

# Data for Brain Reference Architecture of YS24LongitudinallySegmentedDistalCA1andPeriphery

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## Abstract

The hippocampal formation plays a crucial role in learning, memory, and spatial navigation. The connections of four regions of the hippocampal formation (DG, CA3, CA1, S) were investigated in longitudinal axis, transverse axis, and laminar organization, respectively. To define uniform circuits, a group of neurons that have the same meaning of the function, the standard division of longitudinal axis, transverse axis, and laminar organization was decided. Using the algorithm of integrating these three directions, the standard organizational circuits and connections of the hippocampal formation were created.

**Keywords:** Brain Reference Architecture; Hippocampal formation; Longitudinal axis; Transverse axis

## Author roles:

**Yudai Suzuki** Data curation, Methodology, Software, Writing—original draft

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## 1 Context

Brain Reference Architecture (BRA) is the reference architecture for software that realizes cognitive and behavioral functions in a brain-like manner. The architecture primarily consists of the mesoscopic-level anatomical data of the brain and the data of one or more functional mechanisms that are consistent with that knowledge (Yamakawa, 2021). BRA consists of Brain Information Flow (BIF), which represents structural knowledge of the brain, and Hypothetical Component Diagram (HCD)/Function Realization Graph (FRG), which represent brain functionality.

The dataset focuses on the detailed anatomical connections within and around the hippocampal formation, which plays a crucial role in learning, memory, and spatial navigation. The hippocampal formation consists of several regions, including the dentate gyrus (DG), CA3, CA2, CA1, subiculum (S), presubiculum (PrS), parasubiculum (PaS), medial entorhinal cortex (MEC), and lateral entorhinal cortex (LEC). These regions are known to exhibit anatomical differentiation along the longitudinal axis (septal, intermediate, temporal), transverse axis (proximal, distal), and laminar organization (layers 1-6) (Fanselow & Dong, 2010; Lee, GoodSmith, & Knierim, 2020; Ohara et al., 2023).

To create a comprehensive and standardized dataset of the hippocampal formation's anatomical connections, we applied the structure-constrained interface decomposition (SCID) method proposed by Yamakawa (2021). This method allows for the systematic decomposition of brain regions into smaller functional units called "uniform circuits" and the mapping of their connections based on anatomical and physiological evidence.

The resulting dataset, named "YS24LongitudinallySegmentedDistalCA1andPeriphery," provides a detailed and standardized representation of the hippocampal formation's anatomical connections in the Brain Information Flow (BIF) format. This dataset can be used for various purposes, such as understanding the structure-function

relationships in the hippocampus, elucidating the mechanisms of brain disorders involving the hippocampus, and developing computational models of hippocampal function.

The dataset is made publicly available through the Brain Reference Architecture Editorial System (BRAES) to facilitate collaboration and data sharing among researchers in neuroscience, artificial intelligence, and related fields.

Table 1: Abbreviations and formal names of the region of the hippocampal formation treated in this research

Abbreviations	Formal names
DG	dentate area (dentate gyrus)
CA3	CA3 region of Hipp
CA1	CA1 region of Hipp
S	subiculum
LEC	lateral (anterior) entorhinal cortex

Table 2: Abbreviations and formal names of the longitudinal axis treated in this research

Abbreviations	Formal names
s	septal
i	intermediate
t	temporal

Table 3: Abbreviations and formal names of the transverse axis treated in this research

Abbreviations	Formal names
p	proximal
d	distal

Table 4: Abbreviations and formal names of laminar organization treated in this research

Abbreviations	Formal names
L1	layer 1
L2.3	layer 2&3
L2	layer 2
L2fan	fan cells in layer 2
L3	layer 3
L5.6	layer 5&6
L5	layer 5
L5a	layer 5a
L5b	layer 5b
L6	layer 6

We created BIF information based on multiple detailed documents related to the anatomy around the hippocampal formation. In this study, there were five regions of the hippocampal formation (DG, CA3, CA1, S, and LEC), and four of them were ROIs (DG, CA3, CA1, S). Table 1 shows the abbreviations and formal names of the regions of the hippocampal formation that are treated in this study. The hippocampal formation was divided into three axes: longitudinal axis, transverse axis, and laminar organization. Tables 2, 3, and 4 show abbreviations, and formal names for the classification of the longitudinal axis, transverse axis, and laminar organization that are treated in this study.

The circuits were developed using the section “Circuit formulation”. A total of 138 circuits were added. The connections were developed using the section “Connection formulation”. A total of 182 connections were added.

## 2 Method

**SCID method/Function-oriented SCID method** The series of procedures followed to produce the dataset according to structure-constrained interface decomposition (SCID) method (Yamakawa, 2021) or function-oriented SCID method (Yamakawa et al., 2023).

The brief introduction of three steps of SCID method is given as follows:

Step 1. Brain Information Flow (BIF) registering and provisional creation of Hypothetical Component Diagram. This steps include (a) surveying anatomical knowledge in specific brain region (ROI: region of interest), (b) following determination of ROI and TLF (top-level function) consistently and (c) creation of a provisional component diagram (called HCD)

Step 2. Enumerating candidate component diagram.

Step 3. Rejecting diagram that are inconsistent with scientific knowledge.

You can see more details about these steps in (Yamakawa, 2021).

Function-oriented SCID method was proposed to reverse engineer the computational functions of a broad brain regions (Yamakawa et al., 2023). This method consists of four steps:

Step 1. Capability and requirement definition. Define a broad TLF at a high level of abstraction in a broad brain region (e.g. whole brain) and decompose it into a set of requirements to realize it.

Step 2. Function decomposition. Build a set of independent functions that can satisfy all requirements and significant biological constraints.

Step 3. Architecture design. Design a mechanism to realize each function as a component that defines input/output signals with semantics. In doing so, ensure the created components work together to meet all requirements.

Step 4. Brain region mapping. Map the above components to reasonable brain regions concerning input/output signal semantics and internal processing feasibility. However, if no appropriate mapping is found, return to step 2 and revisit the decomposition of the function.

**Sampling strategy** The dataset was created by the authors, including experts in anatomy, through the collection and integration of data from multiple publications. The selection criteria for the referenced publications were based on their inclusion in major academic journals related to anatomy. Detailed information about the referenced publications, such as titles, authors, journals, and publication years, is provided in the "References" sheet of the dataset.

The publications covered in this paper are as follows: [Bienkowski et al. \(2018\)](#); [Dolorfo and Amaral \(1998\)](#); [Fanselow and Dong \(2010\)](#); [Honda and Ishizuka \(2015\)](#); [Honda and Shibata \(2017\)](#); [Lee et al. \(2020\)](#); [Ohara et al. \(2021, 2023\)](#); [Taniguchi, Fukawa, and Yamakawa \(2022\)](#)

**Examination of correspondence of connections in longitudinal axis** [Fanselow and Dong \(2010\)](#) divides the longitudinal axis of the hippocampus into three parts: septal, which is involved in cognitive processes related to learning, spatial memory, exploration, and movement; intermediate, which is involved in converting cognitive and spatial information into motivation and survival behavior; and temporal, which is related to motivational and emotional behavior. Therefore, the direction of the longitudinal axis was divided into three parts: septal, intermediate, and temporal.

Next, we investigated the correspondence of connections in longitudinal axis between regions in the hippocampal formation.

- In [Honda and Shibata \(2017\)](#), the following connections are described to have a projection relationship:
  - CA1→S: CA1<sub>s</sub> projects to S<sub>s</sub>, CA1<sub>i</sub> projects to S<sub>i</sub>, and CA1<sub>t</sub> projects to S<sub>t</sub>.
  - S→PrS: S<sub>s</sub> projects to PrS<sub>s</sub>, S<sub>i</sub> projects to PrS<sub>i</sub>, and S<sub>t</sub> projects to PrS<sub>t</sub>.
  - PrS→MEC: PrS<sub>s</sub> projects to MEC<sub>s</sub>, PrS<sub>i</sub> projects to MEC<sub>i</sub>, and PrS<sub>t</sub> projects to MEC<sub>t</sub>.
  - MEC→PrS: MEC<sub>s</sub> projects to PrS<sub>s</sub>, MEC<sub>i</sub> projects to PrS<sub>i</sub>, and MEC<sub>t</sub> projects to PrS<sub>t</sub>.
  - MEC→CA1: MEC<sub>s</sub> projects to CA1<sub>s</sub>, MEC<sub>i</sub> projects to CA1<sub>i</sub>, and MEC<sub>t</sub> projects to CA1<sub>t</sub>.
- In [Honda and Ishizuka \(2015\)](#), the following connections are described to have a projection relationship:
  - S→PrS: S<sub>s</sub> projects to PrS<sub>s</sub>, S<sub>i</sub> projects to PrS<sub>i</sub>, and S<sub>t</sub> projects to PrS<sub>t</sub>.
  - S→PaS: S<sub>s</sub> projects to PaS<sub>s</sub>, S<sub>i</sub> projects to PaS<sub>i</sub>, and S<sub>t</sub> projects to PaS<sub>t</sub>.
  - S→MEC: S<sub>s</sub> projects to MEC<sub>s</sub>, S<sub>i</sub> projects to MEC<sub>i</sub>, and S<sub>t</sub> projects to MEC<sub>t</sub>.
  - S→LEC: S<sub>s</sub> projects to LEC<sub>s</sub>, S<sub>i</sub> projects to LEC<sub>i</sub>, and S<sub>t</sub> projects to LEC<sub>t</sub>.
- In [Bienkowski et al. \(2018\)](#), the following connections are described to have a projection relationship:
  - DG→CA3: DG<sub>s</sub> projects to CA3<sub>s</sub>, DG<sub>i</sub> projects to CA3<sub>i</sub>, and DG<sub>t</sub> projects to CA3<sub>t</sub>.
  - CA3→CA1: CA3<sub>s</sub> projects to CA1<sub>s</sub>, CA3<sub>i</sub> projects to CA1<sub>i</sub>, and CA3<sub>t</sub> projects to CA1<sub>t</sub>.
  - CA1→S: CA1<sub>s</sub> projects to S<sub>s</sub>, CA1<sub>i</sub> projects to S<sub>i</sub>, and CA1<sub>t</sub> projects to S<sub>t</sub>.
- In [Dolorfo and Amaral \(1998\)](#), the following connections are described to have a projection relationship:

- MEC→DG: MEC<sub>s</sub> projects to DG<sub>s</sub>, MEC<sub>i</sub> projects to DG<sub>i</sub>, and MEC<sub>t</sub> projects to DG<sub>t</sub>.
- LEC→DG: LEC<sub>s</sub> projects to DG<sub>s</sub>, LEC<sub>i</sub> projects to DG<sub>i</sub>, and LEC<sub>t</sub> projects to DG<sub>t</sub>.

Based on these findings, we hypothesized that for the eight regions of the hippocampal formation (DG, CA3, CA1, S, PrS, PaS, MEC, and LEC), connections in longitudinal axis would have a correspondence relationship other than those mentioned in the above literature. In the longitudinal axis, three hypotheses are established:

1. The first hypothesis is established that if the connection of two regions exists, DG<sub>s</sub>, CA3<sub>s</sub>, CA1<sub>s</sub>, S<sub>s</sub>, PrS<sub>s</sub>, PaS<sub>s</sub>, MEC<sub>s</sub>, LEC<sub>s</sub> have a correspondence relationship of the connection.
2. The second hypothesis is established that if the connection of two regions exists, DG<sub>i</sub>, CA3<sub>i</sub>, CA1<sub>i</sub>, S<sub>i</sub>, PrS<sub>i</sub>, PaS<sub>i</sub>, MEC<sub>i</sub>, LEC<sub>i</sub> have a correspondence relationship of the connection.
3. The third hypothesis is established that if the connection of two regions exists, DG<sub>t</sub>, CA3<sub>t</sub>, CA1<sub>t</sub>, S<sub>t</sub>, PrS<sub>t</sub>, PaS<sub>t</sub>, MEC<sub>t</sub>, LEC<sub>t</sub> have a correspondence relationship of the connection.

The above research findings and hypotheses were collected for each pair of source region and target region, and a list of information regarding the correspondence of connections in longitudinal axis was created.

**Examination of correspondence of connections in transverse axes** Lee et al. (2020) divides the transverse axis of the hippocampus into two parts: LEC, CA1<sub>d</sub>, and S<sub>p</sub> are related to the self-centered coordinate system, and MEC, CA1<sub>p</sub>, and S<sub>d</sub> are related to the environment-centered coordinate system. Therefore, the direction of the transverse axis was divided into two parts: proximal and distal.

Next, we investigated the correspondence of connections in transverse axes between regions in the hippocampal formation.

- In Honda and Shibata (2017), the following connections are described to have a projection relationship:
  - CA1→S: CA1<sub>d</sub> projects to S<sub>p</sub>.
  - PrS→MEC: PrS<sub>d</sub> projects to MEC<sub>p</sub>.
  - MEC→PrS: MEC<sub>p</sub> projects to PrS<sub>d</sub>.
- In Honda and Ishizuka (2015), the following connections are described to have a projection relationship:
  - S→PrS: S<sub>d</sub> projects to PrS<sub>d</sub>, and S<sub>d</sub> projects to PrS<sub>p</sub>.
  - S→MEC: S<sub>d</sub> projects to MEC<sub>d</sub>, and S<sub>d</sub> projects to MEC<sub>p</sub>.
  - S→LEC: S<sub>p</sub> projects to LEC<sub>d</sub>, and S<sub>p</sub> projects to LEC<sub>p</sub>.
- In Lee et al. (2020), the following connections are described to have a projection relationship:
  - LEC→CA1: LEC<sub>d</sub> projects to CA1<sub>d</sub>, and LEC<sub>p</sub> projects to CA1<sub>d</sub>.
  - MEC→CA1: MEC<sub>d</sub> projects to CA1<sub>p</sub>, and MEC<sub>p</sub> projects to CA1<sub>p</sub>.
  - CA1→S: CA1<sub>d</sub> projects to S<sub>p</sub>, and CA1<sub>p</sub> projects to S<sub>d</sub>.
  - S→LEC: S<sub>p</sub> projects to LEC<sub>d</sub>, and S<sub>p</sub> projects to LEC<sub>p</sub>.
  - S→MEC: S<sub>d</sub> projects to MEC<sub>d</sub>, and S<sub>d</sub> projects to MEC<sub>p</sub>.

Based on these findings, we hypothesized that for the five regions of the hippocampal formation (CA1, S, PrS, MEC, and LEC), connections in transverse axis would have a corresponding relationship other than those mentioned in the above literature. In the transverse axis, four hypotheses are established.

1. The first hypothesis is established that if the connection of two regions exists, CA1<sub>d</sub>, S<sub>p</sub>, LEC<sub>d</sub> have a correspondence relationship of the connection.
2. The second hypothesis is established that if the connection of two regions exists, CA1<sub>d</sub>, S<sub>p</sub>, LEC<sub>p</sub> have a correspondence relationship of the connection.
3. The third hypothesis is established that if the connection of two regions exists, CA1<sub>p</sub>, S<sub>d</sub>, PrS<sub>p</sub>, MEC<sub>d</sub> have a correspondence relationship of the connection.
4. The fourth hypothesis is established that if the connection of two regions exists, CA1<sub>p</sub>, S<sub>d</sub>, PrS<sub>d</sub>, MEC<sub>p</sub> have a correspondence relationship of the connection.

In addition, the correspondence relationship of connections in transverse axes regarding the two regions of the hippocampal formation (DG, CA3) is described in Lee et al. (2020).

- In Lee et al. (2020), the following connections are described to have a projection relationship:
  - DG→CA3: DG projects to CA3<sub>p</sub>, and DG projects to CA3<sub>d</sub>.
  - CA3→DG: CA3<sub>p</sub> projects to DG.

- MEC→CA3: MEC\_d projects to CA3\_d, MEC\_d projects to CA3\_p, MEC\_p projects to CA3\_d, and MEC\_p projects to CA3\_p.
- LEC→CA3: LEC\_d projects to CA3\_d, LEC\_d projects to CA3\_p, LEC\_p projects to CA3\_d, and LEC\_p projects to CA3\_p.
- CA3→CA1: CA3\_d projects to CA1\_p, and CA3\_p projects to CA1\_d.

The above research findings and hypotheses were collected for each pair of source region and target region, and a list of information regarding the correspondence of connections in transverse axes was created.

**Examination of correspondence of connections in laminar organization** The findings about the correspondence of connections in laminar organization are in [Honda and Shibata \(2017\)](#), [Ohara et al. \(2023\)](#), [Ohara et al. \(2021\)](#), [Taniguchi et al. \(2022\)](#). The above research findings were collected for each pair of source region and target region, and a list of information regarding the correspondence of connections in laminar organization was created.

Regarding the classification of laminar organization, the laminar organization of five regions of the hippocampal formation (DG, CA3, CA1, S, and LEC) was extracted from [an Allen Brain Reference Atlas \(n.d.\)](#). At this time, after discussions with experts, it was decided not to deal with LEC.L3a and LEC.L3b. Furthermore, [Honda and Shibata \(2017\)](#) describes the connections related to LEC.L2\_3 and LEC.L5\_6, so these were extracted as laminar organization. Furthermore, from [Ohara et al. \(2021\)](#), LEC.L2fan, LEC.L5a, and LEC.L5b were extracted as laminar organization.

**Determining ROI and axis classification** In this study, there were five regions of the hippocampal formation (DG, CA3, CA1, S, and LEC), and four of them were ROIs (DG, CA3, CA1, S) (Table 1). We determined the classification of the longitudinal axis, transverse axis, and laminar organization treated in this study (Tables 2, 3, and 4).

Based on the sections “Examination of correspondence of connections in longitudinal axis”, “Examination of correspondence of connections in transverse axes”, and “Examination of the correspondence of connections in laminar organization”, for each region of the hippocampal formation treated in this study, the elements with the smallest grain size in each direction of longitudinal axis, transverse axis, and laminar organization were extracted, and these were used as elements for dividing each direction of longitudinal axis, transverse axis, and laminar organization. Table 5 shows the elements that divide longitudinal axis, transverse axis, and laminar organization in the region of the hippocampal formation. Based on discussions with experts, it was decided not to determine the elements to be divided in the laminar organization of CA1, CA3, DG, and S, and in the transverse axis of DG.

Table 5: Elements that divide longitudinal axis, transverse axis, and laminar organization regarding the regions of the hippocampal formation

Region names	Longitudinal axis	Transverse axis	Laminar organization
DG	Septal, Mid, Temporal		
CA3	Septal, Mid, Temporal	Proximal, Distal	
CA1	Septal, Mid, Temporal	Proximal, Distal	
S	Septal, Mid, Temporal	Proximal, Distal	
LEC	Septal, Mid, Temporal	Proximal, Distal	L1, L2fan, L3, L5a, L5b, L6

---

**Algorithm 1** Segmentation\_process (i, j, k, l)

---

- 1: append "i.j.k.l" to List as uniform circuit = True
  - 2: return
-

---

**Algorithm 2** Algorithm for creating Circuit: Make\_Circuit

For DG, only line 3-5 are executed, with uniform circuit=True.

For CA3, CA1, and S, line 9 and 14 are not executed.

For LEC, "i.j.l" is appended in line 19-21, because connections to DG as "i.j" exists.

For LEC, as l = L2\_3, L2, L5\_6, and L5, "i.l" and "i.j.k.l" are appended in line 19-21.

---

```

1: List=[]
2: for extract element i from region name in Table 5 do
3:   for extract element j from longitudinal axis in Table 5 do
4:     append "i.j" to List as uniform circuit = False
5:   end for
6:   for extract element k from transverse axis in Table 5 do
7:     append "i.k" to List as uniform circuit = False
8:   end for
9:   for extract element l from laminar organization in Table 5 do
10:    append "i.l" to List as uniform circuit = False
11:   end for
12:   for extract element j from longitudinal axis in Table 5 do
13:     for extract element k from transverse axis in Table 5 do
14:       for extract element l from laminar organization in Table 5 do
15:         Segmentation_process (i, j, k, l)
16:       end for
17:     end for
18:   end for
19:   if there is an exception then
20:     append the exception to List
21:   end if
22: end for
23: return List

```

---

**Circuit formulation** The naming convention for abbreviations was decided as follows:

- "abbreviation of region name"\_"s/i/t"\_"p/d". "abbreviation of laminar organization"

The naming convention for formal names was decided as follows:

- "formal name of laminar organization" "of" "septal/intermediate/temporal" "proximal/distal" "formal name of region name"

Circuit was created by using the algorithm Make\_Circuit. For each of the five regions of the hippocampal formation (DG, CA3, CA1, S, LEC), the following circuits were registered not as a uniform circuit:

- "abbreviation of region name"\_"s/i/t"
- "abbreviation of region name"\_"p/d"
- "abbreviation of region name"\_"abbreviation of laminar organization"

Then, using the algorithm Segmentation\_process, by multiplying the elements of three axes, that divide longitudinal axis, transverse axis, and laminar organization, the following circuits were created and registered as a uniform circuit:

- "abbreviation of region name"\_"s/i/t"\_"p/d". "abbreviation of laminar organization"

---

**Algorithm 3** Synthesize\_process (i1-i2, j1-j2, k1-k2, l1-l2)

---

```

1: append "from i1_j1_k1.l1 to i2_j2_k2.l2" to List
2: return

```

---

**Algorithm 4** Algorithm for creating Connection: Make\_Connection

For DG, line 7, 10, 14, and 15 are not executed

For CA3, CA1, and S, line 10 and 15 is not executed

In line 24, about the internal connections of the DG, CA3, CA1, and S, the widely known connections in [Bienkowski et al. \(2018\)](#) were extracted through discussion with experts.

In line 25, in some connections, if a source in ROI is not Uniform Circuit, add "Source\_uc" to Circuit and replace the source of the connection to "Source\_uc".

---

```

1: List=[]
2: for extract source i1 and target i2 from a list of information regarding the correspondence of connections in laminar organization do
3:   append "from i1 to i2" to List
4:   for extract source j1 and target j2 from a list of information regarding the correspondence of connections in longitudinal axis do
5:     append "from i1_j1 to i2_j2" to List
6:   end for
7:   for extract source k1 and target k2 from a list of information regarding the correspondence of connections in transverse axes do
8:     append "from i1_k1 to i2_k2" to List
9:   end for
10:  for extract source l1 and target l2 from a list of information regarding the correspondence of connections in laminar organization do
11:    append "from i1.l1 to i2.l2" to List
12:  end for
13:  for extract source j1 and target j2 from a list of information regarding the correspondence of connections in longitudinal axis do
14:    for extract source k1 and target k2 from a list of information regarding the correspondence of connections in transverse axes do
15:      for extract source l1 and target l2 from a list of information regarding the correspondence of connections in laminar organization do
16:        Synthesize_process (i1-i2, j1-j2, k1-k2, l1-l2)
17:      end for
18:    end for
19:  end for
20:  if there is an exception then
21:    append the exception to List
22:  end if
23: end for
24: append internal connections to List
25: if there is an exception then
26:   append the exception to List of circuits and List of connections
27: end if
28: return List

```

---

**Connection formulation** Connection was created using the algorithm Make\_Connection. Using "a list of information regarding the correspondence of connections in longitudinal axis", "a list of information regarding the correspondence of connections in transverse axes", and "a list of information regarding the correspondence of connections in laminar organization", connections were created. For each pair of the five regions of the hippocampal formation (DG, CA3, CA1, S, LEC), if there is a connection from one region to another region, the following connections were registered:

- "a connection from one region to another region"
- "a connection from one region to another region considering a list of information regarding the correspondence of connections in longitudinal axis"
- "a connection from one region to another region considering a list of information regarding the correspondence of connections in transverse axes"
- "a connection from one region to another region considering a list of information regarding the correspondence of connections in laminar organization"

Then, using the mapping algorithm `Synthesize_process`, we synthesized the connections of longitudinal axis, transverse axis, and laminar organization, and added this connection to a list. From the results of `Synthesize_process`, the following connections were registered:

- "a connection from one region to another region considering a list of information regarding the correspondence of connections in longitudinal axis, transverse axes, and laminar organization"

### 3 Dataset Description

**Repository location** BRA Editorial System (BRAES):  
<https://sites.google.com/wba-initiative.org/braes/data>

**Object name and versions** Please refer to the "Project" sheet in the BRA data for the more detail of data summary.

Table 6: BRA DATA SUMMARY

BRA Data			
Object Name	Template	Including Content(s)	
		BIF	HCD/FRG
YS24LongitudinallySegmentedDistalCA1andPeriphery.bra	<i>version 2.0</i>	√	-

Table 7: BRA IMAGE SUMMARY

Graphic Files: BIF Image, HCD Image, FRG Image	
File Type	Object Name
BIF Image	YS24LongitudinallySegmentedDistalCA1andPeripheryBIF.xml
HCD Image	-
FRG Image	-

**Creation dates** From 2022-09-11 to 2024-07-16.

**Language** English.

**License** The open license under which the data has been deposited (CC-BY 4.0).

**Publication date** 2024-07-16.

### 4 Caveats for Data Usage

The Brain Reference Architecture (BRA) data, including standardized Brain Information Flow (BIF) data, has significant reuse potential for researchers within and beyond neuroscience. Its standardized nature allows for easy integration of mesoscopic brain information, enabling comparative analyses across brain regions. The data's versatility supports various research areas, including understanding brain structure-function relationships, elucidating brain disorder mechanisms, and constructing computational models.

This data includes hypotheses, so caution is required when using it. The hypotheses are included in the three hypotheses described in section "Examination of correspondence of connections in longitudinal axis", the four hypotheses described in section "Examination of correspondence of connections in transverse axes", and the connections created by the algorithm "Synthesize\_process". Methods for verifying the hypotheses are verification using anterograde/retrograde tracers, or verification by selectively expressing fluorescent proteins using transgenic mouse and tracing the labeled axons.

Circuits with "Source\_uc" are a temporary circuit required when executing the algorithm `Make_Connection`, so caution is required when using it. Future challenges include adding CA2, PaS, PrS, and MEC, and adding external connections from/to regions outside the hippocampal formation.

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## Competing interests

The authors have no competing interests to declare.

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