

Analysis of anatomical data in 'The Mind of a Worm'

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1. Introduction

This is a report on computer-aided analysis of anatomical data of synaptic connectivity of *C. elegans* which are described in the paper

J .G. White, E. Southgate, J.N. Tomson and S. Brenner: 'The Structure of the Nervous System of the Nematode *Caenorhabditis elegans*', Phil. Trans. R. Soc. Lond. B **314** pp1-340 (1986)

I will refer to this paper as the original paper and to data therein as the anatomical data, hereafter.

It should be stressed that such analysis become possible by

K. Oshio, Y. Iwasaki, S. Morita, Y. Osana, S. Gomi, E. Akiyama, K. Omata, K. Oka and K. Kawamura: 'Database of Synaptic Connectivity of *C. elegans* for Computation'

From my analysis of the anatomical data, I confirmed that it is almost perfectly self-contained. However, my young colleagues (from K. Oshio to K. Omata in the list of authors of the database) found during their work a few erroneous descriptions in the anatomical data. In addition, I found several inconsistent descriptions. This is a report about such erroneous or inconsistent descriptions in the anatomical data. I expect that you or someone else correct the anatomical data in future and at that moment, I hope, this report help the work.

The report involves three subjects. First, I will discuss several anatomical data described in diagrams of processes which are probably erroneous. They were found by my colleagues while they built the data files. These data are noticed with marks 'wf' on the last column of data file 'synapse_wf.txt'. A few data are actually unaccountable and I cannot correct them. However, some data which my colleagues doubted erroneous might be correctable and I will discuss proof of these data.

The second subject of the following report is inconsistency involved in the anatomical data. I found that they involve such inconsistency that the number of synapses sent by

a neuron A to another neuron B is not equal to that received by the neuron B from A. Although a few of these inconsistent descriptions had been caused by erroneous record during reconstruction from electron microscope image, several inconsistency might be attributed to the nature of synapses that the postsynaptic specialization is invisible and, accordingly, the inconsistency involves important information about synaptic connection.

The third subject is inconsistency involved in the six circuitries in Fig.21 in the original paper. Since many authors refer to those circuitries, I believe that it is worth while to evaluate consistency of those circuitries.

In this report, the word 'synaptic element' denotes what you represented in diagrams of processes with a dot for a chemical synapse and with a short bar for a gap junction. According to our data file 'synapse_wf.txt', the synaptic element on a neuron will be numbered so that the first synaptic element denotes the element which is farthest from the cell body.

2. Erroneous descriptions in diagrams of processes.

In the present section, I will discuss several erroneous data which were found by my colleagues when they created the digital files.

1. The following names of the partner are not found among names of neurons of *C. elegans*.
 - (a) The partner SVPL of the second synaptic element on the process of RMDR. This is noticed with the mark 'wf24' in the file 'synapse_WF.txt'.
 - (b) The partner RMVDL of the twelfth synaptic element on the process of RMGL. This is noticed with the mark 'wf25' in the file 'synapse_WF.txt'.
2. No symbol representing the type of connection is attached to the following synaptic elements. They are noticed with the mark 'wf7' in the file 'synapse_WF.txt'.
 - (a) The 76th synaptic element on the process of AIZL connected to AIYL. I guess that an incoming arrow is missed, since an asterisk is attached to the name of the partner.
 - (b) The 16th synaptic element on the process of AQR connected to AVBR and PVCL. I guess that an outgoing arrow is missed, since the original paper says that AVB is exclusively postsynaptic in the nerve ring.
 - (c) The 41st synaptic element on the process of AQR connected to AVAL and AVBL. I guess that an outgoing arrow is missed, since the original paper says that AVA as well as AVB is exclusively postsynaptic in the nerve ring.
 - (d) The 29th synaptic element on the process of AVBL connected to AQR. I guess that an incoming arrow is missed, since (i) AVB is exclusively postsynaptic in the nerve ring and (ii) an asterisk is attached to the partner name.
 - (e) The 23rd synaptic element on the process of AVBR connected to PVCR. In the same reason as above, I guess that an incoming arrow is missed.
 - (f) The 27th and 28th synaptic elements on the process of OLLR connected to SMDVL. To be consistent with the description of a postsynaptic element at a similar position on SMDVL whose synaptic partner is OLLR, outgoing arrows should be attached.

- (g) The 142nd and 143rd synaptic elements on the process of RIAL connected to BAGR. To be consistent with the description of a presynaptic contact on BAGR to RIAL, incoming arrows should be attached.
 - (h) The 14th synaptic element on RID to PVCL. To be consistent with the fact that PVCL is presynaptic at all other contacts with RID, an incoming arrow should be attached. Principle of homogeneity described in the next section was applied, here.
 - (i) Type of connection at the 3rd synaptic element on the process of RID whose synaptic partner is AVBL is not shown. This is noticed with the mark 'wf8' in the file 'synapse_WF.txt'. A builder of the data file guesses it is a gap junction from the symbol of the synaptic element indicated in the diagram.
3. The type of connection of RIGR to RIBR at the 26th synaptic element is not identified because it is denoted by a left-right arrow. This is noticed with the mark 'wf9' in the file 'synapse_WF.txt'. To be consistent with the fact that all synaptic elements on the process of RIBR connected to RIGR are postsynaptic, the left-right arrow should be replaced with an outgoing arrow. Here, principle of homogeneity was applied again.
 4. The fact that arrows are outgoing in the following descriptions is inconsistent with asterisks attached to partner names, since an asterisk represents that the process is postsynaptic to one of several contacts of a single presynaptic element. They are noticed with the mark 'wf1' in the file 'synapse_WF.txt'.
 - (a) The 26th synaptic element on the process B of ADFR connected to AWBR [The name of the branch of a process is defined in the file 'process_WF.pdf'].
 - (b) The 15th synaptic element on the process of RIAL connected to RMDL.
 - (c) The 12th synaptic element on the process of RIML connected to RIS.
 - (d) The 32nd synaptic element on the process of RMDVL connected to RIAR.

For these data to be consistent, an asterisk should be deleted or the direction of an arrow should be changed in each data. I guess that direction of arrows should be changed in the above mentioned descriptions on ADFR and RIML and that the asterisks should be omitted from the descriptions on RIAL and RMDVL. You will find the reason on the next section.

5. In the diagram of the process in the original paper, one finds many synaptic elements each of which is accompanied by more than one neuron names near a single arrow. When the arrow is outgoing arrow, one can interpret that the synaptic element is presynaptic and it is connected to more than one postsynaptic neurons with a dyadic (or triadic) synapse. However, when a synaptic element is accompanied by an incoming arrow with more than one neuron names, such interpretation is not possible and we suspected that the direction of the arrows should be changed. Such data are noticed in the data file 'synapse_WF.txt' by 'wf2'. However, I guess that you represented more than one postsynaptic elements by a single dot in diagrams for simplicity. In fact several incoming arrows are accompanied by more than one neuron names with asterisks. Accordingly, all descriptions with more than one neuron names with a single incoming arrow are not erroneous. However, the direction of arrows attached to the

following two contacts might be erroneous and arrows attached to these contacts might be outgoing.

- (a) The 25th synaptic element on the branch B of ADFR connected to AIZR and RIAR.
- (b) The 47th synaptic element on the process of AIYR connected to RIAR and RIBR and 48th synaptic element connected to RIAR and AIZR on the process of AIYR. I guess that the arrows attached to these contacts should be outgoing,

The reasons for these statements will be found in the next section.

3. Principles to speculate possibly correct connectivity

In the previous section, I proposed improvement of (possibly) erroneous descriptions in the original data. In the present section, I will summarize reasoning I employed in the previous section in the form of three principles. They will be applied also in the following section to examine inconsistency involved in the original paper.

Principle of send-receive reciprocity:

When a neuron A sends a synapse to a neuron B, the neuron B receives the synapse from the neuron A.

I have already employed this principle, for instance, to speculate that an outgoing arrow is missed from the 16th synaptic element on the process of AQR [the item 2(b) in the previous section]. In fact, if AVBR does not send a synapse to AQR at all, synapses which connect AQR with AVBR are exclusively oriented from AQR to AVBR. My speculation described in 2(b) to (g) and 3 in the previous section were derived by this principle.

This principle was also employed to correct the inconsistent description stated in the item 4 in the previous section. To explain the procedure, the number of the descriptions ' $\rightarrow B$ ' and the number of ' $\leftarrow B$ ' on the diagram of the process of the neuron A are denoted as $N_s(A, B)$ and $N_r(A, B)$, respectively. Similarly, the number of the gap junction with a neuron B in the diagram of A is denoted as $N_g(A, B)$. Then the following relations should be satisfied, if the anatomical data is perfectly self-contained and does not involve any error.

$$\begin{aligned} N_s(A, B) &= N_r(B, A), \\ N_g(A, B) &= N_g(B, A), \end{aligned}$$

I will call these relations **reciprocal relations**.

Actually, I have counted these numbers from 'synapse_WF.txt', 'synapse_WT.txt' and 'synapse_AF.txt'. For instance, contribution from 'synapse_WF.txt' to the number $N_s(A, B)$ is the number of lines on which the entry of the first column is members of the neuron class A and that of the fifth column is 'S'. A connection with a dyadic (triadic) synapse is represented in the diagram of processes by attaching two (three) names of partners near the head of an arrow. In 'synapse_WF.txt', such a connection is described over two (three) lines with 'S' on the fifth column. Accordingly, $N_s(A, B)$ represents the number of presynaptic contacts in stead of presynaptic element.

To represent the violation of reciprocity, the following quantities are introduced:

$$\Delta N_s(A, B) = N_s(A, B) - N_r(B, A), \quad (1)$$

$$\Delta N_r(A, B) = N_r(A, B) - N_s(B, A), \quad (2)$$

$$\Delta N_g(A, B) = N_g(A, B) - N_g(B, A). \quad (3)$$

These three quantities will be called the inconsistency indices, hereafter. By definition, all of these indices should vanish, if the anatomical data correctly describes the synaptic connectivity between neurons A and B.

As for neurons which appeared in the item 4 in the previous section, the inconsistent indices are shown in Table 1. Change of direction of the arrow attached to the 26th synaptic element of ADFR from \rightarrow AWBR to \leftarrow AWBR yields $\Delta N_s(\text{ADFR}, \text{AWBR}) = N_r(\text{ADFR}, \text{AWBR}) = 0$. From the same argument, I guess that the arrow at the 12th synaptic element of RIML whose partner is RIS should be incoming.

On the other hand, the inconsistency index between RIAL and RMDL is not improved by changing the direction of arrows from \rightarrow RMDL to \leftarrow RMDL attached to 15th synaptic element on the process of RIAL. Neither the inconsistent index between RMDVL and RIAR is not improved by change of direction of the arrow attached to the 32nd element on RMDVL. To the inconsistent descriptions in the original data pointed in the item 4(b) and (d) in the previous section, the asterisks should be omitted from partners .

Table 1. Inconsistency index for neurons described in the item 4 in the previous section.

diagram of (A)	partner (B)	$\Delta N_s(A, B)$	$\Delta N_r(A, B)$	$\Delta N_g(A, B)$
ADFR	AWBR	1	-1	0
RIAL	RMDL	-1	-1	0
RIML	RIS	1	-1	0
RMDVL	RIAR	1	0	0

Principle of lateral symmetry : Synaptic connection is almost laterally symmetric.

Given two neuron classes A and B each of which has two members L and R neurons. When AL is connected to BL(R) in a certain region of the process of AL, AR can be connected to BR(L) in the region of the process of AR which is a mirror image of the former. Although the mirror plane is not rigorously geometrical plane, this statement is roughly verified from the structure of neuron processes sketched in the original paper.

I will often extend this principle so that the direction of synapses is laterally symmetric: When the neuron AL is presynaptic (postsynaptic) to a member of B in that region, AR is also presynaptic (postsynaptic) to the counter part of the class B in the region of mirror image. To verify this statement, we should extend arguments beyond geometry so that it is nothing but a hypothesis at this moment.

Principle of homogeneity: When the neuron class A has two members AL and AR, a neuron B is not connected to AL in the region where B is connected to AR.

This statement could be verified by arguments of geometry, unless the neuron process has extremely large curvature.

I will extend this principle so that the direction of synapse between given two neurons does not change alternatively in a small region of processes of these two neurons. A counter example is found, for instance, on the branch C of ADLR where it has two postsynaptic elements from AIAR near four presynaptic elements to AIAR. Accordingly, the direction of synapses cannot be rigorously determined by this principle but it can be referred to when we find any inconsistency which cannot be excluded by other reasoning.

For instance, I speculated that the arrow attached to the 25th synaptic element on the branch B of ADFR stated in the item 5 in the previous section might be outgoing, since (i) all other synaptic elements to RIAR are presynaptic at the region near that synaptic element (by extension of the principle of homogeneity) and (ii) there is a presynaptic contact to AIZL and RIAL, that is, the 24th synaptic element on the branch B of ADFL (by extension of the principle of the lateral symmetry). Similarly, the arrows attached to the 47th and 48th synaptic elements on the process of AIYR stated in the same item might be outgoing, since all other synaptic elements on the same process connected to AIAR, RIBR, RIAR and AIZR are presynaptic (by extension of the principle of homogeneity).

4. Inconsistency of the number of synapses among neuron classes

Erroneous descriptions which have been found during creation of the data files have been corrected in the manner described in the previous two sections. The next task is to find out other inconsistent descriptions which are possibly involved in the original paper and to propose correction of the anatomical data.

4.1 Inconsistency of connection in the nerve ring

For the purpose stated above, number of connections $N_s(A, B)$, $N_r(A, B)$ and $N_g(A, B)$ have been computed from 'synapse_WF.txt', which is equivalent to diagrams of processes sketched in the original paper. When the inconsistency indices were computed from them, it should be noticed that some diagrams describe connection within the ventral cord which are located far from the nerve ring. Subject of discussion in this subsection is restricted to the connection in the nerve ring.

Transversal inconsistency

When I looked at the list of inconsistency indices, I found a type of inconsistency such as

$$\begin{aligned}\Delta N_s(A, B) &= 1 \\ \Delta N_s(A, C) &= -1\end{aligned}$$

This type of inconsistency arises if the partner C of a presynaptic element on the process of A is erroneously recorded as B. I will call this type of inconsistency the transversal inconsistency.

In principle, such a set of inconsistency indices would arise if you overlooked a presynaptic element on B from A and, simultaneously, added the element from A on B which does not exist actually. However, such double misrecording is much less probable than the former type of misrecording. Therefore, when I found such a set of inconsistency indices, I guessed that it arises from the transversal inconsistency.

I looked for the set of lines of the nature described above among the list of inconsistency index and propose the correction described in Table 2.

Table 2. Proposal of correction of partner names in the diagram of processes

diagram of	synaptic element	partner neuron(s)
ADAL	A4 and A5	AVBL 's should be read as AVBR's
ADAL	E22 and E23	SMDVL's should be read as SMDVVR's*
ADAR	A3	AVBL should be read as AVBR
ADAR	C22 and C23	SMDVR's should be read as SMDVL's *
ADFR	B42	SMBDL should be read as SMBDR
AIBL	A43 and A44	RIMR's should be read as RIML's
AIML	A3	AVHR should be read as AVHL
ALML	B18	CEPDL should be read as CEPDR
ASEL	B16	AIYR should be read as AIYL
AVBL	A43	PVPR should be read as PBPL
AVJR	A24	PVNL should be read as PVNR
AVJR	A29	ADLL should be read as ADLR
AVKR	A7	SMBDR should be read as SMBDL
AWBL	B19	SMBDR should be read as SMBDL
BDUL	A15 and A17	PVNL's should be read as PVNR's
CEPDL	A27	SMBDL should be read as SMBDR
CEPDR	A18	RMHL and RICL should be read as RMHR and RICR, respectively
CEPDR	A35	RICR should be read as RICL
ILDR	B25	RMED should be read as RMEV
IL1R	A18 and A20	RMDDL's should be read as RMDDR's
IL1R	A21	RMDL should be read as RMDR
IL2DR	A1	RMER should be read as RMEV
PVR	E8	AVJL should be AVJR
RIAL	A16	SMDVR should be read as SMDVL
RIBR	D29	SIBVR should be read as SIBDR
RICR	E31	SDQR should be read as SDQL
RIGL	A3	BAGL should be read as BAGR
RIGL	A16 and A51	AVKL's should be read as AVKR's
RIH	B18	RIPR should be read as RIPL
RIG	G71	FLPL should be read as FLPR
RIMR	A7	RMFR should be read as RMFL
RIMR	A18	SAAVR should be read as SAADR
RIR	A21	AIZL should be read as AIZR
RIS	A21	AVEL should be read as AVER
RMDL	A28	IL2R should be read as IL2L
RMDVL	A7	SMDVR should be read as SMDVL
RMED	G28	SMBDR should be read as SMBDL
RMFL	C12	AVKL should be read as AVKR
RMFR	A8	RMDR should be read as RMDL
RMGR	C23	RMHL should be read as RMHR
SAADL	A2	RMDDR should be read as RMDDL
SAADL	A3	RMGL should be read as RMGR

Table 2 (continued)

diagram of	synaptic element	partner neuron(s)
SI AVL	A5	RIAL should be read as RIAR
SMBVL	A1,A6,A7,A8,A10,A11	PLNR's should be read as PLNL's
SMVBR	A1,A11, A12, A13	PLNL's should be read as PLNR's
SMDVL	A23	OLLL should be read as OLLR
SMDVL	A27	RIAL should be read as RIAR
URXL	B19	RMGR should be read as RMGL
URXL	C21	RICL should be read as RIGL
URYVL	A15	SIBVL should be read as SIBVR
URYVR	A12	SIBVR should be read as SIBDR
URYVR	A16	RMDDL should be read as RMDDR

Longitudinal inconsistency

I have found another type of inconsistency like

$$\begin{aligned}\Delta N_s(A, B) &= 1 \\ \Delta N_r(A, B) &= -1\end{aligned}$$

This type of inconsistency would arise if a postsynaptic element on B from A and a postsynaptic element on A from B are simultaneously overlooked. Such double misrecording is much less probable than misdrawing of direction of one of two arrows, that is, one outgoing arrow ' $\rightarrow B$ ' attached to the process of the neuron A or one incoming arrow ' $\leftarrow A$ ' attached to the process B. This type of inconsistency will be called the longitudinal inconsistency, hereafter.

Then, there is a question which arrow is erroneously drawn.

An example of the longitudinal inconsistency has been encountered in the first and third lines of Table 1. In that case, I proposed that direction of the arrow ' $\rightarrow AWBR$ ' attached to a synaptic element on the process of ADFR should be reversed from the rule that an asterisk is attached to the name of a postsynaptic partner. In ordinary cases, I applied the principle of lateral symmetry and/or the principle of homogeneity to select an arrow whose direction should be reversed.

In this way, I guess that the direction of several arrows should be reversed as shown in Table 3.

Table 3. Proposal of correction of direction of arrows in diagrams of processes.

diagram of	synaptic element	original description	should be read
ADFR	B25	\leftarrow AIZR, RIAR	\rightarrow AIZR, RIAR
ADFR	B26	\rightarrow AWBR	\leftarrow AWBR
AIAR	A54	\leftarrow ASGR	\rightarrow ASGR
AIYR	A47	\leftarrow RIAR, RIBR	\rightarrow RIAR, RIBR
AIYR	A48	\leftarrow RIAR, AIZR	\rightarrow RIAR, AIZR
AIZL	A59 & A65	\rightarrow ADFL	\leftarrow ADFL
AIZL	A75	\rightarrow RIH	\leftarrow RIH
AIZL	A92	\rightarrow ASIL	\leftarrow ASIL
ASGR	B6	\leftarrow AIAR	\rightarrow AIAR

Table 3 (continued)

diagram of	synaptic element	original description	should be read
ASKL	B12	→ ASJL	← ASJL
AVHL	A13	← AVJL	→ AVJL
AWBL	B4	← AIZL	→ AIZL
DVA	C21	← AIZL	→ AIZL
IL1DL	A1	→ IL1L	← IL1L
IL1R	A11	← URXR	→ URXR
IL2VR	A11	→ OLQVR	← OLQVR
OLL	A15	← CEPDL	→ CEPDL
OLL	C49	→ SAADR	← SAADR
OLLR	A4	← SMDVR, IL1DR	→ SMDVR, IL1DR
RIAL	A15	→ RMDL	← RMDL
RIBR	5E0	← OLQVR	gap junction with OLQVR
RIML	A12	→ RIS	← RIS
RMDVL	A32	→ RIAR	← RIAR

4.2 Number of connection among neuron classes

In the original paper, connection among all neurons are not described; descriptions about the connection within the ventral cord are concerned with neuron classes. For neurons which have synaptic connections within the ventral cord, the number of connection among neurons cannot be computed from the digital data.

I have computed number of connection among neuron classes. Number of connections among the neuron classes α and β is defined as follows;

$$\begin{aligned}
 N_s(\alpha, \beta) &= \sum_{A(\in\alpha)} \sum_{B(\in\beta)} N_s(A, B) \\
 N_r(\alpha, \beta) &= \sum_{A(\in\alpha)} \sum_{B(\in\beta)} N_r(A, B) \\
 N_g(\alpha, \beta) &= \sum_{A(\in\alpha)} \sum_{B(\in\beta)} N_g(A, B)
 \end{aligned}$$

where $\sum_{A(\in\alpha)}$ represents the summation over neurons belonging to the neuron class α .

Although the original paper is almost self-contained, processes of many motoneurons in the ventral cord are not illustrated. Therefore, I could not count the number of connection for A=ASn, DAn, DBn, DDn, VAn, VBn, VCn, and VDn. When A is one of such neuron classes, I speculated the above mentioned number of connections from the reciprocal relations for the number of connection among neurons. For the connection in the nerve ring, we can count the number of connection in which the partner is one of these motoneurons. In the table of synapses in the ventral cord, neuron names instead of neuron classes are described in the column of partners when the partner is the ventral cord motoneuron.

The tables of the number of connection will be uploaded in near future to our home page.

4.3 Inconsistency of number of connections among neuron classes

The reciprocal relations discussed in Section 3 should hold also for any pairs of neuron class α and β . I have computed those numbers from the data files 'synapse_WF.txt', 'synapse_WT.txt' and 'synapse_AF.txt'. Then, I found many combinations of neuron classes for which the reciprocal relation is violated.

To represent the violation of reciprocity, I introduced the three quantities $\Delta N_s(\alpha, \beta)$, $\Delta N_r(\alpha, \beta)$ and $\Delta N_g(\alpha, \beta)$ which are defined by replacing A and B in equations (1) to (3) with α and β respectively. By definition, these three quantities should also vanish if the anatomical data describe connection between neuron classes α and β .

Chemical synapses and/or gap junctions connect 580 pairs of neuron classes. I computed the above three quantities for all of those 580 connections and found that one or more of those three quantities are non-vanishing for 273 pairs of connections. Although their values for most of these 273 combinations are less than four and not serious, there are some appreciable inconsistency as shown in Table 4.

Table 4. Significant Inconsistency among Number of Connections

neuron A	neuron B	$\Delta N_s(A, B)$	$\Delta N_r(A, B)$	$\Delta N_g(A, B)$
PDE	DVA	25	1	0
PVD	PVC	25	1	0
PVD	AVA	24	0	0
IL2	RIP	13	0	0
PDE	AVK	11	0	0
HSN	VCn	10	0	1
IL1	RIP	9	0	0
OLL	RMD	8	1	0
PHB	AVA	8	0	0
AVD	AVA	7	0	0
AVE	SAB	7	0	0
IL1	RMD	7	0	0
IL2	RME	7	0	0
AVE	AVA	6	-1	0
IL2	OLQ	6	-1	0
URX	RIA	6	0	0
I5	M4	5	0	0
IL2	RIH	5	0	0
PVC	AVB	5	0	0
RIA	SMD	5	-2	0
URY	SMD	5	0	0
ADL	AIA	4	0	0
AIB	RIM	4	0	0
AIZ	AIB	4	0	0
AWC	AIY	4	0	0
BAG	RIG	4	-1	0
DVA	AVE	4	0	0
PVN	VDn	4	0	0

Table 4 (continued)

neuron A	neuron B	$\Delta N_s(A, B)$	$\Delta N_r(A, B)$	$\Delta N_g(A, B)$
RIP	OLQ	4	1	0
RMD	RIA	4	-3	0
URA	RIP	4	0	0
URA	RME	4	0	0
VBn	SAA	4	0	0
NSM	M3	-4	0	0
PQR	AVA	-5	0	0
PVM	PDE	-5	1	1

It should be noticed that the inconsistency appears in ΔN_s rather than in ΔN_r . This fact suggests that many postsynaptic elements are overlooked in the original data. To confirm it, I have counted numbers of presynaptic contacts N_s and postsynaptic contacts N_r defined by

$$N_s = \sum_{\alpha} \sum_{\beta} N_s(\alpha, \beta)$$

$$N_r = \sum_{\alpha} \sum_{\beta} N_r(\alpha, \beta)$$

on neurons except the pharyngeal neurons. I found that $N_s = 5369$ while $N_r = 5040$.

The original paper says that there is often some ambiguity as to the identities of postsynaptic elements. I guess that several postsynaptic elements were overlooked because of this ambiguity or did not exist. Accordingly, the discrepancy between the presynaptic contacts and postsynaptic contacts is attributed not to errors of the collection of the original data but to this nature of the structure of synaptic contact.

The discrepancy represented on the first and the fifth lines of Table 4 arises from the inconsistent descriptions in the three tables of ventral cord synapses on PDE, DVA and AVK which is summarized in Table 5. I guess that almost ten postsynaptic elements of synapses from PDE to AVK as well as from PDE to AVK were overlooked.

Table 5. Inconsistent description on the connection to PDE (after the original paper)

Table of	partners	synapses from	synapses to and corecipients
PDE	DVA	1+2m	37, 20AVK, 2PVR, PDE, PVM
PDE	AVK	2+2m	1, 20DVA, HDC
DVA	PDE	22+14m	1, VB11
AVK	PDE	1+10m	2, 2PDE

5. Evaluation of circuitries in Fig.21 in the original paper

The six circuitries shown in Fig.21 in the original paper have been referred to in various papers. I have digitized the circuitries and examined their consistency.

For that purpose, the score of connection between the neuron classes α and β is defined. When α and β are connected by a T-shaped line, $N_{gj}(\alpha, \beta)$ is unity, while it is zero otherwise. In those circuitries, chemical synapses are graded by cross-hatches on arrows. I define the

grade of a chemical synapse between the neuron classes α and β , so that $N_{cs}(\alpha, \beta) = n + 1$, where n is the number of cross-hatches on an arrow from α to β .

In Fig. 21, some connections are described in more than one circuitries. In that case, the grade of a connection should be the same in different diagrams. However, I found that gap junctions which connect eleven pairs of neuron classes are inconsistently illustrated in Fig. 21 and I summarize it in Table 6. For instance, the first line of Table 6 represents that ADF and RIH are connected by a T-shaped line in Fig.21(b), but no gap junction is illustrated in Fig.21(a). Other lines of that table represent remaining ten inconsistently illustrated pairs.

Table 6. Inconsistent descriptions on connectivity with the gap junction in neuron circuitries. The alphabet in the parentheses indicates the circuitries from (a) to (f) in Fig. 21 of the original paper. The numeral represents whether the neuron pair of the left two column are connected (1) or not connected (0) by the gap junction in each circuitry.

neuron A	neuron B	grade of connection
ADF	RIH	0(a), 1(b)
ADL	AVD	1(a), 0 (b), 0(d), 0(e)
AIB	RIG	1(a), 0 (b), 0(c)
AVA	DAn	1(b), 0 (d), 1(e)
AVA	LUA	0(b), 0 (d), 1(e)
AVA	VAn	1(b), 0 (d), 1(e)
AVE	RMD	1(b), 0 (c), 1(d)
AVH	PHB	1(e), 0 (f)
BAG	RIG	2(b), 1 (c)
OLQ	RMD	2(b), 1 (c)
PDE	PVC	0(b), 1 (d), 1(e)

I found that 178 connections by chemical synapses are inconsistently graded in Fig. 21. Among them, the connections whose grade differs by two or more in different circuitries are listed in Table 7. For instance, the first line represents that the connection by the chemical synapse from ADL to AVA is represented by an arrow without a cross-hatch in Fig.21(a) while it is represented by an arrow with two cross-hatches in Figs.21(b), (d) and (e). [The grade 6 of the chemical synapse from PVN to AVD represents that PVN appears twice at the end of an arrow to AVD with two cross-hatches.]

Table 7. Inconsistent grades of connection with chemical synapses in circuitries in Fig. 21.

neuron A	neuron B	grade of connection
ADL	AVA	1(a), 3(b), 3(d), 3(e)
ADL	AVB	1(a), 3(b), 3(d)
ADL	AVD	1(a), 1(b), 3(d), 2(e)
ADA	RIM	0(c), 2(f)
ADA	RIP	0(c), 2(f)
ADA	SMD	0(c), 2(f)
AIZ	AVE	3(a), 1(b), 3(d)
ASH	AVD	2(a), 1(b), 3(d), 2(e)
ALA	AVE	1(b), 3(d)

Table 7 (continued)

neuron A	neuron B	grade of connection
ALM	PVC	1(b), 3(d), 2(e)
AQR	AVD	1(b), 3(d), 2(e)
AQR	PVC	1(b), 3(d), 2(e)
AQR	RIA	1(b), 3(c)
AUA	AVE	3(a), 1(b), 3(d)
AVA	DAn	2(b), 0(d), 2(e)
AVA	VAn	2(b), 0(d), 2(e)
AVD	DAn	2(b), 0(d), 2(e)
AVD	VAn	2(b), 0(d), 2(e)
AVE	DAn	2(b), 0(d)
AVE	VAn	2(b), 0(d)
AVF	AVB	3(b), 3(d), 1(f)
AVJ	AVE	1(b), 3(d), 1(f)
AVJ	PVC	1(b), 3(d), 2(e), 1(f)
AVK	AVE	1(b), 3(d), 2(e)
AVK	RIM	0(c), 2(e)
AVK	SMD	0(c), 2(e)
AWB	RIA	1(a), 3(c)
DVA	AIZ	0(a), 1(d), 3(e)
DVA	AQR	1(b), 1(d), 3(e)
DVA	AUA	0(a), 1(d), 3(e)
DVA	AVE	1(b), 3(d), 3(e)
DVA	SMB	2(c), 1(d), 3(e)
BAG	AVE	1(b), 3(d)
BAG	RIG	1(b), 3(c)
DVA	DBn	1(d), 3(e)
DVA	RIR	1(d), 3(e), 2(f)
DVA	VBn	0(d), 3(e)
DVB	RIG	1(b), 3(c), 2(e)
DVC	AIB	1(a), 3(e)
DVC	AVA	3(b), 3(d), 1(e)
DVC	RMF	1(c), 3(e)
DVC	RIG	1(b), 3(c), 3(e)
FLP	AVE	1(b), 3(d)
HSN	AIZ	1(a), 3(f)
HSN	AWB	0(a), 3(f)
LUA	AVD	1(b), 3(d), 1(e)
LUA	PVC	1(b), 3(d), 1(e)
OLL	RMD	3(b), 1(c)
PDE	DVA	1(d), 3(e)
PHB	AVD	0(b), 3(d), 1(e)
PHB	PVC	1(b), 3(d), 2(e)
PHC	PVC	1(b), 3(d), 1(e)
PLM	AVA	1(b), 3(d), 1(e)

Table 7 (continued)

neuron A	neuron B	grade of connection
PLM	AVD	1(b), 3(d), 1(e)
PQR	AVD	1(b), 3(d), 2(e)
PVC	AVE	1(b), 1(d), 3(e)
PVC	DBn	2(b), 1(d), 3(e)
PVC	VBn	2(b), 0(d), 3(e)
PVD	PVC	1(b), 3(d), 1(e)
PVM	PVC	1(b), 3(d), 1(e)
PVN	AVB	3(b), 3(d), 0(e), 0(f)
PVN	AVD	1(b), 6(d), 2(e), 1(f)
PVP	AVH	1(b), 2 (e), 0(f)
PVN	PVC	1(b), 3(d), 1(e), 1(f)
PVP	AVA	1(b), 3(d), 1(e)
PVP	PVC	2(b), 3(d), 1(e)
PVP	RIG	1(b), 3(c), 2(e)
RIB	AIZ	0(a), 2(c)
RIB	AVE	1(b), 2(c), 3(d)
RIF	ALM	0(b), 3(f)
RIF	PVP	1(b), 1(e), 3(f)
RIG	AIZ	0(a), 2(b), 2(c)
RIG	AVE	1(b), 2(c), 3(d)
RIH	AIZ	1(a), 3(b)
RIH	RIF	3(b), 0(f)
RIH	RIP	0(b), 2(c)
RIS	AVE	1(b), 3(c), 3(d)
RIR	RIA	3(c),1(f)
RIS	AVK	3(c), 0 (e)
RMG	AVE	1(b), 1(c), 3(d)
SDQ	AVA	1(b), 3(d), 3(e)
URX	AUA	1(a), 3(c)

6. Conclusion

It should be emphasized the anatomical data is almost perfectly self-contained. Although the above description gives an wrong impression that the anatomical data involves many errors, it is much less than the huge information involved in it. I wish that my analysis is useful for better understanding of the neuronal system of *C. elegans*

In conclusion, I express my regrets, first of, all to you and your colleagues and secondly to my young colleagues who created the data files for their elaborate and patient work.