cycles (**Fig. 5b** and **video 4**; see also [Romani and Tsodyks \(2015\)](#) for a similar model of cyclical sweeps spanning several theta cycles). The underlying mechanism is straightforward. Suppose that the bump first sweeps to the left arm from the current location, it will sweep back to the current location first due to the attraction of the external input. Then in the next round, the bump will sweep to the right arm, since the neurons on the left arm are suppressed due to adaptation. This cycling process repeats constantly between the two upcoming arms before the external input enters one of the two arms (i.e., before the decision is made). At the single cell level, this bump cycling phenomenon gives rise to the “cycle skipping” effect ([Kay et al., 2020](#); [Deshmukh et al., 2010](#); [Brandon et al., 2013](#)), where a neuron whose place field is on one of the two arms fires on every other LFP theta cycle before the decision is made (**Fig. 5c** left panel and **Fig. 5d** upper panel). For example, a pair of cells with firing fields on each of the two arms will fire in regular alternation on every other theta cycle (**Fig. 5c** right panel and **Fig. 5d** lower panel). These cell-level firing patterns agree well with the experimental observations ([Kay et al., 2020](#)).

In summary, our model, extended to a T-maze structure, explains the constant cycling of two possible future scenarios in a T-maze environment. The underlying mechanism relies on delayed adaptation, which alternately causes neurons on one arm to be more suppressed than those on the other arm. Such high-speed cycling may contribute to the quick and continuous sampling among multiple future scenarios in real-world decision-making and planning. We also note that there is a cyclical effect in the sweep lengths across oscillation cycles before the animal enters the left or right arm (see **Fig. 5b** lower panel), which may be interesting to check in the experimental data in future work (see Discussion for more details).

## Robust phase coding of position with place cells

As the firing rate shows large variability when the animal runs through the firing field ([Fenton and Muller, 1998](#)), it has been suggested that the theta phase shift provides an additional mechanism to improve the localization of animals ([O'keefe and Burgess, 2005](#)). Indeed, [Jensen and Lisman \(2000\)](#) showed that taking phase into account leads to a significant improvement in the accuracy of localizing the animal. To demonstrate the robustness of phase coding, previous experiments showed two intriguing findings: a linear relationship between the firing frequency of



**Figure 5.**

Constant cycling of future positions in a T-maze environment. **a**, An illustration of an animal navigating a T-maze environment with two possible upcoming choices (the left and right arms). **b**, Upper panel: Snapshots of constant cycling of theta sweeps on two arms when the animal is approaching the choice point. Red triangle marks the location of the external input. Note that the red triangle moves slightly towards the choice point in the 200 ms duration. Lower panel: Constant cycling of two possible future locations. The black, red and blue traces represent the bump location on the center, left and right arms, respectively. The green line marks the location of the external moving input. **c**, Left panel: the firing rate trace of a neuron A on the left arm when the animal approaches the choice point. Right panel: the firing rate traces of a pair of neurons when the animal approaches the choice point, with neuron A (red) on the left arm and neuron B (blue) on the right arm. Dashed lines separate theta cycles. **d**, Upper panel: the auto-correlogram of the firing rate trace of probe neuron A. Lower panel: the cross-correlogram between the firing rate trace of neuron A and the firing rate trace of neuron B.



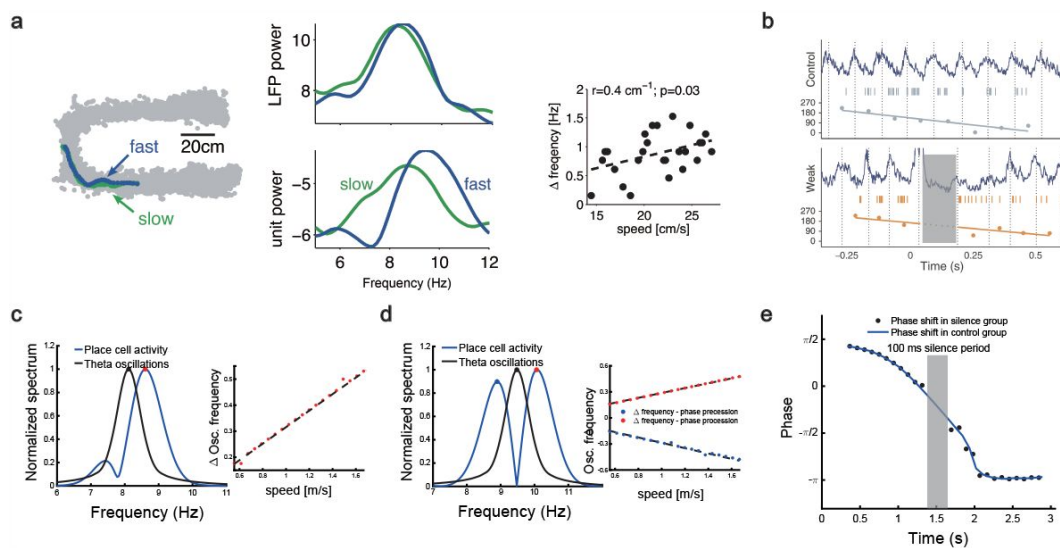
place cells and the animal's moving speed ([Geisler et al., 2007](#)) ([Fig. 6a](#)), and the continued phase shift after interruption of hippocampal activity ([Zugaro et al., 2005](#)) ([Fig. 6b](#)). We show that our model can also reproduce these two phenomena.

To investigate the relationship between the single cell's oscillation frequency and the moving speed as the animal runs through the firing field, we consider a unimodal cell with predominant phase precession as studied in [Geisler et al. \(2007\)](#). As we see from [Fig. 3d](#) and [Fig. 4a&b](#), when the animal runs through the firing field of a place cell, the firing rate oscillates because the activity bump sweeps around the firing field center. Therefore, the firing frequency of a place cell has a baseline theta frequency, which is the same as the bump oscillation frequency. Furthermore, due to phase precession, there will be half a cycle more than the baseline theta cycles as the animal runs over the firing field, and hence single cell oscillatory frequency will be higher than the baseline theta frequency ([Fig. 6c](#)). The faster the animal runs, the faster the extra half cycle can be accomplished. Consequently, the firing frequency will increase more (a steeper slope in [Fig. 6c](#) red dots) than the baseline frequency. This linear relationship ensures that the firing phase of a unimodal cell in each theta cycle is locked with the relative location of the animal in the firing field of that cell, which supports a robust phase-position code. Notably, in our model, the speed modulation of the place cells' firing frequency is not the cause of theta phase shift, but rather a result of oscillatory tracking. This is different from the dual oscillator model ([Lengyel et al., 2003](#)), which assumes that phase precession is caused by a speed-dependent increase in the dendritic oscillation frequency (see Discussion for more details).

In a different experiment, ([Zugaro et al., 2005](#)) found that the firing phase of a place cell continues to precess even after hippocampal activity was transiently silenced for up to 250 ms (around 2 theta cycles) ([Fig. 6b](#)). To reproduce this phenomenon, we also study a unimodal cell by manually turning off the network activity for a few hundred milliseconds (by setting  $r(x, t) = 0$  for all neurons) and then letting the network dynamics evolves again with all parameters unchanged. Based on the theoretical analysis ([Eq. 8](#)), we see that the firing phase is determined by the location of the animal in the place field, i.e.,  $v_{ext}t$ . This means that the firing phase keeps tracking the animal's physical location. No matter how long the network is inactivated, the new firing phase will only be determined by the new location of the animal in the place field. Therefore, the firing phase in the first bump oscillation cycle after the network perturbation is more advanced than the firing phase in the last bump oscillation cycle right before the perturbation, and the amount of precession is similar to that in the case without perturbation ([Fig. 6e](#)). This agrees well with the experimental observation ([Fig. 6b](#)), and indicates that the phase-position code is robust to the perturbation of the hippocampal dynamics.

Overall, our model reproduces these two experimental findings, and suggests that there exists a one-to-one correspondence between the firing phase of a place cell and the travelled distance in the neuron's place field, which is independent of the animal's running speed or the perturbation duration ([Fig. S4](#)). This agrees well with experimental observations ([O'Keefe and Recce, 1993](#)) that theta phase correlates better with the animal's location than with time ([Fig. 6f&g](#)). In addition to the results for unimodal cells as introduced above, our model predicts new results for bimodal cells. First, in contrast to a unimodal cell, a bimodal cell will have two peaks in its firing frequency, with one slightly higher than the LFP theta baseline (due to phase precession) and the other slightly lower than the LFP theta baseline (due to phase procession). The precession-associated frequency positively correlates with the running speed of the animal, while the procession-associated frequency negatively correlates with the running speed ([Fig. 6d](#)). Second, similar to the preserved phase shift in unimodal cells, both the phase precession and procession of a bimodal cell after transient intrahippocampal perturbation continue from the new location of the animal (see [Fig. S5](#)), no matter how long the silencing period lasts. The two predictions could be tested by experiments.





**Figure 6.**

Robust phase coding of position. **a**, speed modulation of place cell firing frequency, adapted from *Geisler et al. (2007)*. Oscillation frequency of the place cell is higher in the faster run trial (blue) than that in the slower run trial (green). The frequency difference is linearly increased with the running speed. **b**, Phase precession is preserved after stimulation-induced perturbation (grey shaded area of the yellow part), adapted from *Zugaro et al. (2005)*. **c**, left: normalized spectrum of bump oscillation (black curve) and the oscillation of a unimodal cell (blue curve). Right: linear relationship between the frequency difference and the running speed. **d**, same as **c** but for a bimodal cell. **e**, silencing the network activity for 100 ms (grey shaded area) when the external moving input passes through the center part of the place field of a unimodal cell. Theta phase shifts of the unimodal cell are shown with (black points) or without (blue curve) silencing the network.

## Discussion

### Model contributions

In this paper, we have proposed a CANN with firing rate adaptation to unveil the underlying mechanism of place cell phase shift during locomotion. We show that the interplay between intrinsic mobility (owing to firing rate adaptation) and extrinsic mobility (owing to the location-dependent sensory inputs) leads to an oscillatory tracking state, which naturally accounts for theta sweeps where the decoded position oscillates around the animal's physical location at the theta rhythm. At the single neuron level, we show that the forward and backward bump sweeps account for, respectively, phase precession and phase procession. Furthermore, we show that the varied adaptation strength explains the emergence of bimodal and unimodal cells, that is, as the adaptation strength increases, forward sweeps of the bump gradually suppress backward sweeps, and as a result, neurons initially exhibiting both significant phase precession and procession (due to a low level adaptation) will gradually exhibit only predominant phase precession (due to a high level adaptation).

### Computational models for theta phase shift and theta sweeps

As a subject of network dynamics, oscillatory tracking has been studied previously in an excitatory-inhibitory neural network ([Folias and Bressloff, 2004](#)), where it was found that decreasing the external input strength can lead to periodic emission of traveling waves in the network (Hopf instability), which is analogous to the oscillatory tracking state in our model. However, their focus was on the mathematical analysis of such dynamical behavior, while our focus is on the biological implications of oscillatory tracking, i.e., how can it be linked to phase precession and procession of hippocampal place cells.

Due to their potential contributions to the temporal sequence learning involved in spatial navigation and episodic memory ([Mehta et al., 1997](#); [2002](#); [Yamaguchi, 2003](#)), theta phase precession and forward theta sweeps have been modelled in the field for decades. These models can be divided into two main categories, with one relying on the mechanism of single cell oscillation ([O'Keefe and Recce, 1993](#); [Kamondi et al., 1998](#); [Lengyel et al., 2003](#); [O'Keefe and Burgess, 2005](#); [Mehta et al., 2002](#)), and the other relying on the mechanism of recurrent interactions between neurons ([Tsodyks et al., 1996](#); [Romani and Tsodyks, 2015](#); [Kang and DeWeese, 2019](#)). A representative example of the former is the oscillatory interference model ([O'Keefe and Recce, 1993](#); [Lengyel et al., 2003](#)), which produces phase precession via the superposition of two oscillatory signals, with one from the baseline somatic oscillation at the LFP theta frequency (reflecting the inputs from the medial septal pacemaker ([Stewart and Fox, 1990](#))), and the other from the dendritic oscillation whose frequency is slightly higher. While these models can explain a large variety of experimental phenomena, it remain unclear how oscillation of individual neurons has a frequency higher than the baseline theta frequency. Here, our model provides a network mechanism for how such higher-frequency oscillation emerges.

A representative model relying on neuronal recurrent interactions is the activation spreading model ([Tsodyks et al., 1996](#)). This model produces phase precession via the propagation of neural activity along the movement direction, which relies on asymmetric synaptic connections. A later version of this model considers short-term synaptic plasticity (short-term depression) to implicitly implement asymmetric connections between place cells ([Romani and Tsodyks, 2015](#)), and reproduces many other interesting phenomena, such as phase precession in different environments. Different from these two models, our model considers firing rate adaptation to implement symmetry breaking and hence generates activity propagation. To prevent the activity bump from spreading away, their model considers an external theta input to reset the bump location at the end of each theta cycle, whereas our model generates an internal oscillatory state, where the activity bump travels back due to the attraction of external location input once it

spreads too far away. Moreover, theoretical analysis of our model reveals how the adaptation strength affect the direction of theta sweeps, as well as offers a more detailed understanding of theta cycling in complex environments.

## Beyond the linear track environment

Besides the linear track environment, the mechanism of generating theta sweeps proposed in our model can also be generalized to more complex environments. For instance, in a T-maze environment, our model explains the constant cycling of theta sweeps between left and right arms. Such cycling behavior may be important for high-speed actions such as predating and escaping which require animals to make decision among several future scenarios at the sub-second level. Similar alternative activity sweeps in the T-maze environment has been studied in a previous paper ([Romani and Tsodyks, 2015](#)), which showed that the frequency of alternation correlates with overtly deliberative behaviors such as head scans (frequency at 1 Hz or less) ([Johnson and Redish, 2007](#)). In contrast to our model, the network activity in their model propagates continuously from the current location on the center arm till the end of the outer arm, which takes a few theta cycles (i.e., 1 second or more). In our model, the network bump alternately sweeps to one of the two outer arms at a much higher frequency ( $\sim 8$  Hz), which may be related to fast decision-making or planing in natural environments ([Kay et al., 2020](#)). Furthermore, our model can also be easily extended to the multiple-arms ( $> 2$ ) environment ([Gillespie et al., 2021](#)) or the cascade-T environment ([Johnson and Redish, 2007](#)) with the underlying mechanism of generating theta cycling remaining unchanged. In addition to the linear and T-maze environments, phase shift has also been reported when an animal navigates in an open field environment. However, due to the lack of recorded neurons, decoding theta sweeps in the 2D environment is not as straightforward as in the 1D case. While theta sweeps in the 1D case have been associated with goal-directed behaviors and spatial planning ([Wikenheiser and Redish, 2015](#)), it remains unclear whether such conclusion is applicable to the 2D case. Our preliminary result shows that in the 2D CANN where neurons are arranged homogeneously according to their relative firing locations, the activity bump will sweep along the tangent direction of the movement trajectory, similar to the 1D case (see SI.4 and Fig. S6 for details). It will be interesting to explore theta sweeps in the open field environment in detail when more experimental data is available.

## Model predictions and future works

Our model has several predictions which can be tested in future experiments. For instance, the height of the activity bump in the forward sweep window is higher than that in the backward sweep window ([Fig. 4c](#)) due to the asymmetric suppression effect from the adaptation. For bimodal cells, they will have two peaks in their firing frequency as the animal runs across the firing fields, with one corresponding to phase precession and the other corresponding to phase procession. Similar to unimodal cells, both the phase precession and procession of a bimodal cell after transient intrahippocampal perturbation will continue from the new location of the animal ([Fig. S5](#)). Interestingly, our model of the T-maze environment showed an expected phenomenon that as the animal runs towards the decision point, the theta sweep length also shows cyclical patterns ([Fig. 5b](#) lower panel). An intuitive explanation is that, due to the slow dynamics in firing rate adaptation (with a large time constant compared to neural firing), a long sweep leads to an adaptation effect on the neurons at the end of the sweep path. Consequently, the activity bump cannot travel as far due to the adaptation effect on those neurons, resulting in a shorter sweep length compared to the previous one. In the next round, the activity bump exhibits a longer sweep again because those neurons have recovered from the previous adaptation effect. We plan to test this phenomenon in future experiments.

In the current study, we have modeled the place-cell population in the hippocampus with a CANN and adopted firing rate adaptation to generate theta phase shift. In fact, this model can be easily extended to the grid cell population without changing the underlying mechanism. For instance, we can induce the torus-like connection profile (periodic boundary in the 2D space) ([Samsonovich and](#)

[McNaughton, 1997](#); [McNaughton et al., 2006](#)) or the locally inhibitory connection profile ([Burak and Fiete, 2009](#); [Couey et al., 2013](#)) in the CANN structure to construct a grid cell model, and by imposing firing rate adaptation, neurons in the grid cell network will also exhibit phase shift as the animal moves through the grid field, as reported in previous experimental studies ([Hafting et al., 2008](#); [Van Der Meer and Redish, 2011](#)). Notably, although for both grid cells and place cells, CANNs can generate theta phase shift, it does not mean that they are independent from each other. Instead, they might be coordinated by the same external input from the environment, as well as by the medial septum which is known to be a pacemaker that synchronises theta oscillations across different brain regions ([King et al., 1998](#); [Wang, 2002](#)). We will investigate this issue in future work.

Our model also suggests that the “online” theta sweep and the “offline” replay may share some common features in their underlying mechanisms ([Romani and Tsodyks, 2015](#); [Hopfield, 2010](#); [Kang and DeWeese, 2019](#); [Jahnke et al., 2015](#)). We have shown that the activity bump with strong adaptation can move spontaneously when the external input becomes weak enough (see previous sections). Such non-local spreading of neural activity has a speed much faster than the conventional speed of animals (the external input speed in our model, see [Fig. 2d](#)), which resembles the fast spreading of the decoded position during sharp-wave ripple events ([Diba and Buzsáki, 2007](#); [Foster and Wilson, 2006](#); [Karlsson and Frank, 2009](#); [Dragoi and Tonegawa, 2011](#)). This indicates that these two phenomena may be generated by the same neural mechanism of firing rate adaptation, with theta sweeps originating from the interplay between the adaptation and the external input, while replay originating from only the adaptation, since the external input is relatively weak during the “offline” state. This hypothesis seems to be supported by the coordinated emergence of theta sequences and replays during the post-natal development period ([Muessig et al., 2019](#)), as well as their simultaneous degradation when the animal travelled passively on a model train ([Drieu et al., 2018](#)).

Nevertheless, it is important to note that the CANN we adopt in the current study is an idealized model for the place cell population, where many biological details are missed ([Amari, 1977](#); [Tsodyks and Sejnowski, 1995](#); [Samsonovich and McNaughton, 1997](#); [Tsodyks, 1999](#)). For instance, we have assumed that neuronal synaptic connections are translation-invariant in the space. In practice, such a connection pattern may be learned by a synaptic plasticity rule at the behavioral time scale when the animal navigates actively in the environment ([Bittner et al., 2017](#)). In future work, we will explore the detailed implementation of this connection pattern, as well as other biological correspondences of our idealized model, to establish a comprehensive picture of how theta phase shift is generated in the brain.

## Materials and Methods

### General summary of the model

We consider a one-dimensional continuous attractor neural network (1D CANN), in which neurons are uniformly aligned according to their firing fields on a linear track (for the T-maze case, see Methods. below; for the case of the open field (2D CANN), see SI.4). Denote  $U(x, t)$  the synaptic input received by the place cell at location  $x$ , and  $r(x, t)$  the corresponding firing rate. The dynamics of the network is written as

$$\tau \frac{dU(x, t)}{dt} = -U(x, t) + \rho \int_{-\infty}^{\infty} J(x, x') r(x', t) dx' - V(x, t) + I^{ext}(x, t), \quad (9)$$

where  $\tau$  is the time constant of  $U(x, t)$  and  $\rho$  the neuron density. The firing rate  $r(x, t)$  is given by

$$r(x, t) = \frac{gU(x, t)^2}{1 + k\rho \int_{-\infty}^{\infty} U(x', t)^2 dx'}, \quad (10)$$

where  $k$  controls the strength of the global inhibition (divisive normalization),  $g$  denotes a gain factor.  $J(x, x')$  denotes the connection weight between place cells at location  $x$  and  $x'$ , which is written as:

$$J(x, x') = \frac{J_0}{\sqrt{2\pi}a} \exp\left[-\frac{(x - x')^2}{2a^2}\right], \quad (11)$$

where  $J_0$  controls the strength of the recurrent connection and  $a$  the range of neuronal interaction. Notably,  $J(x, x')$  depends on the relative distance between two neurons, rather than the absolute locations of neurons. Such translation-invariant connection form is crucial for the neutral stability of the attractor states of CANNs (Wu et al., 2016).  $I^{ext}(x, t)$  represents the external input which conveys the animal location information to the hippocampal network, which is written as:

$$I^{ext}(x, t) = \alpha \exp\left[-\frac{(x - v_{ext}t)^2}{4\sigma^2}\right], \quad (12)$$

with  $v_{ext}$  denoting the animal's running speed and  $\alpha$  controlling the input strength to the hippocampus.  $\sigma$  denotes the width of the external input  $I^{ext}$ , which is set to be equal to the recurrent connection width  $a$  in the main text and the following derivation.  $V(x, t)$  denotes the adaptation effect of the place cell at location  $x$ , which increases with the synaptic input (and hence the place cell's firing rate), i.e.,

$$\tau_v \frac{dV(x, t)}{dt} = -V(x, t) + mU(x, t), \quad (13)$$

with  $\tau_v$  denoting the time constant of  $V(x, t)$  and  $m$  the adaptation strength. Note that  $\tau_v \gg \tau$ , meaning that adaptation is a much slower process compared to the neural firing.

## Stability analysis of the bump state

We derive the condition under which the bump activity is the stable state of the CANN. For simplicity, we consider the simplest case that there is no external input and adaptation in the network, i.e.,  $m = \alpha = 0$ . In this case, the network state is determined by the strength of the recurrent excitation and global inhibition. When the global inhibition is strong ( $k$  is large), the network is silent, i.e., no bump activity emerges in the CANN. When the global inhibition is small, an activity bump with the Gaussian-shaped profile emerges, which is written as:

$$\bar{U}(x, t) = A_u \exp\left\{-\frac{[x - z(t)]^2}{4a^2}\right\}, \quad (14)$$

$$\bar{r}(x, t) = A_r \exp\left\{-\frac{[x - z(t)]^2}{2a^2}\right\}, \quad (15)$$



with  $A_u$  and  $A_r$  representing the amplitudes of the synaptic input bump and the firing rate bump, respectively.  $z(t)$  represents the bump center, and  $a$  is the range of neuronal interaction (defined in Methods.). To solve the network dynamics, we substitute Eqs. 14 & 15 into Eqs. 9 & 10, which gives (see SI.2 for more details of the derivation):

$$\tau \frac{dA_u}{dt} = -A_u + \frac{\rho J_0}{\sqrt{2}} A_r, \quad (16)$$

$$A_r = \frac{A_u^2}{1 + \sqrt{2\pi k \rho a} A_u^2}, \quad (17)$$

These two equations describes how the bump amplitudes change with time. For instance, if neurons are weakly connected (small  $J_0$ ) or they are connected sparsely (small  $\rho$ ), the second term on the right-hand side of Eq. 16 is small, and  $A_u$  will decay to zero, implying that the CANN cannot sustain a bump activity. By setting  $dA_u/dt = 0$ , we obtain:

$$A_u = \frac{\rho J_0 \pm \sqrt{\rho^2 J_0^2 - 8\sqrt{2\pi k \rho a}}}{4\sqrt{\pi k \rho a}}, \quad (18)$$

$$A_r = \frac{\sqrt{2}}{\rho J_0} A_u. \quad (19)$$

It is straightforward to check that only when:

$$k < k_c = \rho J_0^2 / 8\sqrt{2\pi a}, \quad (20)$$

$A_u$  have two real solutions (indicated by the  $\pm$  sign in Eq. 18), i.e., the dynamic system (Eqs. 16 & 17) has two fixed points. It can be checked that only  $A_u = \left( \rho J_0 + \sqrt{\rho^2 J_0^2 - 8\sqrt{2\pi k \rho a}} \right) / \left( 4\sqrt{\pi k \rho a} \right)$  is the stable solution.

## Analysis of the intrinsic mobility of the bump state

We derive the condition under which the bump of the CANN moves spontaneously in the attractor space without relying on external inputs. As the adaptation strength increases, the bump activity becomes unstable and has tendency to move away from its location spontaneously. Such intrinsic mobility of the CANN has been shown in previous studies (Bressloff, 2011; Wu et al., 2016; Mi et al., 2014). We set  $a = 0$  (no external input), and investigate the effect of adaptation strength  $m$  on the bump dynamics. Our simulation result shows that during the spontaneous movement,  $V(x, t)$  can also be represented by a Gaussian-shaped bump, which is written as

$$\bar{V}(x, t) = A_v \exp \left\{ -\frac{[x - z(t) + d(t)]^2}{4a^2} \right\}, \quad (21)$$

where  $A_v$  denotes the amplitude of the adaptation bump, and  $d(t)$  the displacement between the bump centers of  $U(x, t)$  and  $V(x, t)$ . This displacement originates from the slow dynamics of adaptation, which leads to the adaptation bump always lags behind the neural activity bump. Similar to Methods., we substitute the bump profiles Eqs. (14, 15, 21) into the network dynamics Eqs. (9, 10, 13), and obtain:

$$\tau \left[ A_u \frac{x-z}{2a^2} \frac{dz}{dt} + \frac{dA_u}{dt} \right] \mathcal{N}(x, z, 2a) = (-A_u + \frac{\rho J_0}{\sqrt{2}} A_r) \mathcal{N}(x, z, 2a) - A_v \mathcal{N}(x, z-d, 2a), \quad (22)$$

$$A_r = \frac{A_u^2}{1+k\rho\sqrt{2\pi a}A_u^2}, \quad (23)$$

$$\tau_v \left[ A_v \frac{x-z+d}{2a^2} \frac{d(z-d)}{dt} + \frac{dA_v}{dt} \right] \mathcal{N}(x, z-d, 2a) = -A_v \mathcal{N}(x, z-d, 2a) + mA_u \mathcal{N}(x, z, 2a), \quad (24)$$

where  $\mathcal{N}(x, z, 2a) = \exp \left\{ -\frac{[x-z]^2}{4a^2} \right\}$ .

At first glance, the resulting equations given by Eqs. (22) and (24) may seem intractable due to the high dimensionality (i.e.,  $2N$ , where  $N$  is the number of neurons in the network). However, a key property of CANNs is that their dynamics are dominated by a few motion modes, which correspond to distortions of the bump shape in terms of height, position, width, etc. **Fung et al. (2010)**. By projecting the network dynamics onto its dominant motion modes **Fung et al. (2010)** (which involves computing the inner product of a function  $f(x)$  with a mode  $u_n(x)$ ), we can significantly simplify the network dynamics. Typically, projecting onto the first two motion modes is sufficient to capture the main features of the dynamics, which are given by,

$$u_0(x, t) = \exp \left\{ -\frac{[x-z(t)]^2}{4a^2} \right\}, \quad (25)$$

$$u_1(x, t) = [x-z(t)] \exp \left\{ -\frac{[x-z(t)]^2}{4a^2} \right\}. \quad (26)$$

By projecting the network dynamics onto these two motion modes, we obtain:

$$-A_u + \frac{\rho J_0}{\sqrt{2}} A_r - A_v \exp\left(-\frac{d^2}{8a^2}\right) = 0, \quad (27)$$

$$\tau A_u v_{int} = d A_v \exp\left(-\frac{d^2}{8a^2}\right), \quad (28)$$

$$\frac{d}{4a^2} \tau_v A_v \exp\left(-\frac{d^2}{8a^2}\right) v_{int} = -A_v \exp\left(-\frac{d^2}{8a^2}\right) + mA_u, \quad (29)$$

$$\tau_v \left(1 - \frac{d^2}{4a^2}\right) v_{int} = d. \quad (30)$$

Note that we assume that the bump height keep as constant over time, i.e.,  $dA_u/dt = dA_v/dt = 0$  is assumed. Eqs. 27-30 describes the relationships between bump features  $A_u$ ,  $A_r$ ,  $A_v$ ,  $v_{int}$  and  $d$ , where  $v_{int} = dz/dt$  representing the intrinsic moving speed of the bump center. By solving these equations together with eqn. 23, we obtain,

$$A_u = \frac{\rho J_0 + \sqrt{\rho^2 J_0^2 - 8\sqrt{2\pi k \rho a}(1 + \sqrt{\frac{m\tau}{\tau_v}})^2}}{4\sqrt{\pi k \rho a}(1 + \sqrt{\frac{m\tau}{\tau_v}})}, \quad (31)$$

$$A_r = \frac{\rho J_0 + \sqrt{\rho^2 J_0^2 - 8\sqrt{2\pi k \rho a}(1 + \sqrt{\frac{m\tau}{\tau_v}})^2}}{2\sqrt{2\pi k \rho^2 a J_0}}, \quad (32)$$

$$A_v = \sqrt{\frac{m\tau}{\tau_v}} \exp\left[\frac{1 - \sqrt{\frac{\tau}{m\tau_v}}}{2}\right] \frac{\rho J_0 + \sqrt{\rho^2 J_0^2 - 8\sqrt{2\pi k \rho a}(1 + \sqrt{\frac{m\tau}{\tau_v}})^2}}{4\sqrt{\pi k \rho a}(1 + \sqrt{\frac{m\tau}{\tau_v}})}, \quad (33)$$

$$d = 2a\sqrt{1 - \sqrt{\frac{\tau}{m\tau_v}}}, \quad (34)$$

$$v_{int} = \frac{2a}{\tau_v} \sqrt{\frac{m\tau_v}{\tau} - \sqrt{\frac{m\tau_v}{\tau}}}. \quad (35)$$

Eqs. 31-33 describe the amplitudes of the bumps of synaptic input, firing rate, and adaptation in the CANN, respectively, and Eq. 34 describes the displacement between the neural activity and adaptation bumps. From Eq. 35, we see that for the bump to travel spontaneously, it requires  $m > \tau/\tau_v$ , i.e., the adaptation strength is larger than a threshold given by the ratio between two time constants  $\tau$  and  $\tau_v$ . As the adaptation strength increases (larger  $m$ ), the travelling speed of the bump increases (larger  $v_{int}$ ).

## Analysis of the oscillatory tracking behaviour of the bump state

When both the external input and the adaptation are applied to the CANN, the bump activity can oscillate around the external input if the strengths of the external input and the adaptation are appropriated. The simulation shows that during the oscillatory tracking, the bump shape is roughly unchanged, and the oscillation of the bump center can be approximated as a sinusoidal wave expressed as:

$$z(t) = c_0 \sin(\omega t) + d_0 + v_{ext}t, \quad (36)$$

where  $c_0$  and  $\omega$  denote, respectively, the oscillation amplitude and frequency, and  $d_0$  denotes a constant offset between the oscillation center and the external input.

Similar to the analysis in Methods., we substitute the expression of  $z(t)$  (Eq. 36) into Eqs. (14, 15, 21), and then simplify the network dynamics by applying the projection method (see SI.3 for more detailed derivation). We obtain,

$$(m+1)A_u - \frac{\rho J_0}{\sqrt{2}} \frac{A_u^2}{1 + \sqrt{2\pi ak\rho A_u^2}} - \alpha = 0, \quad (37)$$

$$\omega^2 = \frac{\alpha}{\tau\tau_v A_u}, \quad (38)$$

$$mA_u \exp\left(-\frac{d^2}{8a^2}\right) = A_v, \quad (39)$$

$$d_0 = \tau_v v, \quad (40)$$

$$\sqrt{\frac{2(\tau A_u + \alpha\tau_v)}{\alpha\tau_v} \left[ 4a^2 \left( \ln \frac{\tau_v mA_u}{\tau A_u + \alpha\tau_v} \right) - \tau_v^2 v^2 \right]} = c_0, \quad (41)$$

Eqs. 37-41 describe the relationships among 6 oscillation features  $A_u$ ,  $A_r$ ,  $A_v$ ,  $c_0$ ,  $d_0$  and  $\omega$ . By solving these equations, we obtain:

$$A_u = \frac{J_0 + 2\sqrt{\pi ak\alpha}}{2\sqrt{\pi ak}(1+m)}, \quad (42)$$

$$A_r = \frac{A_u^2}{1 + \sqrt{2\pi ak\rho A_u^2}}, \quad (43)$$

$$A_v = \sqrt{\left( \frac{\tau A_u + \alpha\tau_v}{\tau_v} \right) mA_u}, \quad (44)$$

$$c_0 = A_v \sqrt{\frac{2}{\alpha mA_u} \left[ 8a^2 \ln \frac{mA_u}{A_v} - \tau_v^2 v^2 \right]}, \quad (45)$$

$$d_0 = \tau_v v, \quad (46)$$

$$\omega = \sqrt{\frac{\alpha}{\tau\tau_v A_u}}. \quad (47)$$

It can be seen from Eq. 45 that for the bump activity to oscillate around the external input (i.e., the oscillation amplitude  $c_0 > 0$ ), it requires that  $8a^2 \ln(mA_u/A_v) - \tau_v^2 v^2 > 0$ . This condition gives the boundary (on the parameter values of the input strength  $\alpha$  and the adaptation strength  $m$ ) that separate two tracking states, i.e., smooth tracking and oscillatory tracking (see Fig. 2g and Fig. S2 for the comparison between the simulation results and theoretical results).

Note that to get the results in Eqs. 37–41, we have assumed that the amplitudes of neural activity bumps and the adaptation bump remain unchanged during the oscillation (i.e.,  $A_w$ ,  $A_v$ ,  $A_r$  are constants). However, this assumption is not satisfied when the SFA strength  $m$  is large (see previous sections and Fig. 4). In such a case, we carry out simulation to analyze the network dynamics.

## Implementation details of the linear track environment

For the linear track environment, we simulate an 1D CANN with 512 place cells topographically organized on the one-dimensional neuronal track. Since we are interested in how the neuronal firing phase shifts as the animal moves through the firing field of a place cell, we investigate the place cell at location  $x = 0$  and ignore the boundary effect, that is, we treat the linear track with the infinite length. The neural firing time constant is set to be 3 ms, while the time constant of spike frequency adaptation is much longer, which is set to be 144 ms. The density of place cells on the linear track is set to be  $256/\pi$ . The excitatory interaction range of place cells is set to be  $0.4m$ , while the maximum excitatory connection strength  $J_0$  is set to be 0.2. The gain factor is set to be 5. The global inhibition strength  $k$  is set to be 5. The moving speed of the virtual animal  $v_{ext}$  is set to be 1.5 m/s. For the simulation details, we use the first-order Euler method with the time step  $\delta t$  set to be 0.3 the duration of simulation  $T$  set to be 10 s. These parameters are commonly used in all plots related to the linear track environment (see Table.1 for a summary).

For the two key parameters, i.e., the external input strength  $\alpha$  and the adaptation strength  $m$ , we vary their values in different plots. Specifically, for illustrating the smooth tracking state in Fig. 2c, we set  $\alpha = 0.19$  and  $m = 0$ . For illustrating the travelling wave state (intrinsic mobility of the bump state) in Fig. 2d, we set  $\alpha = 0$  and  $m = 0.31$ . For plotting the relationship between the intrinsic speed  $v_{int}$  and the adaptation strength  $m$  shown in Fig. 2e, we keep  $\alpha = 0$ , but vary  $m$  in the range between 0 and 0.1 with a step of 0.05. For plotting the overall phase diagram including all three moving states as shown in Fig. 2g, we vary  $\alpha$  in the range between 0.05 and 0.16 with a step of 0.001, and  $m$  in the range between 0.9 and 1.8 with a step of 0.01. To generate bimodal cell firing patterns in Fig. 3a and Fig. 4a,e, we choose  $\alpha = 0.19$  and  $m = 3.02$ . To generate unimodal firing patterns in Fig. 4b,f&h, we choose  $\alpha = 0.19$  but a relatively larger adaptation strength with  $m = 3.125$ . The values of these two parameters in different plots are summarized in Table. 2.

## Implementation details of the T-maze environment

### Parameter configurations during simulation

To simulate the T-maze environment, we consider a CANN in which place cells are topographically organized in a T-shaped area which consists of a vertical central arm and two horizontal left and right arms (Fig. 5a). The width of the central arm is set to be 0.84 m and the length is set to be 3.14 m. The widths of the two horizontal arms are also set to be 0.84 m, while the lengths of both arms are set to be 2.36 m. The connection strength between two neurons is determined by the distance between them, which is written as:

$$J(x, x'; y, y') = \frac{J_0}{2\pi a^2} \exp \left[ -\frac{(x - x')^2 + (y - y')^2}{2a^2} \right]. \quad (48)$$



| Parameters                                            | Values    |
|-------------------------------------------------------|-----------|
| Number of place cells: $N$                            | 512       |
| Time constant of neural firing: $\tau$                | 3ms       |
| Time constant of spike frequency adaptation: $\tau_v$ | 144ms     |
| Neuron density: $\rho$                                | $256/\pi$ |
| Recurrent connection range (Gaussian width): $a$      | 0.4 m     |
| Width of external input (Gaussian width): $\sigma$    | 0.4 m     |
| Recurrent connection strength: $J_0$                  | 0.2       |
| Gain factor: $g$                                      | 5         |
| Global inhibition strength: $k$                       | 5         |
| Moving speed of the external input: $v_{ext}$ (m/s)   | 1.5       |
| Time interval: $\delta t$                             | 0.3 s     |
| Simulation duration: $T$                              | 10 s      |

**Table 1.**

**Commonly used parameter values in the simulation of the linear track environment.**

| Figures/parameters                                | $\alpha$        | $m$          |
|---------------------------------------------------|-----------------|--------------|
| An example of smooth tracking (Fig. 2c)           | 0.19            | 0            |
| An example of traveling wave (Fig. 2d)            | 0               | 0.31         |
| Intrinsic speed vs. adaptation strength (Fig. 2e) | 0               | 0:0.05:0.1   |
| Phase diagram (Fig. 2g)                           | 0.05:0.001:0.16 | 0.9:0.01:1.8 |
| Oscillatory tracking (bimodal) (Fig. 4a,e,g)      | 0.19            | 3.02         |
| Oscillatory tracking (unimodal) (Fig. 4b,f,h)     | 0.19            | 3.125        |

**Table 2.**

**Figure specific parameter values for input strength  $\alpha$  and adaptation strength  $m$ .**

Here  $(x, y)$  and  $(x', y')$  represent the coordinates of two neurons in the T-maze environment,  $a$  is the recurrent connection range which is set to be 0.3, and  $J_0$  controls the connection strength which is set to be 0.0125. Since we are interested in investigating theta sweeps when the animal is running on the central arm towards the junction point, the external input is restricted on the central arm which is modelled by a Gaussian-like moving bump written as:

$$I^{ext}(x, y) = \alpha \exp \left[ -\frac{(x - x_0)^2 + (y - y_0)^2}{2a^2} \right], \quad (49)$$

where  $x_0 = 0$  and  $y_0 = v_{ext}t$  represent the center location of the external input with a moving speed  $v_{ext} = 1.5$  m/s. In the simulation, we used the first-order Euler method with the time step  $\delta t = 0.3$  s and the duration of simulation  $T = 4.2$ s. The parameters used are summarized in [Table.3](#).

### Calculating auto-correlogram and cross-correlogram

To show the “cycle skipping” effect of a single place cell in the T-maze environment, we calculate the auto-correlogram of the firing rate trace of a place cell whose firing field encodes a location on the left arm (the upper panel in [Fig. 5d](#)). Assume the firing trace of the place cell is  $f(t)$  (showed in left panel in [Fig. 5c](#)), the auto-correlogram is calculated as:

$$(f * f)(\tau) \triangleq \int_{-\infty}^{\infty} f(t)f(t + \tau)dt, \quad (50)$$

where  $\tau$  represents the time offset.

To show the “alternative cycling” effect of a pair of place cells with each of them encoding a location on each of the two outward arms, we calculate the cross-correlogram between their firing traces (the lower panel in [Fig. 5d](#)). It measures the similarity of the two firing traces as a function of the temporal offset of one relative to the other. Assume the firing traces of the two place cells are  $f(t)$  and  $g(t)$ , respectively, the cross-correlogram is calculated as:

$$(f * g)(\tau) \triangleq \int_{-\infty}^{\infty} f(t)g(t + \tau)dt, \quad (51)$$

### Details of generating the probability heatmap of theta phase shift

In [Fig. 4g](#) we described the smoothed probability heatmaps of theta phase versus normalized position in the place field of both bimodal and unimodal cells. Generally, these two plots are similar to the traditional spike plot of phase and position traveled in the place field ([O'Keefe and Recce, 1993](#); [Skaggs et al., 1996](#)). However, in our rate-based model, the phase of neuronal spike is not directly modelled, rather we use the phase of firing rate peak to represent the phase shift in neuronal firing. Here we describe the implementation details of generating the heatmaps.

The x-axis denotes the normalized position in the place field, with -1 representing the position where the animal just enters the place field, and 1 representing the position where the animal just leaves the place field. In our simulation, the firing field of a place cell with preferred location at  $x_0$  is defined as  $x \in (x_0 - 2.5 * a, x_0 + 2.5a)$ , with  $a$  roughly the half size of the firing field. Consider the animal is at  $x_t$  at time  $t$  (note that  $x_t = v_{ext}t$ ), then its normalized position  $\tilde{x}_t$  is calculated as  $\tilde{x}_t = (x_t - x_0)/(5a)$ . The y-axis represents the phase of neuronal activity, which is in the range of  $(0^\circ, 720^\circ)$ . To calculate the phase at every time step, we divide the duration of the animal traversing the linear track into multiple theta cycles according to the bump's oscillation. We can

| Parameters                                            | Values           |
|-------------------------------------------------------|------------------|
| Number of cells central/left/right: $N_1, N_2, N_3$   | 3000/1500/1500   |
| Time constant of neural firing: $\tau$                | 3 ms             |
| Time constant of spike frequency adaptation: $\tau_v$ | 144 ms           |
| Neuron density: $\rho$                                | $(128/\pi)^2$    |
| Recurrent connection range (Gaussian width): $a$      | 0.3              |
| Recurrent connection strength: $J_0$                  | $1.25 * 10^{-2}$ |
| Gain factor: $g$                                      | 20               |
| Global inhibition strength: $k$                       | 1.25             |
| Moving speed of the external input: $v_{ext}$ (m/s)   | 1.5              |
| Input strength: $\alpha$                              | 2                |
| Adaptation strength: $m$                              | 3.96             |
| Time interval: $\delta t$                             | 0.3 s            |
| Simulation duration: $T$                              | 3.3 s            |

**Table 3.**

**Parameters values in the simulation of the T-maze environment**

calculate the phase by  $\theta_t = (t - t_0)/T$ , with  $t_0$  referring to the beginning of the present theta cycle and  $T$  referring to the theta period. Denote the firing rate of the  $i$ -th neuron at time  $t$  as  $r_i(\tilde{x}_t, \theta_t)$ , the probability heatmap is calculated by,

$$p(\tilde{x}, \theta_t) = C \sum_{i=1}^{N_c} \theta_i r_i(\tilde{x}, \theta_t), \quad (52)$$

where  $C = 1 / \sum_t \sum_{i=1}^{N_c} \theta_i r_i(\tilde{x}, \theta_t)$  is the normalization factor.

## Spike generation from the firing rate

To understand phase shift based on spiking time rather than the peak firing rate, we convert the firing rate into spike trains according to the Poisson statistics (note that our analysis is rate-based, but converting to spike-based does not change the underlying mechanism). For the  $i$ th place cell which encodes position  $x_i$  on the linear track, the number of spikes  $n_i$  it generates within a time interval  $\Delta t$  satisfies a Poisson distribution, which is expressed as,

$$P(n_i | z) = \frac{[f_i(z)\Delta t]^{n_i}}{n_i!} e^{-f_i(z)\Delta t}, \quad (53)$$

where  $z$  is the animal's location, and  $f_i(z)$  is the tuning function of cell  $i$ , which is given by

$$f_i(z) = A_r \exp \left[ -\frac{(x_i - z)^2}{2a^2} \right], \quad (54)$$

where  $A_r$  denotes the amplitude of the neural activity bump and  $a$  the range of recurrent interaction.

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## Author Contributions

TC, ZJ and SW conceptualized and designed the research. TC, ZJ, JZ, and YM analyzed the model and performed the simulations. ZJ, WZ, TH, NB and SW interpreted the results. ZJ, TC, DB, NB and SW wrote the manuscript.

## Competing interests

Authors declare that they have no competing interests.

## Data and materials availability

All code for reproducing the figures in the main text are available in the supplementary materials.

## List of material contained in the Supplementary Material

- Supplementary text (pdf file)
- Figures S1-S4
- Video 1-4
- Code for reproducing all the figures in the main text

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**Reviewer #1 (Public Review):**

Continuous attractor networks endowed with some sort of adaptation in the dynamics, whether that be through synaptic depression or firing rate adaptation, are fast becoming the leading candidate models to explain many aspects of hippocampal place cell dynamics, from hippocampal replay during immobility to theta sequences during run. Here, the authors show that a continuous attractor network endowed with spike frequency adaptation and subject to feedforward external inputs is able to account for several previously unaccounted aspects of theta sequences, including (1) sequences that move both forwards and backwards, (2) sequences that alternate between two arms of a T-maze, (3) speed modulation of place cell firing frequency, and (4) the persistence of phase information across hippocampal inactivations.

I think the main result of the paper (findings (1) and (2)) are likely to be of interest to the hippocampal community, as well as to the wider community interested in mechanisms of neural sequences. In addition, the manuscript is generally well written and the analytics are impressive. However, several issues should be addressed, which I outline below.

Major comments:

In real data, population firing rate is strongly modulated by theta (i.e., cells collectively prefer a certain phase of theta - see review paper Buzsaki, 2002) and largely oscillates at theta frequency during run. With respect to this cyclical firing rate, theta sweeps resemble "Nike" check marks, with the sweep backwards preceding the sweep forwards within each cycle before the activity is quenched at the end of the cycle. I am concerned that (1) the summed population firing rate of the model does not oscillate at theta frequency, and (2) as the authors state, the oscillatory tracking state must begin with a forward sweep. With regards to (1), can the authors show theta phase spike preference plots for the population to see if they match data? With regards to (2), can the authors show what happens if the bump is made to sweep backwards first, as it appears to do within each cycle?

I could not find the width of the external input mentioned anywhere in the text or in the table of parameters. The implication is that it is unclear to me whether, during the oscillatory tracking state, the external input is large compared to the size of the bump, so that the bump lives within a window circumscribed by the external input and so bounces off the interior walls of the input during the oscillatory tracking phase, or whether the bump is continuously pulled back and forth by the external input, in which case it could be comparable to the size of the bump. My guess based on Fig 2c is that it is the latter. Please clarify and comment.

I would argue that the "constant cycling" of theta sweeps down the arms of a T-maze was roughly predicted by Romani & Tsodyks, 2015, Figure 7. While their cycling spans several theta cycles, it nonetheless alternates by a similar mechanism, in that adaptation (in this case synaptic depression) prevents the subsequent sweep of activity from taking the same arm as the previous sweep. I believe the authors should cite this model in this context and consider the fact that both synaptic depression and spike frequency adaptation are both possible mechanisms for this phenomenon. But I certainly give the authors credit for showing how this constant cycling can occur across individual theta cycles.

The authors make an unsubstantiated claim in the paragraph beginning with line 413 that the Tsodyks and Romani (2015) model could not account for forwards and backwards sweeps. Both the firing rate adaptation and synaptic depression are symmetry breaking models that should in theory be able to push sweeps of activity in both directions, so it is far from obvious to me that both forward and backward sweeps are not possible in the Tsodyks and Romani model. The authors should either prove that this is the case (with theory or simulation) or excise this statement from the manuscript.

The section on the speed dependence of theta (starting with line 327) was very hard to understand. Can the authors show a more graphical explanation of the phenomenon? Perhaps a version of Fig 2f for slow and fast speeds, and point out that cells in the latter case fire with higher frequency than in the former?

I had a hard time understanding how the Zugaro et al., (2005) hippocampal inactivation experiment was accounted for by the model. My intuition is that while the bump position is determined partially by the location of the external input, it is also determined by the immediate history of the bump dynamics as computed via the local dynamics within the hippocampus (recurrent dynamics and spike rate adaptation). So that if the hippocampus is inactivated for an arbitrary length of time, there is nothing to keep track of where the bump should be when the activity comes back on line. Can the authors please explain more how the model accounts for this?

Can the authors comment on why the sweep lengths oscillate in the bottom panel of Fig 5b during starting at time 0.5 seconds before crossing the choice point of the T-maze? Is this oscillation in sweep length another prediction of the model? If so, it should definitely be remarked upon and included in the discussion section.

Perhaps I missed this, but I'm curious whether the authors have considered what factors might modulate the adaptation strength. In particular, might rat speed modulate adaptation strength? If so, would have interesting predictions for theta sequences at low vs high speeds.

I think the paper has a number of predictions that would be especially interesting to experimentalists but are sort of scattered throughout the manuscript. It would be beneficial to have them listed more prominently in a separate section in the discussion. This should include (1) a prediction that the bump height in the forward direction should be higher than in the backward direction, (2) predictions about bimodal and unimodal cells starting with line 366, (3) prediction of another possible kind of theta cycling, this time in the form of sweep length (see comment above), etc.



- <https://doi.org/10.7554/eLife.87055.2.sa1>

### Reviewer #2 (Public Review):

In this work, the authors elaborate on an analytically tractable, continuous-attractor model to study an idealized neural network with realistic spiking phase precession/procession. The key ingredient of this analysis is the inclusion of a mechanism for slow firing-rate adaptation in addition to the otherwise fast continuous-attractor dynamics. The latter continuous-attractor dynamics classically arises from a combination of translation invariance and nonlinear rate normalization.

For strong adaptation/weak external input, the network naturally exhibits an internally generated, travelling-wave dynamics along the attractor with some characteristic speed. For small adaptation/strong external stimulus, the network recovers the classical externally driven continuous-attractor dynamics. Crucially, when both adaptation and external input are moderate, there is a competition with the internally generated and externally generated mechanisms leading to an oscillatory tracking regime. In this tracking regime, the population firing profile oscillates around the neural field tracking the position of the stimulus. The authors demonstrate by a combination of analytical and computational arguments that oscillatory tracking corresponds to realistic phase precession/procession. In particular the authors can account for the emergence of unimodal and bimodal cells, as well as some other experimental observations with respect the dependence of phase precession/procession on the animal's locomotion.

The strengths of this work are at least three-fold: 1) Given its simplicity, the proposed model has a surprisingly large explanatory power of the various experimental observations. 2) The mechanism responsible for the emergence of precession/procession can be understood as a simple yet rather illuminating competition between internally driven and externally driven dynamical trends. 3) Amazingly, and under some adequate simplifying assumptions, a great deal of analysis can be treated exactly, which allows for a detailed understanding of all parametric dependencies. This exact treatment culminates with a full characterization of the phase space of the network dynamics, as well as the computation of various quantities of interest, including characteristic speeds and oscillating frequencies.

As mentioned by the authors themselves, the main limitation of this work is that it deals with a very idealized model and it remains to see how the proposed dynamical behaviors would persists in more realistic models. For example, the model is based on a continuous attractor model that assumes perfect translation-invariance of the network connectivity pattern. Would the oscillating tracking behavior persist in the presence of connection heterogeneities? Another limitation is that the system needs to be tuned to exhibit oscillation within the theta range and that this tuning involves a priori variable parameters such as the external input strength. Is the oscillating-tracking behavior overtly sensitive to input strength variations? The author mentioned that an external pacemaker can serve to drive oscillation within the desired theta band but there is no evidence presented supporting this. A final and perhaps secondary limitation has to do with the choice of parameter, namely the time constant of neural firing which is chosen around 3ms. This seems rather short given that the fast time scale of rate models (excluding synaptic processes) is usually given by the membrane time constant, which is typically about 15ms. I suspect this latter point can easily be addressed.

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### Author Response

The following is the authors' response to the original reviews.

# Reviewer #1:

*Continuous attractor networks endowed with some sort of adaptation in the dynamics, whether that be through synaptic depression or firing rate adaptation, are fast becoming the leading candidate models to explain many aspects of hippocampal place cell dynamics, from hippocampal replay during immobility to theta sequences during run. Here, the authors show that a continuous attractor network endowed with spike frequency adaptation and subject to feedforward external inputs is able to account for several previously unaccounted aspects of theta sequences, including (1) sequences that move both forwards and backwards, (2) sequences that alternate between two arms of a T-maze, (3) speed modulation of place cell firing frequency, and (4) the persistence of phase information across hippocampal inactivations. I think the main result of the paper (findings (1) and (2)) are likely to be of interest to the hippocampal community, as well as to the wider community interested in mechanisms of neural sequences. In addition, the manuscript is generally well written, and the analytics are impressive. However, several issues should be addressed, which I outline below.*

## Major comments:

- 1. In real data, population firing rate is strongly modulated by theta (i.e., cells collectively prefer a certain phase of theta - see review paper Buzsaki, 2002) and largely oscillates at theta frequency during run. With respect to this cyclical firing rate, theta sweeps resemble "Nike" check marks, with the sweep backwards preceding the sweep forwards within each cycle before the activity is quenched at the end of the cycle. I am concerned that (1) the summed population firing rate of the model does not oscillate at theta frequency, and (2) as the authors state, the oscillatory tracking state must begin with a forward sweep. With regards to (1), can the authors show theta phase spike preference plots for the population to see if they match data? With regards to (2), can the authors show what happens if the bump is made to sweep backwards first, as it appears to do within each cycle?*

Thank you for raising these two important points. As the reviewer mentioned, experimental data does show that the population activity (e.g., calculated from the multiunit activity of tetrode recording) is strongly modulated by theta. While we mainly focused on sweeps of bump position, the populational activity also shows cyclical firing at the theta frequency (we added Fig. S7 to reflect this). This is also reflected in Fig. 4d where the bump height (representing the overall activity) oscillates at individual theta cycles. The underlying mechanism of cyclical population activity is as follows: the bump height is determined by the amount of input the neuron received (which located at the center of the bump). While the activity bump sweeps away from the external input, the center neuron receives less input from the external input, and hence the bump height is smaller. Therefore, not only the position sweeps around the external input, also the populational activity sweeps accordingly at the same frequency.

For the "Nike" check marks: we first clarify that the reason for we observed a forward sweep preceding a backward sweep is that we always force the artificial animal runs from left to right on the track where we treated "right" as "forward". At the beginning of simulation, the external input to the network moves towards right, and therefore the activity bump starts from a position behind the animals and sweeps towards right (forward). In general, this means that the bump will never do a backward sweep first in our model. However, this does not mean that the forward sweeps precede the backward sweeps in each theta cycle. Experimentally, to determine the "0" phase of theta cycles, the LFP signal in CA1 was first bandpass filtered and then Hilbert transformed to get the phase at each time point. Then, a phase histogram of multiunit activity in CA1 was calculated across locomotor periods; the

phase of maximal CA1 firing on the histogram was then defined to be “0” phase. Since we didn’t model LFP oscillation in the attractor model, we cannot obtain a “0” phase reference like the experimental procedure. Instead, we define the “0” phase using the “population activity quenched time”, where phase “0” is defined as the minimum population activity during oscillation cycles, which happens when the activity bump is farthest from the animal position. In this way, we observed a “Nike” pattern where the activity bump begins with a backward sweep towards the external input and then followed up with a forward sweep. This was showed in Fig. 3b in the main text.

*1. I could not find the width of the external input mentioned anywhere in the text or in the table of parameters. The implication is that it is unclear to me whether, during the oscillatory tracking state, the external input is large compared to the size of the bump, so that the bump lives within a window circumscribed by the external input and so bounces off the interior walls of the input during the oscillatory tracking phase, or whether the bump is continuously pulled back and forth by the external input, in which case it could be comparable to the size of the bump. My guess based on Fig 2c is that it is the latter. Please clarify and comment.*

Thank you for your comment. We added the width of the external input to the text and table (see table 1). The bump is continuously pulled back and forth by the external input, as guessed by the reviewer. Experimentally, theta sweeps live roughly in the window of place field size. This is also true in our model, where theta sweep length depends on the strength of recurrent connections which determines the place field size. However, it also depends on the adaptation strength where large adaptation (more intrinsic mobility) leads to large sweep length. We presume that the reason for the reviewer had the guess that the bump may live within a window bounded by the external input is that we also set the width of external input comparable to the place field size (in fact, we don’t know how wide the external location input to the hippocampal circuits is in the biological brain, but it might be reasonable to set the external input width as comparable to the place field size, otherwise the location information conveyed to the hippocampus might be too dispersed). We added a plot in the SI (see Fig. S1) to show that when choosing a smaller external input width, but increasing the adaptation strength, the activity bump lives in a window exceeding the external input.

We clarified this point by adding the following text to line 159

“... It is noteworthy that the activity bump does not live within a window circumscribed by the external input bump (bouncing off the interior walls of the input during the oscillatory tracking state), but instead is continuously pulled back and forth by the external input (see Fig. S1).”

*1. I would argue that the "constant cycling" of theta sweeps down the arms of a T-maze was roughly predicted by Romani & Tsodyks, 2015, Figure 7. While their cycling spans several theta cycles, it nonetheless alternates by a similar mechanism, in that adaptation (in this case synaptic depression) prevents the subsequent sweep of activity from taking the same arm as the previous sweep. I believe the authors should cite this model in this context and consider the fact that both synaptic depression and spike frequency adaptation are both possible mechanisms for this phenomenon. But I certainly give the authors credit for showing how this constant cycling can occur across individual theta cycles.*

Thank you for raising this point. We added the citation of Romani & Tsodyks’ model in the context (line 304). As the reviewer pointed out, STD can also act as a potential mechanism for this phenomenon. We also gave the Romani & Tsodyks’ model credit for showing how this “cycling spanning several theta cycles” can account for the phenomenon of slow (~1Hz) and

deliberative behaviors, namely, head scanning (Johnson and Redish, 2007). We commented this in line 302

“... As the external input approaches the choice point, the network bump starts to sweep onto left and right arms alternatively in successive theta cycles (Fig. 5b and video 4; see also Romani and Tsodyks (2015) for a similar model of cyclical sweeps spanning several theta cycles) ...”

1. *The authors make an unsubstantiated claim in the paragraph beginning with line 413 that the Tsodyks and Romani (2015) model could not account for forwards and backwards sweeps. Both the firing rate adaptation and synaptic depression are symmetry breaking models that should in theory be able to push sweeps of activity in both directions, so it is far from obvious to me that both forward and backward sweeps are not possible in the Tsodyks and Romani model. The authors should either prove that this is the case (with theory or simulation) or excise this statement from the manuscript.*

Thank you for your comment. Our claim about the Tsodyks and Romani (2015) model's inability to account for both forward and backward sweeps was inappropriate. We made this claim based on our own implementation of the Tsodyks and Romani (2015) model and didn't find a parameter region where the bump oscillation shows both forward and backward sweeps. It might be due to the limited parameter range we searched from. Additionally, we also note some difference in these two models, where the Romani & Tsodyks' model has an external theta input to the attractor network which prevent the bump to move further. This termination may also prevent the activity bump to move backward as well. We didn't consider external theta input in our model, and the bump oscillation is based on internal dynamics. We have deleted that claim from line 424 in the revised paper, and revised that portion of the manuscript by adding the following text to line 424:

“...Different from these two models, our model considers firing rate adaptation to implement symmetry breaking and hence generates activity propagation. To prevent the activity bump from spreading away, their model considers an external theta input to reset the bump location at the end of each theta cycle, whereas our model generates an internal oscillatory state, where the activity bump travels back due to the attraction of external location input once it spreads too far away. Moreover, theoretical analysis of our model reveals how the adaptation strength affect the direction of theta sweeps, as well as offers a more detailed understanding of theta cycling in complex environments...”

1. *The section on the speed dependence of theta (starting with line 327) was very hard to understand. Can the authors show a more graphical explanation of the phenomenon? Perhaps a version of Fig 2f for slow and fast speeds, and point out that cells in the latter case fire with higher frequency than in the former?*

Thank you for raising this valuable point. There are two different frequencies showed in Fig. 6 a,c & d. One is the bump oscillation frequency, the other is the firing frequency of single cell. To help understanding, we included experimental results (from Geisler et al, 2007) in Fig. 6a. It showed that when the animal increases its running speed, the LFP theta only increases a bit (compare the blue curve and the green curve), while the single cell firing rate oscillation frequency increases more. In our model, we first demonstrated this result using unimodal cells which have only significant phase precession (Fig. 6c). While the animal runs through the firing field of a place cell, the firing phase will always precess for half a cycle in total. Therefore, faster running speed means that the half cycle will be accomplished faster, and hence single cell oscillation frequency will be higher. We also predicted the results on bimodal cells (Fig. 6d). To make this point clearer, we modified Fig. 6 by including experimental results, and rewrote the paragraph as follows (line 337):

“...As we see from Fig. 3d and Fig. 4a&b, when the animal runs through the firing field of a place cell, its firing rate oscillates, since the activity bump sweeps around the firing field center of the cell. Therefore, the firing frequency of a place cell has a baseline theta frequency, which is the same as the bump oscillation frequency. Furthermore, due to phase precession, there will be a half cycle more than the baseline theta cycles as the animal runs over the firing field, and hence single cell oscillatory frequency will be higher than the baseline theta frequency (Fig. 6c). The faster the animal runs, the faster the extra half cycle is accomplished. Consequently, the firing frequency of single cells will increase more (a steeper slope in Fig. 6c red dots) than the baseline frequency....”

1. I had a hard time understanding how the Zugaro et al., (2005) hippocampal inactivation experiment was accounted for by the model. My intuition is that while the bump position is determined partially by the location of the external input, it is also determined by the immediate history of the bump dynamics as computed via the local dynamics within the hippocampus (recurrent dynamics and spike rate adaptation). So that if the hippocampus is inactivated for an arbitrary length of time, there is nothing to keep track of where the bump should be when the activity comes back online. Can the authors please explain more how the model accounts for this?

Thank you for the comments. The easiest way to understand how the model account for the experimental result from Zugaro et al., (2005) is from Eq. 8:

$$\Phi_f = -\arcsin\left[\frac{d_0 + v_{ext}t_f}{c_0}\right].$$

This equation says that the firing phase of a place cell is determined by the time the animal traveled through the place field, i.e., the location of the animal in the place field (with  $d_0, c_0$  and  $v_{ext}$  all constant, and  $t_f$  the only variable). No matter how long the hippocampus is inactivated (for an arbitrary length of time), once the external input is on, the new phase will continue from the new location of the animal in the place field. In other words, the peak firing phase keeps tracking the location of the animal. To make this point clearer, we modified Fig. 6 by including experimental results from Zugaro et al., (2005), and updated the description from line 356:

“...Based on the theoretical analysis (Eq. 8), we see that the firing phase is determined by the location of the animal in the place field, i.e.,  $v_{ext} t_f$ . This means that the firing phase keeps tracking the animal's physical location. No matter how long the network is inactivated, the new firing phase will only be determined by the new location of the animal in the place field. Therefore, the firing phase in the first bump oscillation cycle after the network perturbation is more advanced than the firing phase in the last bump oscillation cycle right before the perturbation, and the amount of precession is similar to that in the case without perturbation (Fig. 6e) ...”

1. Can the authors comment on why the sweep lengths oscillate in the bottom panel of Fig 5b during starting at time 0.5 seconds before crossing the choice point of the T-maze? Is this oscillation in sweep length another prediction of the model? If so, it should definitely be remarked upon and included in the discussion section.

We appreciate the reviewer's valuable attention of this phenomenon. We thought it was a simulation artifact due to the parameter setting. However, we found that this phenomenon is quite robust to different parameter settings. While we haven't found a theoretical

explanation, we provide a qualitative explanation for it: this length oscillation frequency may be coupled with the time constant of the firing rate adaptation. Specifically, for a longer sweep, the neurons at the end of the sweep are adapted (inhibited), and hence the activity bump cannot travel that long in the next round. Therefore, the sweep length is shorter compared to the previous one. In the next round, the bump will sweep longer again because those neurons have recovered from the previous adaptation effect. We think this length oscillation is quite interesting and will check that in the experimental data in future works. We added this point in the main text as a prediction in line 321:

“...We also note that there is a cyclical effect in the sweep lengths across oscillation cycles before the animal enters the left or right arm (see Fig. 5b lower panel), which may be interesting to check in the experimental data in future work (see Discussion for more details) ...”

And line 466:

“...Our model of the T-maze environment showed an expected phenomenon that as the animal runs towards the decision point, the theta sweep length also shows cyclical patterns (Fig. 5b lower panel). An intuitive explanation is that, due to the slow dynamics in firing rate adaptation (with a large time constant compared to neural firing), a long sweep leads to an adaptation effect on the neurons at the end of the sweep path. Consequently, the activity bump cannot travel as far due to the adaptation effect on those neurons, resulting in a shorter sweep length compared to the previous one. In the next round, the activity bump exhibits a longer sweep again because those neurons have recovered from the previous adaptation effect. We plan to test this phenomenon in future experiments...”

1. *Perhaps I missed this, but I'm curious whether the authors have considered what factors might modulate the adaptation strength. In particular, might rat speed modulate adaptation strength? If so, would have interesting predictions for theta sequences at low vs high speeds.*

Thank you for raising up this important point. As we pointed out in line 279: “...the experimental data (Fernandez et al, 2017) has indicated that there is a laminar difference between unimodal cells and bimodal cells, with bimodal cells correlating more with the firing patterns of deep CA1 neurons and unimodal cells with the firing patterns of superficial CA1 neurons. Our model suggests that this difference may come from the different adaptation strengths in the two layers...”. Our guess is that the adaptation strength might reflect some physiological differences of place cells in different pyramidal layers in the hippocampus. For example, place cells in superficial layer and deep layer receive different amount of input from MEC and sensory cortex, and such difference may contribute to a different effect of adaptation of the two populations of place cells.

Our intuition is that animal's running speed may not directly modulate the adaptation strength. Note that the effect of adaptation and adaptation strength are different. As the animal rapidly runs across the firing field, the place cell experiences a dense firing (in time), therefore the adaptation effect is large; as the animal slowly runs across the field, the place cell experiences sparse firing (in time), and hence the adaptation effect is small. In these two situations, the adaption strength is fixed, but the difference is due to the spike intervals.

From Eq. 45-47, our theoretical analysis shows several predictions of theta sequences regarding to the parameters in the network. For example, how the sweep length varies when the running speed changes in the network. We simulated the network in both low running speed and high running speed (while kept all other parameters fixed), and found that the sweep length at low speed is larger than that at high speed. This is different from previously data, where they showed that the sweep length increases as the animal runs faster (Maurer et



al, 2012). However, we are not sure how other parameters are changed in the biological brain as the animal runs faster, e.g., the external input strength and the place field width might also vary as confounds. We will explore this more in the future and investigate how the adaptation strength is modulated in the brain.

*1. I think the paper has a number of predictions that would be especially interesting to experimentalists but are sort of scattered throughout the manuscript. It would be beneficial to have them listed more prominently in a separate section in the discussion. This should include (1) a prediction that the bump height in the forward direction should be higher than in the backward direction, (2) predictions about bimodal and unimodal cells starting with line 366, (3) prediction of another possible kind of theta cycling, this time in the form of sweep length (see comment above), etc.*

Thank you for pointing this out. We updated the manuscript by including a paragraph in Discussion summarizing the prediction we made throughout the manuscript (from line 459):

“...Our model has several predictions which can be tested in future experiments. For instance, the height of the activity bump in the forward sweep window is higher than that in the backward sweep window (Fig. 4c) due to the asymmetric suppression effect from the adaptation. For bimodal cells, they will have two peaks in their firing frequency as the animal runs across the firing fields, with one corresponding to phase precession and the other corresponding to phase procession. Similar to unimodal cells, both the phase precession and procession of a bimodal cell after transient intrahippocampal perturbation will continue from the new location of the animal (Fig. S5). Interestingly, our model of the T-maze environment showed an expected phenomenon that as the animal runs towards the decision point, the theta sweep length also shows cyclical patterns (Fig. 5b lower panel). An intuitive explanation is that, due to the slow dynamics in firing rate adaptation (with a large time constant compared to neural firing), a long sweep leads to an adaptation effect on the neurons at the end of the sweep path. Consequently, the activity bump cannot travel as far due to the adaptation effect on those neurons, resulting in a shorter sweep length compared to the previous one. In the next round, the activity bump exhibits a longer sweep again because those neurons have recovered from the previous adaptation effect. We plan to test this phenomenon in future experiments...”

#### **Reviewer #2:**

*In this work, the authors elaborate on an analytically tractable, continuous-attractor model to study an idealized neural network with realistic spiking phase precession/procession. The key ingredient of this analysis is the inclusion of a mechanism for slow firing-rate adaptation in addition to the otherwise fast continuous-attractor dynamics. The latter which continuous-attractor dynamics classically arises from a combination of translation invariance and nonlinear rate normalization. For strong adaptation/weak external input, the network naturally exhibits an internally generated, travelling-wave dynamics along the attractor with some characteristic speed. For small adaptation/strong external stimulus, the network recovers the classical externally driven continuous-attractor dynamics. Crucially, when both adaptation and external input are moderate, there is a competition with the internally generated and externally generated mechanism leading to oscillatory tracking regime. In this tracking regime, the population firing profile oscillates around the neural field tracking the position of the stimulus. The authors demonstrate by a combination of analytical and computational arguments that oscillatory tracking corresponds to realistic phase precession/procession. In particular the authors can account for the emergence of a unimodal and bimodal cells, as well as some other experimental observations with respect the dependence of phase precession/procession on the animal's locomotion. The strengths of this work are*

*at least three-fold: 1) Given its simplicity, the proposed model has a surprisingly large explanatory power of the various experimental observations. 2) The mechanism responsible for the emergence of precession/procession can be understood as a simple yet rather illuminating competition between internally driven and externally driven dynamical trends. 3) Amazingly, and under some adequate simplifying assumptions, a great deal of analysis can be treated exactly, which allows for a detailed understanding of all parametric dependencies. This exact treatment culminates with a full characterization of the phase space of the network dynamics, as well as the computation of various quantities of interest, including characteristic speeds and oscillating frequencies.*

*1. As mentioned by the authors themselves, the main limitation of this work is that it deals with a very idealized model and it remains to see how the proposed dynamical behaviors would persist in more realistic models. For example, the model is based on a continuous attractor model that assumes perfect translation-invariance of the network connectivity pattern. Would the oscillating tracking behavior persist in the presence of connection heterogeneities?*

Thank you for raising up this important point. Continuous attractor models have been widely used in modeling hippocampal neural circuits (see McNaughton et al, 2006 for a review), and researchers often assumed that there is a translation-invariance structure in these network models. The theta sweep state we presented in the current work is based on the property of the continuous attractor state. We do agree with the reviewer that the place cell circuit might not be a perfect continuous attractor network. For a simpler case where the connection weights are sampled from a Gaussian distribution around  $J_0$ , the theta sweep state still exhibit in the network (see Fig. S8 for an example). We also believe that the model can be extended to more complex cases where there exist over-representations of the “home” location and decision points in the real environment, i.e., the heterogeneity is not random, but has stronger connections near those locations, then the theta sweeps will be more biased to those location. However, if the heterogeneity breaks the continuous attractor state, the theta sweep state may not be presented in the network.

*1. Can the oscillating tracking behavior be observed in purely spiking models as opposed to rate models as considered in this work?*

Thank you for pointing this out. The short answer is yes. If the translation-invariance of the network connectivity pattern hold in the network, i.e., the spiking network is still a continuous attractor network (see the work from Tsodyks et al, 1996; and from Yu et al. "Spiking continuous attractor neural networks with spike frequency adaptation for anticipative tracking"), then the adaptation, which has the mathematical form of spike frequency adaptation (instead of firing rate adaptation), will still generate sweep state of the activity bump. We here chose the rate-based model because it is analytically tractable, which gives us a better understanding of the underlying dynamics. Many of the continuous attractor model related to spatial tuning cell populations are rate-based (see examples Zhang 1996; Burak & Fiete 2009). However, extending to spike-based model would be straightforward.

*1. Another important limitation is that the system needs to be tuned to exhibit oscillation within the theta range and that this tuning involves a priori variable parameters such as the external input strength. Is the oscillating-tracking behavior overtly sensitive to input strength variations?*

Thank you for pointing this out. In rodent studies, theta sequences are thought to result from the integration of both external inputs conveying sensory-motor information, and intrinsic

network dynamics possibly related to memory processes (see Drieu and Zugaro 2019; Drieu et al, 2018). We clarified here that, in our modeling work, the generation of theta sweeps also depends on both the external input and the intrinsic dynamics (induced by the firing rate adaptation). Therefore, we don't think the dependence of theta sweeps on the prior parameter – the external input strength – is a limitation here. We agreed with the reviewer that the system needs to be tuned to exhibit oscillation within the theta range. However, the parameter range of inducing oscillatory state is relatively large (see Fig. 2g in the main text). It will be interesting to investigate (and find experimental evidence) how the biological system adjusts the network configuration to implement the sweep state in network dynamics.

1. *The author mentioned that an external pacemaker can serve to drive oscillation within the desired theta band but there is no evidence presented supporting this.*

Thank you for pointing this out. We made this argument based on our initial simulation before but didn't go into the details of that. We have deleted that argument in the discussion and rewrote that part. We will carry out more simulations in the future to verify if this is true. See our changes from line 418 to line 431:

“... A representative model relying on neuronal recurrent interactions is the activation spreading model. This model produces phase precession via the propagation of neural activity along the movement direction, which relies on asymmetric synaptic connections. A later version of this model considers short-term synaptic plasticity (short-term depression) to implicitly implement asymmetric connections between place cells, and reproduces many other interesting phenomena, such as phase precession in different environments. Different from these two models, our model considers firing rate adaptation to implement symmetry breaking and hence generates activity propagation. To prevent the activity bump from spreading away, their model considers an external theta input to reset the bump location at the end of each theta cycle, whereas our model generates an internal oscillatory state, where the activity bump travels back due to the attraction of external location input once it spreads too far away. Moreover, theoretical analysis of our model reveals how the adaptation strength affect the direction of theta sweeps, as well as offers a more detailed understanding of theta cycling in complex environments...”

1. *A final and perhaps secondary limitation has to do with the choice of parameter, namely the time constant of neural firing which is chosen around 3ms. This seems rather short given that the fast time scale of rate models (excluding synaptic processes) is usually given by the membrane time constant, which is typically about 15ms. I suspect this latter point can easily be addressed.*

Thank you for pointing this out. The time constant we currently chose is relatively short as used in other studies. We conducted additional simulation by adjusting the time constant to 10ms, and the results reported in this paper remain consistent. Please refer to Fig S9 for the results obtained with a time constant of 10 ms.

### **Reviewer #3:**

*With a soft-spoken, matter-of-fact attitude and almost unwittingly, this brilliant study chisels away one of the pillars of hippocampal neuroscience: the special role(s) ascribed to theta oscillations. These oscillations are salient during specific behaviors in rodents but are often taken to be part of the intimate endowment of the hippocampus across all mammalian species, and to be a fundamental ingredient of its computations. The gradual anticipation or precession of the spikes of a cell as it traverses its place field, relative to the theta phase, is seen as enabling the prediction of the future - the short-term future position of the animal at least, possibly the future in a wider cognitive sense*

as well, in particular with humans. The present study shows that, under suitable conditions, place cell population activity "sweeps" to encode future positions, and sometimes past ones as well, even in the absence of theta, as a result of the interplay between firing rate adaptation and precise place coding in the afferent inputs, which tracks the real position of the animal. The core strength of the paper is the clarity afforded by the simple, elegant model. It allows the derivation (in a certain limit) of an analytical formula for the frequency of the sweeps, as a function of the various model parameters, such as the time constants for neuronal integration and for firing rate adaptation. The sweep frequency turns out to be inversely proportional to their geometric average. The authors note that, if theta oscillations are added to the model, they can entrain the sweeps, which thus may superficially appear to have been generated by the oscillations.

1. The main weakness of the study is the other side of the simplicity coin. In its simple and neat formulation, the model envisages stereotyped single unit behavior regulated by a few parameters, like the two time constants above, or the "adaptation strength", the "width of the field" or the "input strength", which are all assumed to be constant across cells. In reality, not only assigning homogeneous values to those parameters seems implausible, but also describing e.g. adaptation with the simple equation included in the model may be an oversimplification. Therefore, it remains important to understand to what extent the mechanism envisaged in the model is robust to variability in the parameters or to eg less carefully tuned afferent inputs.

Thank you for pointing out this important question. As the reviewer pointed out, there is an oversimplification in our model compared to the real hippocampal circuits (also see Q1 and Q3 from reviewer2). We also pointed out that in the main text line 504:

"...Nevertheless, it is important to note that the CANN we adopt in the current study is an idealized model for the place cell population, where many biological details are missed. For instance, we have assumed that neuronal synaptic connections are translation-invariant in the space..."

To investigate model robustness to parameter setting, we divided all the parameters into two groups. The first group of parameters determines the bump state, i.e., width of the field  $a$ , neuronal density  $\rho$ , global inhibition strength  $k$ , and connection strength  $J_0$ . The second group of parameters determines the bump sweep state (which based on the existence of the bump state), i.e., the input strength  $\alpha$  and the adaptation strength  $m$ . For the first group of parameters, we refer the reviewer to the Method part: stability analysis of the bump state. This analysis tells us the condition when the continuous attractor state holds in the network (see Eq. 20, which guides us to perform parameter selection). For the second group of parameters, we refer the reviewer to Fig. 2g, which tells us when the bump sweep state occurs regarding to input strength and adaptation strength. When the input strength is small, the range of adaptation strength is also small (to get the bump sweep state). However, as the input strength increases, we can see from Fig. 2g that the range of adaptation strength (to get the bump sweep state) also linearly increases. Although there exists other two state in the network when the two parameters are set out of the colored area in Fig. 2g, the parameter range of getting sweep state is also large, especially when the input strength value is large, which is usually the case when the animal actively runs in the environment.

To demonstrate how the variability affect the results, we added variability to the connection weights by sampling the connection weights from a Gaussian distribution around  $J_0$  (this introduces heterogeneity in the connection structure). We found that the bump sweep state still holds in this condition (see Fig. S8 as well as Q1 from reviewer2). For the variability in other parameter values, the results will be similar. Although adding variability to these

parameters will not bring us difficulty in numerical simulation, it will make the theoretical analysis much more difficult.

*1. The weak adaptation regime, when firing rate adaptation effectively moves the position encoded by population activity slightly ahead of the animal, is not novel - I discussed it, among others, in trying to understand the significance of the CA3-CA1 differentiation (2004). What is novel here, as far as I know, is the strong adaptation regime, when the adaptation strength  $m$  is at least larger than the ratio of time constants. Then population activity literally runs away, ahead of the animal, and oscillations set in, independent of any oscillatory inputs. Can this really occur in physiological conditions? A careful comparison with available experimental measures would greatly strengthen the significance of this study.*

Thank you for raising up this interesting question.

Re: "...firing rate adaptation effectively moves the position encoded by population activity slightly ahead of the animal, is not novel...", We added Treves, A (2004) as a citation when we introduce the firing rate adaptation in line 116

To test if the case of "...the adaptation strength  $m$  is at least larger than the ratio of time constants..." could occur in physiological conditions, it requires a measure of the adaptation strength as well as the time constant of both neuron firing and adaptation effect. The most straightforward way would be in vivo patch clamp recording of hippocampal pyramidal neurons when the animal is navigating an environment. This will give us a direct measure of all these values. However, we don't have these data to verify this hypothesis yet. Another possible way of measure these values is through a state-space model. Specifically, we can build a state space model (considering adaptation effect in spike release) by taking animal's position as latent dynamics, and recorded spikes as observation, then infer the parameters such as adaptation strength and time constant in the slow dynamics. Previous work of state-space models (without firing rate adaptation) in analyzing theta sweeps and replay dynamics have been explored by Denovellis et al. (2021), as well as Krause and Drugowitsch (2022). We think it might be doable to infer the adaptation strength and adaptation time constant in a similar paradigm in future work. We thank the reviewer for pointing out that and hope our replies have clarified the concerns of the reviewer.