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Data Article

Validation of memory assessment in the Starmaze task: Data from 14 month-old APPPS1 mice and controls

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ABSTRACT

This article describes navigation data of 14 month-old APPPS1 and C57Bl6 in the Starmaze task. These data were acquired as positive controls of memory deficit in a model of the familial form of Alzheimers's disease (see Schmitt et al., Flexibility as a marker of early cognitive decline in humanized Apolipoprotein E $\varepsilon 4$ (ApoE4) mice, Neurobiol Aging, 2021). They were acquired in a reduced version of the Starmaze environment and accompanied by a number of acquisitions in different control groups at 6 and 14 months to assess the robustness of the procedure and its associated memory scores. These data illustrate the extraction of a variety of navigation scores (including search strategy, spatial learning and memory) and provide a reference of navigation data in the Starmaze task for healthy 6-month-old controls, normal aging and a model of pathological memory deficit.

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Specifications Table

Subject	Neuroscience: Behavioral
Specific subject area	Behavioral assessment of memory using a navigation task as a behavioral assessment of memory
Type of data	Table Figure Excel Spreadsheet Text file (raw trajectories)
How data were acquired	Mice trajectories in the Starmaze (Rondi-Reig et al., 2005) were tracked and recorded using SMART 2.5 (Bioseb) software. X and Y coordinates were processed with our own developed software, NAT (Navigation Analysis Tool (Jarlier et al., 2013)), to compute the assessment scores presented here.
Data format	Raw Analyzed
Parameters for data collection	A white noise of 50 dB was broadcast via 4 loudspeakers. The brightness of the room was between 90 and 100 lux. The maze is surrounded by black curtains arranged in square, on which 2D and 3D visual cues are attached.
Description of data collection	X and Y trajectory coordinates recorded every 0.04 s during a navigation task.
Data source location	Institution: IBPS City/Town/Region: Paris Country: France Latitude and longitude (and GPS coordinates, if possible) for collected samples/data: 48.847, 2.359
Data accessibility	With the article (spreadsheets) Repository name: Mendeley Data Data identification number: doi: 10.17632/ggdyxxynj8.1 Direct URL to data: https://data.mendeley.com/datasets/ggdyxxynj8/1 (preview)
Related research article	J. Schmitt, A.-L. Paradis, M. Boucher, L. Andrieu, P. Barnéoud, L. Rondi-Reig. Flexibility as a marker of early cognitive decline in humanized Apolipoprotein E ε4 (ApoE4) mice. Neurobiol Aging. 2021. https://doi.org/10.1016/j.neurobiolaging.2021.01.013

Value of the Data

- These data highlight robust navigation scores that evaluate spatial and sequence aspects of episodic-like memory and validate the ability of the Starmaze task to detect a deficit of this memory in APPPS1 mice, a model of the familial form of Alzheimer's disease.
- These data can be useful to labs or companies needing a behavioral paradigm to assess spatial and sequence memory in transgenic mice models and/or mice treated with pharmacological agents targeting memory.
- These data may be used as reference when assessing spatial and sequence memory in mice during normal or pathological aging.

1. Data Description

To first ensure the robustness of the scores used to evaluate memory from the Starmaze task, we tested if their values were stable (i.e., did not significantly differ) across different batches of control mice at 6 or 14 months (see data files 'Robustness_6months.xslx' and

'Robustness_14months.xlsx' respectively, in Navigation and Memory Scores). We thus compared a C57BL/6 ($N = 15$, 'manip 8') and two ApoE3 batches ($N = 14$, 'manip 9' and $N = 15$, 'manip 7') at 6 months, as well as two batches of C57/BL6 ($N = 15$, 'manip 8' and $N = 12$, 'manip 4') at 14 months. The data for each score are reported on separate sheets named according to the score (Travelled distance, Localization Score, repeated sequence score, Recall sequence score and Number of dead ends revisits). Each sheet consists of 10 columns detailing the identification code of the mice, their group and their individual scores at each experimental session (8 in total). Note that the repeated sequence score is only available from session 4, and that the recall sequence score is computed between consecutive sessions (Sn/Sn+1).

Additional raw scores ('Time', 'Number of visited alleys', 'Direct Path Score', '% correct 1st turn' and '% of direct path') are provided for the sake of completeness but were not further analyzed in the following because they were considered less informative and globally redundant with the other ones. In particular, the time and number of visited alleys relate to distance, and the orientation choice at the first intersection, which determines the percentage of correct first turns by session, also contributes to the localization score, just as the direct path score and the associated percentage of direct path can be considered special cases of the localization score as well.

We also eliminated the recall sequence score from further analysis because of a significant difference between the two C57BL/6 groups at 14 months (Genotype effect: $F(1, 53.9) = 5.04$, $p = 0.0289$, two-way ANOVA-type). The four other analyzed parameters were considered as robust (Table 1).

These four scores were then compared between 14-month-old APPPS1 mice ($N = 10$) and 14-month-old C57BL/6 control mice ($N = 12$) to evaluate the ability of a reduced configuration of the Starmaze to detect memory deficits (see data file 'Starmaze_APPPPS1_14months.xlsx', in Navigation and Memory Scores). Data for each score are reported in separate sheets organized in columns. The first two columns provide the identification code and group of the mice. The 40 following columns report their individual score at each experimental trial (5 trials per session multiplied by 8 days). We observed consistent impairments of the APPPS1 on the 4 parameters (Fig. 1). For each parameter (travelled distance -TD-, localization score -LS-, repeated sequence score -RSS- and dead end revisit number -DERN-), there was a genotype effect (TD: $F(1, 20) = 20.05$, $p = 0.0002$; LS: $F(1, 33) = 14.03$, $p = 0.0013$; RSS: $F(1, 25) = 14.71$, $p = 0.008$; DERN: $F(1, 31.3) = 12.40$, $p = 0.0013$). All parameters but the repeated sequence score also showed a session effect (TD: $F(7, 140) = 22.76$, $p < 0.0001$, two-way ANOVA;

Table 1
Robustness assessment for the different Starmaze scores.
Comparisons across control groups were performed separately at 6 months (3 batches: 2 ApoE3, n = 14 and n = 15, and 1 C57BL/6, n = 15) and 14 months (2 batches of C57BL/6, n = 15 and n = 12) using a two-way ANOVA with factors Group and Session. Italic font highlights a score that significantly varies across the 14-month-old batches for the Group factor, and is therefore considered as a non-robust parameter. *Bold: p-value<0.05.

Starmaze Parameters	Cognitive function	Age (months)	Statistical model	Group factor *F* value	Group effect *P* value
Travelled distance (cm)	Learning of the task	6 14	Two-way ANOVA	$F(2, 41) = 0.77$ $F(1, 25) = 0.33$	0.4718 0.5724
Repeated sequence score	Sequence memory inside sessions	6 14	Two-way ANOVA-TYPE	$F(2, 52.3) = 0.49$ $F(1, 32.9) = 0.00$	0.6178 0.9938
Recall sequence score	*Sequence memory between sessions*	*6* *14*		*F(2, 80.8) = 0.57* *F(1, 53.9) = 5.04*	*0.5678* ***0.0289****
Number of revisits in dead ends	Working memory	6 14		$F(2, 88.3) = 0.82$ $F(1, 49.7) = 2.22$	0.4440 0.1425
Localization score	Spatial memory	6 14		$F(2, 52.4) = 0.47$ $F(1,49.2) = 0.29$	0.6245 0.5934

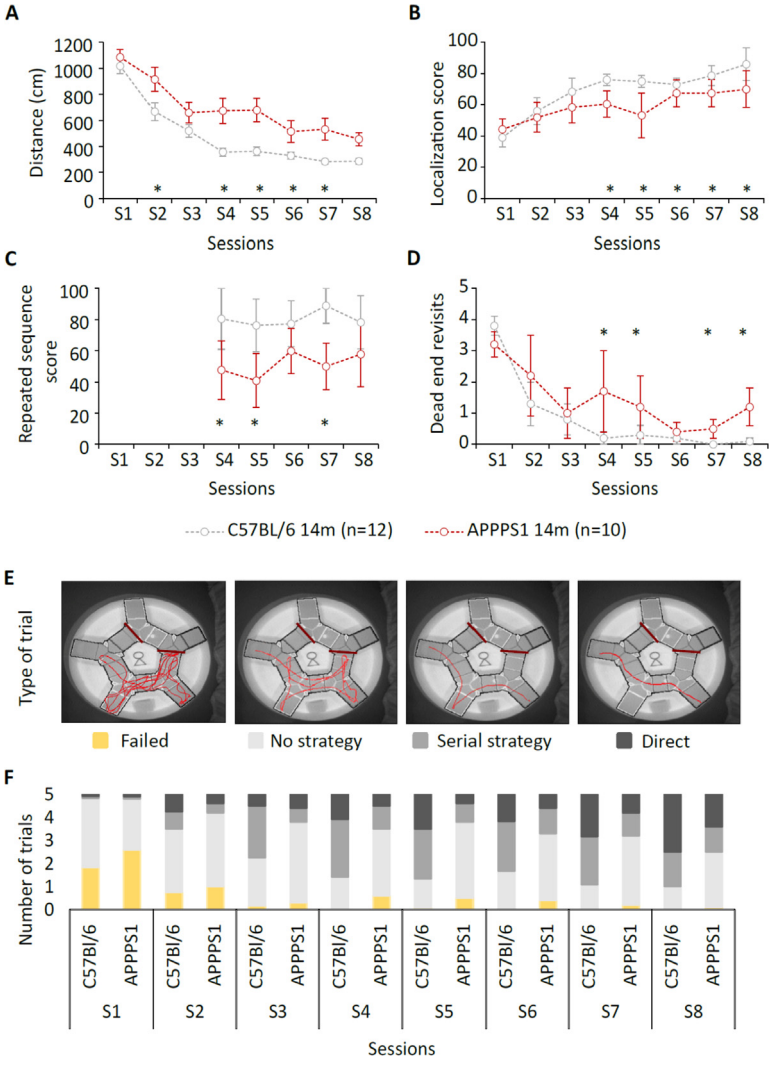

Fig. 1. The Starmaze reveals memory deficits in 14 months APPPS1 mice.
Comparison of APPPS1 (N=10) and C57Bl6 (N=12) behavior at 14 months in the Starmaze. A: Travelled distance. Data are represented as mean +/sem. B: Localization score. Data are represented as median +/mad (median absolute deviation). C: Repeated sequence score. Data are represented as median +/mad. D: Dead end revisit number. Data are represented as median +/mad. E: Examples of trials illustrating search strategies. Failed: the mouse does not reach the platform in the allotted time. Direct: efficient sequence of turns to the goal with no dead-end visit. Serial strategy: visit of the dead-end between the start and the goal. No strategy: all other situations. Dark red lines show the blocking walls added to reduce the Starmaze. F: Distribution of trial types by session and genotype. *: Genotype effect $p < 0.05$, Post hoc analysis with Student's t- test performed after a two-way ANOVA for distance or with Fisher's test performed after two-way ANOVA-type for other parameters in a specific session (Table 2).

LS: $F(5.14, 154) = 19.61$, $p < 0.0001$; DERN: $F(4.82, 148) = 18.70$, $p < 0.001$ but RSS: $F(3.22, 97.7) = 0.85$, $p = 0.4745$) and an interaction effect was found for the localization score ($F(5.14, 154) = 2.16$, $p = 0.0537$). Post-hoc tests for each session showed that APPPS1 were impaired in particular in session S2 and in sessions S4 to S7 for the travelled distance, in sessions S4 to S8 for the localization score, in sessions S4, S5 and S7 for the repeated sequence score, and in sessions S4, S5, S7 and S8 for the dead end revisit number (Table 2).

Table 2
Comparison of 14-month-old APPPS1 ($N = 10$) and C57BL/6 ($N = 12$) mice in the Starmaze.
Top: Effects of factors Genotype, Session (repeated) and their interaction on each parameter of the Starmaze, and on the distance travelled in the cued version of the Morris water maze. Bottom: Post-hoc analyses comparing 14-month-old APPPS1 and C57BL/6 mice at each session in all above parameters. The repeated sequence score was computed only from session S4. A two-way ANOVA analysis was followed by Student's T-tests and a two-way ANOVA-type analysis was followed by Fisher's tests. Failed, Direct and Serial refer to the search strategies used by the mice to reach the platform. The results of the cued morris water maze are provided to ensure that the learning deficits of the APPPS1 in the Starmaze are not due to visuo-motor deficits compared to C57bl6. Bold: p-value<0.05 for main effects, $p<0.1$ for interaction.

Statistical model	Parameters	Factor	*F* value	*p*-value
Two-way ANOVA	Travelled distance	Genotype	$F(1, 20) = 20.05$	**0.0002**
		Session	$F(7, 140) = 22.76$	**< 0.0001**
		Genotype*Session	$F(7, 140) = 1.73$	0.1067
Two-way ANOVA-type	Localization score	Genotype	$F(1, 33) = 14.03$	**0.0013**
		Session	$F(5.14, 154) = 19.61$	**< 0.0001**
		Genotype*Session	$F(5.14, 154) = 2.16$	**0.0537**
	Repeated sequence score	Genotype	$F(1, 25) = 14.71$	**0.0008**
		Session	$F(3.22, 97.7) = 0.85$	0.4745
		Genotype*Session	$F(3.22, 97.7) = 0.76$	0.5255
	Dead end revisit number	Genotype	$F(1, 31.3) = 12.40$	**0.0013**
		Session	$F(4.82, 148) = 18.70$	**<0.0001**
		Genotype*Session	$F(4.82, 148) = 1.75$	0.122
Two-way binomial GLMM	Direct strategy	Genotype	$F(1, 20) = 0.87$	0.3524
		Session	$F(7, 140) = 7.82$	**<0.0001**
		Genotype*Session	$F(7, 140) = 1.12$	0.3552
	Serial strategy	Genotype	$F(1, 20) = 2.62$	0.1076
		Session	$F(7, 140) = 6.3$	**<0.0001**
		Genotype*Session	$F(7, 20) = 1.28$	0.2633
	No Strategy	Genotype	$F(1, 140) = 14.51$	**0.0002**
		Session	$F(7, 140) = 3.32$	**0.0026**
		Genotype*Session	$F(7, 140) = 4.01$	**0.0005**

(*continued on next page*)

Table 2 (*continued*)

Statistical model	Parameters	Factor	*F* value	*p*-value
Two-way ANOVA	Distance to cued platform in Morris water maze	Genotype	$F(1, 20) = 0.155$	0.6978
		Session	$F(7, 140) = 2.033$	0.055
		Genotype*Session	$F(7, 140) = 0.292$	0.9563

	Session by session analyses (*p*-values)							
Score\Session	S1	S2	S3	S4	S5	S6	S7	S8
Travelled distance	0.4334	**0.0047**	0.1062	**0.0003**	**0.0003**	**0.0323**	**0.0045**	0.0506
Localization score	0.8463	0.2243	0.3098	**0.0004**	**0.001**	**0.0477**	**0.0012**	**0.0133**
Repeated sequence score	–	–	–	**0.0047**	**0.0005**	0.0582	**0.004**	0.0745
Dead end revisit number	0.8493	0.0695	0.2266	**0.0027**	**0.0157**	0.0668	**0.0014**	**0.002**
Direct strategy	0.6766	0.6194	0.4699	0.3659	0.0586	0.4174	0.1224	0.1082
Serial strategy	0.9196	0.3421	**0.0135**	**0.0421**	**0.0486**	0.1536	0.1348	0.5828
No Strategy	0.1392	0.3896	**0.0095**	**0.007**	**0.0003**	**0.0251**	**0.0005**	**0.0076**
Distance to cued platform	0.6884	0.572	0.191	0.72	0.6228	0.0956	0.6272	0.2758

We further analyzed the trajectories of the APPPS1 mice and their controls (see associated raw trajectories) to determine which search strategies they used when learning the task (see Fig. 1F). These trajectories are recorded as separate text files for the X and Y coordinates. There is one file per trial and per mouse, named JxEy-IC.txt, where x is the day of recording, y the trial number and IC the identification code of the mouse. The files are arranged in directories by day of recording (from day 1 to day 8). We thus observed that APPPS1 mice performed more trials without strategy, confirming the learning impairment of APPPS1 mice (see Table 2, second part for statistics) (Fig. 1F).

To ensure that the deficits of the APPPS1 in the Starmaze were not explained by a visuo-motor impairment, we verified that their performances were not significantly different from those of C57BL/6 mice in the cued version of the Morris water maze (see Table 2 and data file 'Cued_Watermaze_Distance_APPPS1_14months.xslx', in Navigation and Memory Scores). The data file reports for each mouse the distance travelled between the start point and the visible goal platform at each trial (8 trials in total).

2. Experimental Design, Materials and Methods

2.1. Mice

C10 homozygous Thy1.APPmutxPS1M146L (hereafter called APPPS1) [1] were used as positive controls for spatio-temporal memory deficit at middle-aging stage. Mice were obtained from Charles River France (Saint Germain Nuelles, France). C57BL/6JRj male mice aged 14 months ($n = 12$) were obtained from Charles River France (Saint Germain Nuelles, France) to be used as controls for the APPPS1 mice.

Additional C57BL/6JRj male mice aged 6 months ($n = 15$) and 14 months ($n = 15$) were obtained from Janvier Labs (Saint Berthevin, France). The ApoE3 mice were obtained from Taconic Biosciences (Germantown, USA). All 6 month-old mice were used as controls in Schmitt et al., 2021 [2].

The list of the mice used in this dataset is provided in the data file 'List_of _mice_and_genotypes.xlsx' with their identification code and genotype.

Animals were housed in a 12 h dark/light cycle in a temperature-controlled room (20 +/- 1 °C) with food and water ad libitum. They were housed by groups of 3 or 4 mice per cage until one week before the start of the experiment, at which point mice were isolated in individual cages until the end of the first experiment, which lasted approximately 1 month.

Mice performed the tests in the following order: Shirpa protocol [3], Starmaze [4] and cued Morris water maze [5].

2.2. Starmaze paradigm

The Starmaze is a star-shaped water maze consisting of 5 central alleys forming a pentagon and 5 peripheral alleys starting from each vertex of the pentagon. In order to reduce the acquisition period, we here used a reduced Starmaze: some alleys were made inaccessible by blocking them with walls (see Fig. 1E). The alleys are 42 (central) or 47 (peripheral) cm long, 25 cm wide and 30 cm high [4]. The Starmaze is filled with water made opaque with a non-toxic dye (Accuscan OP 301) up to about 5 cm from the top of the walls. A platform is immersed 1 cm below the water surface. The Starmaze is surrounded by black curtains arranged in square on which 2D and 3D visual cues are attached. The cues are grouped into groups of 2 or 3. All cues are present in two copies but each configuration of 2 or 3 cues is unique. The brightness of the room was between 90 and 100 lux. A white noise of 50 dB was broadcast via 4 loudspeakers during all trials.

A trial begins with the mouse released by the experimenter always at the same departure point. The mouse is then left to swim until it finds the platform or 90 s maximum. If the mouse

finds the platform, it is left 20 s on the platform before being picked up by the experimenter. If the mouse does not find the platform before the end of the 90 s, it is placed on the platform for 20 s. At the end of each trial, the mouse is placed in a cage containing a towel for drying before being returned to its home cage while waiting for the next trial, during 30 to 60 min. The acquisition phase consisted of 5 trials per day for 8 days (also named sessions in the data files).

2.3. Starmaze scores

Mice trajectories were tracked and the distances travelled during a trial were measured using SMART 2.5 (Bioseb) software. X and Y trajectory coordinates were recorded every 0.04 s during the navigation task, and processed with our own developed software, NAT (Navigation Analysis Tool) [6], to extract the following behavioral parameters:

- the localization score, calculated by allocating a mark at each choice point (100 if the mouse moves toward the platform, 0 otherwise) and averaging the marks allocated at all the intersections encountered during a trial [7];
- the repeated sequence score, attributing a maximal mark if the moves made at each choice point of trial Ti+1 reproduce the choices made at trial Ti, in a same learning session [8];
- the recall sequence score, calculated like the repeated sequence score, to compare the sequence performed in the first trial on day $X + 1$ with the most repeated sequence performed on day X;
- the number of dead ends (peripheral arms not containing the platform) revisits;
- the time to reach the platform, capped at 90 s per trial;
- the percentage of correct first turns, which indicates the proportion of trials per session where the mouse makes a correct decision at the first intersection;
- the number of visited alleys averaged across trials.

All these scores are reported at the session level in the data files 'Robustness_6months.xslx' and 'Robustness_14months.xlsx' for the 6 and 14-month-old control mice.

2.4. Search strategies

The visualization of the trajectories (see raw trajectories) allowed to identify two types of trajectories that reveal an efficient strategy to reach the goal during the acquisition of the task:

- the direct trajectory, which corresponds to the most efficient sequence of turns to the goal with no visit of dead ends;
- the serial strategy, which includes a systematic visit of the dead end between the start and the platform.

The other types of trajectories corresponded to mice travelling more alleys to reach the platform, and were labelled as 'no strategy'.

2.5. Morris water maze in cued version

The 14-month-old APPPS1 mice ($N = 10$) and their C57BL/6 controls ($N = 12$) were subjected to a navigation task in the Morris water maze with a visible platform to ensure that possible deficits observed during the Starmaze task are not due to vision or swimming deficits. The pool is a circular tank of 150 cm in diameter. It is filled with water at 20 +/− 1 °C made opaque with a non-toxic dye (Accuscan OP 301). An opaque black curtain is placed around the pool so that the mouse cannot use distal landmarks and a flag is placed on the platform (12 cm in diameter)

to make it visible. The protocol is carried out in 2 days with 4 trials per day separated by 45 to 60 min each. The platform location is changed at each trial; the starting point is always opposite to the platform and the head of the mouse is directed towards the center of the water maze at the beginning of each trial. A trial lasts a maximum of 90 s. If the mouse does not find the platform during those 90 s, it is guided to the platform. The success at this task is monitored using the distance travelled by the mouse from the starting point to the visible platform. Distances were recorded by the tracking software (SMART 2.5, Bioseb). They are reported for each mouse and each trial (8 in total) in the data file 'Cued_Watermaze_Distance_APPPS1_14months.xslx'.

2.6. Statistical analysis

The distance travelled in the Starmaze was analyzed using a two-way analysis of variance (ANOVA) with factors Genotype, Session and their interaction, performed on raw data for the robustness assessment (Table 1) and the comparison of APPPS1 vs. C57Bl6 at 14 months (Table 2). Repeated measures on the factor session were taken into account in each model and AR(1) variance-covariance structure was used.

The Localization score was analyzed using a two-way ANOVA-type with factors Group, Session and their interaction on ranked data for the robustness assessment (Table 1) and the comparison of APPPS1 with C57Bl6 at 14 months (Table 2).

For the other three Starmaze parameters, i.e. repeated sequence score, recall sequence score and Dead end revisit number, a two way ANOVA-type was performed on ranked data for the score robustness assessment (Table 1), the comparison of APPPS1 vs C57Bl6 at 14 months (Table 2). The analysis was followed by comparisons of groups with post hoc tests at each session.

To compare the use of search strategies between groups, a two-way GLMM with binomial distribution was performed on raw data for the number of Direct, Serial and No strategy trials (Table 2) followed by Bonferroni-Holm adjustment if necessary.

A two-way analysis of variance (ANOVA) on factors Genotype and Session (repeated) was also performed on the travelled distance in the indexed version of the Morris water maze, when significant deficits were found in the Starmaze task (Table 2).

Ethics Statement

All experiments were approved by Sorbonne University Ethical Committee and conducted in full compliance with standards for the care and use of laboratory animals, according to French and European Community (Directive 2010/63/EU) legislation.

CRediT Author Statement

Julien Schmitt: Investigation, Data acquisition, Data curation, Formal analysis, Writing – original draft; **Anne-Lise Paradis:** Supervision, Formal analysis, Writing – review & editing, Writing – original draft; **Mathieu Boucher:** Formal analysis, Writing – original draft; **Laurent Andrieu:** Formal analysis, Writing – original draft; **Pascal Barnéoud:** Funding acquisition, Project administration, Writing – original draft; **Laure Rondi-Reig:** Conceptualization, Funding acquisition, Project administration, Supervision, Writing – review & editing, Writing – original draft.

Declaration of Competing Interest

JS, PB and LA were full-time employees of Sanofi when this study was performed. The CNRS, LRR and her lab have financial interest in the sale of the Starmaze task.

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Supplementary Materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.dib.2021.107266.

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