



Mohamed Helmy <mmhelmy@gmail.com>

Concerning Yuan et al 2025

Mohamed Helmy <mmhelmy@gmail.com>

Tue, Dec 16, 2025 at 6:46 AM

To: Nature Communications <naturecommunications@nature.com>, "jleutgeb@ucsd.edu" <jleutgeb@ucsd.edu>, sleutgeb@ucsd.edu, naturecommunicationsproduction@springernature.com, zhongmin.lu@springernature.com, n.lebot@nature.com

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Dear Colleagues

This concerns the article:

Li Yuan, Jose F. Figueroa, Ameen Khan, Gautam Narayan, Jill K. Leutgeb, and Stefan Leutgeb. Time cell sequences during delay intervals are not dependent on brain state and do not support hippocampus-dependent working memory. *Nat Commun* **16**, 7470 (2025). doi.org/10.1038/s41467-025-62498-z.

Please scroll down for past correspondence relating to this matter.

Briefly, the methods used may not produce the results published, nor support the purported proof which appears to raise questions concerning the seminal works by Professors O'Keefe, Moser, and Moser, and for which they received a Nobel prize.

The editor, Dr. Lu, "...glanced through those technical questions (not essentially concerns) about methods of this paper..." and duly recommended "...The reader...to seek answers from Methods section, Results section and the transparent review file we published along with the paper...". She also "...checked those aforementioned contents online and they are accessible...".

I do not know the difference between 'technical questions, essentially concerns, and methods and results' with regards to scientific publications.

The methodical failure of the results, essentially concerns with the technical implications of the paper, have been transparently published on www.nanyangscandal.com. Please click on *Academic Corruption* followed by Theta Pop. Possible relation between Dr. Lu and the Leutgeb Labs, and what appears to be nonsensical material underpinning the mathematical construct of the technique underpinning Dr. Lu's doctoral thesis, are also explored.

Kind regards,
Mohamed Helmy
MD, PhD

www.nanyangscandal.com

On Thu, Dec 11, 2025 at 6:08 AM Nature Communications <naturecommunications@nature.com> wrote:

Dear Dr Helmy,

Hope this email finds you well.

We have received responses from the editor.

Regarding your concerns, it is recommended by the editor that you can seek answers from Methods

section, Results section and the transparent review file we published along with the paper. Please check them in the online materials firstly. Hope this helps.

Kind regards,
Abby

Abby Bian
Senior Editorial Assistant, *Nature Communications*
Springer Nature

From: Zhongmin Lu <zhongmin.lu@springernature.com>
Sent: Wednesday, December 10, 2025 9:45 AM
To: Nature Communications <naturecommunications@nature.com>
Subject: RE: Concerning Yuan et al 2025

Hi, Abby,

Thank you for passing this along.

I glanced through those technical questions (not essentially concerns) about methods of this paper.

The reader, Dr Mohamed Helmy, should be able to seek answers from Methods section, Results section and the transparent review file we published along with the paper.

I have checked those aforementioned contents online and they are accessible.

So please go ahead and advise this reader to check these online materials firstly.

Best,
Zhongmin

From: Mohamed Helmy <mmhelmy@gmail.com>
Sent: Saturday, December 6, 2025 7:52 PM
To: jleutgeb@ucsd.edu <jleutgeb@ucsd.edu>; sleutgeb@ucsd.edu <sleutgeb@ucsd.edu>; Nature Communications <naturecommunications@nature.com>; NatureCommunicationsProduction <naturecommunicationsproduction@springernature.com>
Cc: j.okeefe@ucl.ac.uk <j.okeefe@ucl.ac.uk>; may-britt.moser@ntnu.no <may-britt.moser@ntnu.no>; edvard.moser@ntnu.no <edvard.moser@ntnu.no>; Jozsef.Csicsvari@ist.ac.at <Jozsef.Csicsvari@ist.ac.at>
Subject: Concerning Yuan et al 2025

Dear Colleagues

This concerns the article:

Li Yuan, Jose F. Figueroa, Ameen Khan, Gautam Narayan, Jill K. Leutgeb, and Stefan Leutgeb. Time cell sequences during delay intervals are not dependent on brain state and do not support hippocampus-dependent working memory. *Nat Commun* **16**, 7470 (2025). doi.org/10.1038/s41467-025-62498-z

[1] It is difficult to discern between the "...hyperdrive..." and "...neuropixels..." populations, listed by the authors in **Figure S8**:

(a) The "...Average # retraining days after surgery..." is quoted for both groups *hyperdrive* and *neuropixels* under the Figure S8 tab and shown in Figure S8(c). On average, the *hyperdrive* group required about 10 days to be trained, while the *neuropixels* group was trained in about 3 days. Was this significant difference justified?

(b) The article states that "...Anesthesia was induced with isoflurane (2–3% mixture in oxygen, 1 L/min), and buprenorphine (1 mg/kg) was administrated as an analgesic..." [*sic*] for surgery of the *hyperdrive* group. How was anesthesia maintained?

[2] The authors state "...Neuropixels 1.0 probes (IMEC)..." and reference Jun et al. (2017) "...were chronically implanted in eleven pretrained rats with combined treadmill-on and off training by following the same general surgical procedures as for hyperdrive implants. The use of a metal drive and protection case for the Neuropixels implants was adopted from the design described in a previous study..." and reference Vöröslakos *et al.* (2021). The former had authors who were at that time working at [imec](#) while the latter appears to not have a relation to imec. The latter is a methods paper with many methods. What is the relation of the N/neuropixels used in this article with imec or IMEC if any?

[3] The authors state: "...The action potential (AP) band signals were recorded with a gain of 500 and a sampling frequency of 30,000 Hz, while the LFP band signals of matching AP channels were recorded with a gain of 250 and a sampling frequency of 2,500 Hz...". Was there no gain for the signals measured using *hyperdrive*?

[4] The authors state: "...Population activity and SWRs...During trials in the alternation task, rats remained stationary in the reward areas for short periods, and in treadmill-off trials, in the delay area. SWRs and bursts with co-active cells were observed during these recording segments. SWRs were identified using LFP recordings from a channel confirmed to be in the hippocampal CA1 layer based on histological verification. The signal was bandpass filtered between 150 and 250 Hz. SWR events were defined as periods when the filtered signal power exceeded three standard deviations above the mean for at least 50 ms. To further analyze the temporal activation pattern of principal neurons in the delay and reward areas, we selected recording sessions with at least 20 recorded principal cells and identified population events. A population event was defined as a 200 ms time bin when >1/5 of all neurons became active, but with neurons only included in the count if they were silent during the preceding 100 ms window (spike count ≤ 1). We reasoned that a criterion that directly selects brief periods of heightened neuronal activity, as otherwise also characteristic for SWRs, is best suited to analyze neuronal activity patterns. The population event onset was the first spike time of any of the neurons that were active in the event. If at least 20 population events were detected in the delay or reward area, the recording session was included for further analysis of population activity. In total, 12 recording sessions from 4 of the 5 rats met the analysis threshold..."

I am finding it difficult to reconcile these data with those mentioned in relation to *hyperdrive*. Were all signals bandpass filtered between 150 and 250 Hz? Are population events equivalent to LFP - this cannot be the case because for some reason only one of four channels were used to measure LFP with *hyperdrive* despite LFP appearing to be the signal of interest.

[5] The authors state: "...We trained 6–10 weeks old rats to collect chocolate sprinkles at

two corners of the figure-eight maze (i.e., the reward locations) with food only available at the reward location if the rats chose the opposite turn compared to the previous trial..." [sic]. Is this testing place, or is it testing memory? i.e. reward condition, rather than "...reward area...reward areas...reward location...reward locations...reward zone....delay area...delay zone...delay condition..." mentioned by the authors, and/or a "...delay zones..." referenced by the authors. In any case, I believe the diagrams mentioning reward and/or delay should indicate that absence of reward is possible. For accuracy as well as clarity.

[6] If I understand the title of the article more or less correctly, and if time is not completely dissociated from space, then the article in question raises questions concerning the works of Professors O'Keefe, and Moser & Moser, and for which a Nobel prize was awarded (2014). Since the publisher will not tell who the other reviewer(s) was/were with Professor Jozsef Csicsvari, I have cc-ed our colleagues here for their input if any. It would be interesting to view the related peer review file available.

[7] The authors specifically stated that: "...The reference was connected to the ground using a silver wire (AGW1010, World Precision Instruments) attached to a ground screw implanted above the cortex...". What is the justification for using bare silver wire when coated wire is available from the same provider? Of what material was the "...ground screw..." made? If it was not silver....then? If it was silver then from where was it sourced? In addition, why was (at least the tip of) the uncoated silver wire not chlorided prior to surgery? Of course, the part in contact with body fluid will eventually chloride, if patchily in space and over an unknown period of time. Any attempt to record theta waves before the tip of the uncoated silver wire gains a AgCl coating is difficult to imagine ("...ground screw..." to one side for the moment). Because the signal will be, from a DC perspective, all over the place. And no amount of filtering, fiddling with the gain, so on, can do anything about it.

Kind regards
Mohamed Helmy
MD, PhD

www.nanyangscandal.com

REFERENCES IN ORDER OF APPEARANCE

Li Yuan, Jose F. Figueroa, Ameen Khan, Gautam Narayan, Jill K. Leutgeb, and Stefan Leutgeb. Time cell sequences during delay intervals are not dependent on brain state and do not support hippocampus-dependent working memory. *Nat Commun* **16**, 7470 (2025). doi.org/10.1038/s41467-025-62498-z

James J. Jun, Nicholas A. Steinmetz, Joshua H. Siegle, Daniel J. Denman, Marius Bauza, Brian Barbarits, Albert K. Lee, Costas A. Anastassiou, Alexandru Andrei, Çağatay Aydın, Mladen Barbic, Timothy J. Blanche, Vincent Bonin, João Couto, Barundeb Dutta, Sergey L. Gratiy, Diego A. Gutnisky, Michael Häusser, Bill Karsh, Peter Ledochowitsch, Carolina Mora Lopez, Catalin Mitelut, Silke Musa, Michael Okun, Marius Pachitariu, Jan Putzeys, P. Dylan Rich, Cyrille Rossant, Wei-lung Sun, Karel Svoboda, Matteo Carandini, Kenneth D. Harris, Christof Koch, John O'Keefe, and Timothy D. Harris. Fully integrated silicon probes for high-density recording of neural activity. *Nature* **551**, 232–236 (2017). doi.org/10.1038/nature24636

Mihály Vöröslakos, Peter C Petersen, Balázs Vöröslakos, and György Buzsáki. Metal microdrive and head cap system for silicon probe recovery in freely moving rodent. *Elife* (2021) 10.7554/eLife.65859.