From store receipts to finding solution for the brain

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Brain exhibits large number of seemingly unrelated features in multiple levels. Hence, we often think that it is very difficult to solve this system. Can we actually find a way to utilize these large numbers of features to solve the system? Is there a condition where large number of unrelated findings provides certain advantages in solving a system? Let us get some insights from a problem that we may encounter occasionally. I will tell it here as a story.

I used to shop from a small corner store called "Super Dollar Store". This shop does not provide a detailed bill. They type only names and numbers of items that were sold, and the total amount. The cost of each item includes taxes and is in multiples of a whole dollar - so the name "Super Dollar Store". They do it by changing the size of the sachets and packets according to the market price. I buy coffee, sugar and milk from this shop. I have been lazy to ask the exact price of each of the items. One day as I was sitting at home, I thought of figuring this out just by looking at the receipts. Can I do it?

[Solving the system means finding the price of each item. Different combination of items on different days shows different total amounts. This Dollar store problem involves finding the solution (costs of) for coffee, sugar and milk (only 3 variables); whereas, in the case of the brain there are large number of variables. If we can solve this problem, then the deep principle of the method may be transferred towards discovering the solution for the brain. Huge ambition! But will it work? However, it is reasonable to assume that if the principle can work for a small problem, then it must work for a large problem.].

I do not clean up my room very often. So, I decided to look for previous receipts. I got one. I started solving the puzzle. Since I cannot use mathematical equations to solve the brain, I should be solving the dollar store problem without any mathematical equations. Hence, I am trying to solve it by trial and error method. However, knowing how the process work mathematically does not hurt. Therefore, I will be writing them down as well. This will help us to know the deep underlying principle and the necessary conditions for finding the solution, which can be transferred to solve a large system such as the brain.

Total cost = cost of coffee + cost of sugar + cost of milk

Total cost = (number sachets of coffee x cost of 1 sachet of coffee) + (number sachets of sugar x cost of 1 sachet of sugar) + (number of packets of milk x cost of 1 packet of milk)

 $m_1 = number of sachets of coffee$ $x_1 = \frac{s}{sachet of coffee}$ $m_2 = number of sachets of sugar$ $x_2 = \frac{s}{sachet of sugar}$ $m_3 = number of packets of milk$ $x_3 = \frac{p}{packet of milk}$ $y_1 = total cost printed in the receipt$

Step I

I got one receipt and it shows that I bought 1 sachet of coffee, 2 sachets of sugar and 3 packets of milk one day. This can be written as follows.

 $m_1x_1 + m_2x_2 + m_3x_3 = y_1$

 $1x_1 + 2x_2 + 3x_3 = 22$ (1)

Solving the system means to figure out the actual cost of one sachet of coffee, sugar and one packet of milk. We may quickly reach a solution that cost per coffee, sugar and milk in dollars can be written as \$1, \$3, and \$5 respectively. At the first look, we may think that it is correct. But if we try other numbers, there are many other possible combinations of values for each item that can give the same total cost. For example, cost of coffee, sugar and milk can also be respectively a) \$4, \$3, \$4, b) \$2, \$4, \$4, c) \$2, \$7, \$2 and, d) \$3, \$5, \$3 etc. In fact, many combinations of values are possible. So we can say that there are many solutions for the current system. If the price was in cents (not in whole dollars), then it is likely that

there will be infinitely many solutions. So, the information derived from once receipt alone is not helping us to figure out the actual cost per sachet of coffee & sugar or packet of milk.

Inference: When a system has more than one variable (coffee, sugar, milk etc.) and it exhibits different findings (total value or result), then to understand (to solve) the system we have to examine multiple findings at the same time.

[When we examine only one finding from the nervous system, we will not be able to solve the system. We are likely to end up in many possible solutions. For example, many mechanisms were proposed as candidate solutions for storing memories. In fact, all of them have some relationships with brain's functions. However, to understand the actual solution, we need to use large number of findings from different levels. This is similar to the need for more information from our example of coffee, sugar and milk situation. Now, it forces us to examine findings from additional areas of brain research. This is an inevitable step in solving any system].

[I know that some of the readers who already know where we are going will be bored by now. They can directly go to Stage VI, where there is an interesting example that we will not encounter in linear algebra! It gives us some hint as to what was preventing us from solving the nervous system]

Step II

So, I looked again for my receipts of my previous purchases. Within a few minutes, I found another receipt. This shows that one day I had purchased only coffee and milk, which can be written as follows.

 $m_1 x_1 + m_2 x_2 + 0 x_3 = y_2$ 2x₁ + 0x₂ + 1x₃ = 7------(2)

Along with the previous information, this new information has brought some limitations/rigidity to the system that will direct us towards the cost of each item. Now, we need values for x_1 , x_2 and x_3 that will simultaneously satisfy both equations (1) and (2). In other words, the new equation has brought some constraints that enable us to get directions towards the correct solution. By mere trial and error method, we can try to figure out the cost of individual items that can result in equation (2). Since the costs are multiples of a whole dollar, then the possible costs of coffee and milk respectively can be\$3& \$1, \$2 & \$3, and \$1&\$5. When these values are applied to equation (1), then the possible values for coffee, sugar, and milk respectively are \$3, \$8, \$1 and \$1, \$3, and \$5. However, we are not sure which combination of these values is correct. However, we have narrowed down the possibilities to two combinations of values. This indicates that as we increase the number of findings with different combinations of variables, then the additional constraints within these equations allow us to narrow down the possible solutions. This is progress.

[In the case of the nervous system, we can look for additional findings of the system from different levels. We can ask the following questions. What type of an inter-connectable explanation will enable us to explain sleep? What type of an inter-connectable mechanism can explain various findings and correlations between long-term potentiation (LTP), which is an electrophysiological finding that has found many correlations with learning and memory? How can we explain consolidation of memory (apparent transfer of locations of memory storage from the hippocampus to the cortex) in terms of the operational mechanism of generation of memory? The candidate mechanism is expected to provide inter-connectable explanations for all the findings of the system. As we narrow down the candidate mechanisms, then examination of additional findings from the system will eventually guide to the solution/s. In systems with large number of findings (many variables), it is most likely that the system has a unique solution. By examining which of the candidate mechanism/s continue to show matching explanations, we will be able to continue this process until we reach one unique solution].

Step III

Now, I am in search of more receipts to solve the puzzle. What we are actually looking for is a different combination of items, which will provide us more constraints so that we can figure out what the solution is. I got one more. It can be written as follows.

 $m_1x_1 + m_2x_2 + m_2x_3 = y_3$ $3x_1 + 4x_2 + 5x_3 = 40$ (3) Now, we can directly go and plug in the possible values of x_1 , x_2 , and x_3 that we got after trying to solve equation (2) into equation (3) and see which one fits correctly. We get the correction solution as \$1 for coffee, \$3 for sugar, and \$5 for milk. Again, this reiterates the fact that each new combination of variables provides additional constraints that guides us towards reaching the correct solution.

The conclusion from the above exercise is the following.

1. Any single bill or single finding by itself will not help us solve a system with several findings. It is necessary to simultaneously examine more than one finding to move towards the solution.

2. We need to gather more combinations of properties and figure out the constraints offered by their combinations. Then use them to narrow down the possible solutions. Always make sure that the possible solutions match with all the previous findings.

3. As we use more equations and bring additional constraints, the number of possibilities reduces. We will be moving closer and closer to the final solution. Continue this exercise until we figure out the correct solution.

4. In a system with large number of findings, we can ignore observations with redundant features. Any observation with unique features should be included. In a system with large number of disparate findings, we can always expect a unique solution.

Step IV

Once we have collected enough number of receipts (findings) to reach a solution, it is time to verify whether we are correct or not. For this, we can examine additional findings from the system. For this, we can look for more previous receipts. Yes. I found one more receipt. Here, I returned one sachet of coffee from a previous purchase since the expiry date was over. So, the shopkeeper reduced the price of it from my total bill. It can be written as follows.

 $-m_1x_1 + m_2x_2 + m_3x_3 = y_4$ $-1x_1 + 1x_2 + 2x_3 = 12$ (4)

Now, we can plug the values of x_1 , x_2 , and x_3 from our solution and see it matches with the bill. Yes, we can find it correct.

[In the case of the brain, we can use additional findings to verify whether the unique solution we arrived is correct or not. We can look at more findings to confirm that our findings are correct. Even though this is all what we need, in science we go one further step for its final confirmation. This is the step of making testable predictions and verifying them. It is explained in the next step].

Step V

The next step of verifying the solution is to make predictions. Here, we can plan to purchase a different combination of items and predict the bill. Now go to the shop and buy a new combination. To make it complicated, you may even return one item if you think it has some valid problems. Luckily, I found a reason. The expiry date printed on the pack of milk that I bought on the day before is not readable – a valid reason for returning the packet. Now, I can expect the following.

 $m_1x_1 + m_2x_2 - m_3x_3 = y_5$

 $1x_1 + 1x_2 - 1x_3 = -1 - \dots$ (5)

So here I made a prediction that the shopkeeper will refund1\$& I found it to be correct. Now after doing this ultimate test, we can confirm the prices of each item.

Step VI

An apparently "trivial" error can lead to a more complicated scenario.

Imagine the amounts of the bill in each of the first three conditions were increased by 1\$.So instead of equations (1), (2) and (3), we need to re-write them as follows.

$1x_1 + 2x_2 + 3x_3 = 23$	(6)
$2x_1 + 0x_2 + 1x_3 = 8$	(7)
$3x_1 + 4x_2 + 5x_3 = 41$	(8)

Here, we will fail to reach a solution however hard we try. Difficulties in finding the solution for the nervous system can be compared to a similar condition. Now we have to ask some questions such as a) Is the billing machine making an error in calculations? b) Is the shopkeeper charging an extra dollar for no reason? c) Are they billing for one more item every time? In fact, the shopkeeper was charging \$1 for a small carry bag each time! So, we have to now re-write the system of linear equations by adding that variable to every equation to obtain a new system of linear equations (9), (10) and (11) as follows.

$1x_1 + 2x_2 + 3x_3 + 1x_4 = 23$	(9)
$2x_1 + 0x_2 + 1x_3 + 1x_4 = 8 - \dots -$	(10)
$3x_1 + 4x_2 + 5x_3 + 1x_4 = 41$	(11)

As the number of variables increases, trial and error method will become more and more difficult. But it can be carried out if we are ready to spend time and make effort. Since we know that we can proceed to solve the system algebraically, let us do it. What we need to do is to find a way to remove the common factor $1x_4$ from all the equations. This can be achieved by subtracting one equation from another one and use the new equations to solve the system. We can proceed further, thinking that it will eventually help us to find the solution. Since the coefficients of the variable x_4 are the same, we can minus between equations (9), (10) and (11) and eliminate this variable from the equations.

(11) - (10), we get $1x_1 + 4x_2 + 4x_3 = 33$	· (12)	
(10) - (9), we get $1x_1 - 2x_2 - 3x_3 = 33$	- (13)	
(12) - (13), we get $6x_2 + 6x_3 = 48$	(14)	

Since 6 is a common factor in all the elements, we can divide the equation (14) by 6

 $(14) \div 6$, we get $1x_2 + 1x_3 = 8$ ------(15)

(11) - (9), we get $2x_1 + 2x_2 + 2x_3 = 18$ ------(16)

Since 2 is a common factor in all the elements, we can divide the equation (16) by 2

 $(16) \div 2$, we get $1x_1 + 1x_2 + 1x_3 = 9$ ------(17)

Now (17) - (15) shows that $1x_1 = 1$. Therefore, the cost of coffee is \$1 per sachet.

When x_1 is substituted with \$1 in equations ((9), (10), (11) and (17), we get the following equations (18), (19), (20) and (21) respectively.

$2x_2 + 3x_3 + 1x_4 = 22$	(18)
$0x_2 + 1x_3 + 1x_4 = 6$	
$4x_2 + 5x_3 + 1x_4 = 38$	(20)
$1x_2 + 1x_3 + 0x_4 = 8$	

The next steps are carried out to reduce the number of variables in equations to two by methods of subtraction or addition. Since coefficients of x_4 in majority of equations are 1, then we can try to eliminate it.

(18) - (19), we get $2x_2 + 2x_3 = 16$ ------ (22) (20) - (19), we get $4x_2 + 2x_3 = 38$ ------ (23)

Eliminating the variable x₄ did not result in finding any new relationships other than (21)

We can also make other approaches to reduce the number of variable in an equation as follows.

(21) - (19), we get $1x_2 - 1x_4 = 2$ ------ (24) (18) - (21), we get $1x_2 + 2x_3 + 1x_4 = 14$ ------ (25) (20) - (21), we get $3x_2 + 4x_3 + 1x_4 = 30$ ------ (26)

We can write the final simplified equations as

 $1x_1 = 1$ $1x_3 + 1x_4 = 6$ $1x_2 + 1x_3 = 8$ (19)
(21)

It is not possible to solve the system of linear equations containing equations (9), (10) and (11). A new problem is preventing us from solving the new system. This is due to the presence of 4 variables; but only 3 equations are available. It was possible to solve the system of linear equations containing equations (1), (2) and (3), because there were having only three variables.

To solve the system of three equations (9), (10), and (11) having four variables, we need to obtain at least one more equation (27) to make a new system of linear equations for finding its solution as follows.

$1x_1 + 2x_2 + 3x_3 + 1x_4 = 23$	(9)
$2x_1 + 0x_2 + 1x_3 + 1x_4 = 8$	(10)
$3x_1 + 4x_2 + 5x_3 + 1x_4 = 41$	(11)
$2x_1 + 3x_2 + 2x_3 + 1x_4 = 22$	(27)

This can be solved as follows.

(11) - (27), we get $1x_1 + 1x_2 + 3x_3 = 19$ ------ (28) (23) - (17), we get $2x_3 = 10$. Hence, $x_3 = 5$ Substituting values of x_3 in equation (14), we get $6x_2 = 18$. Hence, $x_2 = 3$

Substituting values for x_1 , x_2 , x_3 and x_4 in any of the equations (9), (10), (11), or (12), we get $x_4 = 1$. Availability of the fourth equation (equation number 27) has now provided us with a solvable system of linear equations. In fact we arrived at the solution very quickly. In short, to solve a system of linear equations the number of equations must be at least equal to the number of variables.

Let us now imagine that we have all the above four equations but without the common variable $1x_4$, as shown below.

$1x_1 + 2x_2 + 3x_3 = 23$	(9)
$2x_1 + 0x_2 + 1x_3 = 8$	(10)
$3x_1 + 4x_2 + 5x_3 = 41$	(11)
$2x_1 + 3x_2 + 2x_3 = 22$	(27)

Let us try to solve this system of linear equations.

$(27) - (10)$, we get $3x_2 + 1x_3 = 14$	(29)
(9) x 2, we get $2x_1 + 4x_2 + 6x_3 = 46$	(30)
(29) - (10), we get $4x_2 + 5x_3 = 38$	(31)
(29) x 5, we get $15x_2 + 5x_3 = 70$	(29)
$(29) - (31)$, we get $11x_2 = 32$	(32)

 $x_2 = 32/11$. We are not getting the value of x_2 as a whole number. We have set it as a precondition for this problem. Hence, we can say that we are getting a wrong solution.

In this last case, we made a system of linear equations consisting of equations (9), (10), (11), and (27), where there are four equations and only three variables. Still we could not solve this system. This shows that if we ignore one variable from the system, it will not allow us to solve the system however hard we try. This difficulty has many similarities to our current difficulties in solving the nervous system.

Conclusion

We all know that the functions of the nervous system are not as simple as that of a small system of linear equations. Even though the example shown here might look simple, it highlights certain facts. In a system of linear equations, each variable has specific relationships with other variables and are determined by the values of their coefficients. It can be noted that in the early part of **Step VI**, removal of x_4 from equations (9), (10) and (11) caused changes in the coefficients of remaining variables. Even though the coefficient of x_4 is 1 in all the equations, it provides certain specific constraints to the relationship between variables, which depends on the values of the coefficients of those variables in each equation. This highlights the fact that brain functions with different properties results from combinations of different factors. Hence, to solve the nervous system it will be necessary to use the variable of first-person internal sensations, which is the unique and most important function of the system under examination.

Even in a simple of system of linear equations, eliminating one variable does not allow us to solve the system. It is only when we bring the variable of internal sensation into the findings that we will be in a position to align the constraints provided by different findings of the nervous system to reach the solution. We need to make sure that we have sufficient number of findings (equations) such that all the variables are included in the system at least once. If we have large number of findings so that a) number of equations are much more than the number of variables, and b) different combinations of variables are present in them, then we can try to use different sets of equations (having all the variables) to solve the system. If we are having difficulties to solve the system by using a subset of findings, then we can use another subset of findings and continue this process until we reach the solution.

In the case of the nervous system, we have been ignoring the formation of first-person inner sensations thinking that it is something very difficult to understand. This unique function of the nervous system is associated with most of the higher brain functions such as perception, memory, thought process, hypothesis building, voluntary motor actions, language, emotions, and consciousness. Ignoring it is similar to ignoring the cost of the small carry bag that we demonstrated. When we try to solve a system with multiple features, we should be aware of everything, including those features that we often ignore for "trivial" reasons such as the cost of the plastic bag or "obvious" reasons such as difficulties in studying the first-person inner sensations.

Specialization and super-specialization of each area of research has led to the accumulation of huge amount of information and it has become very difficult to undertake examination of large number of findings simultaneously. However, this is similar to having large number of equations with different combinations of variables. In fact, they provide a condition with surplus number of equations needed to solve the system. This situation provides tremendous opportunity to solve the system by selecting different subsets of those findings so that all the variables are included in that system at least once. This provides an added advantage that the remaining findings (equations) can be used to verify whether the derived solution is correct or not. While trying to use findings from several fields of brain research for this purpose, one is likely to be called "Jack of all trades; but master of none". Nevertheless, being a Jack-Of-All-Trades provides one an opportunity to understand the constraints offered by the variables associated with them and use them to figure out the solution that can interconnect all the findings.

In the case of the nervous system, more than fifty major findings from different fields of brain sciences can be used for this purpose. A subset of these findings can be used to arrive at the solution and the rest of the findings can be used to verify the derived solution. Even though trying to solve the system using many findings by trial and error method will take lots of time and effort, it is possible to eliminate the several values for many variables at various stages. We can also eliminate all the tested solutions that failed in the previous attempts using different subsets of findings. This will enable to narrow down the possibilities and eventually guide towards the correct solution. Since a system having disparate findings can have only a unique solution, trial and error method can result in the correct solution even though it is expected to be a tedious exercise.

We solved the problem of the Super Dollar Store using numbers (whole numbers). Actually, numbers do not exist; we made them. But we used them so frequently that we knew that we can rely on the outcomes either when we used them in trial and error methods as in Steps I, II & III or in mathematical methods as in Steps IV, V & VI. We believed in the result that we got, because it matched the logic and the values fit in all the equations. Similarly, when we solve the nervous system using large number of findings by including the variable of internal sensations present in most of its functions, then the result that we get can be trusted. If it allows us to make predictions, then we can test them.

How does the example from Super Dollar Store contribute towards solving the nervous system?

The example of finding a unique solution for a system of linear algebraic equations highlights the importance of viewing internal sensations generated during a higher brain function as one of the variables in that function's equation. However, one may argue that findings of brain functions do not behave like linear algebraic equations. Here we will examine some of the properties of system operations that operate very precisely as mathematical equations. This will highlight the need for treating them exactly same as mathematical equations for obtaining the unique solution of the nervous system. In this exercise, we need to stick with the logical arguments behind each finding. Then only we can take advantage of the deep principle of reaching a solution that can interconnect different variables in the system.

Associative learning should make specific changes at the location of convergence of pathways through which these stimuli propagate. Tracing down these pathways have confirmed that locations of convergence are the places where learning generated changes occur (for example amygdala and hippocampus).	(1)
As long as the learning generated change persists, arrival of one of the sensory stimuli participated in learning will induce internal sensation of the second stimulus with which it was associatively learned and generate motor action that the second stimulus would have generated by itself. The latter is necessary to fulfill the requirements of a conditioning paradigm.	(2)
Memory is first-person internal sensation accessible only to the owner of the nervous system, which is a cue-induced cue-specific hallucination about the item whose memories are being retrieved (Ref. 1).	(3)
Internal sensation of higher brain functions occurs only within a narrow range of oscillating extracellular potentials. Extracellular ionic changes reflect the net effect of intracellular changes in the surrounding region. This necessitates that the operational mechanism is contributing to/ associated with the vector components of those oscillations.	(4)
No cellular or molecular changes were observed during memory retrieval. This indicates that memory retrieval takes place by a passive reactivation of the learning generated change.	(5)
It is possible to associate (associatively learn) more than one pair of items within a second, which can then be retrieved again within one second. This shows that both learning and memory retrieval take place in millisecond time-scales.	(6)

Solution for the system can be found by asking the question, "What should be the anatomical location where changes should occur to satisfy the above six conditions?" This is exactly same as finding the solution for the three mathematical equations (1), (2) and (3). If we find one candidate location with a suitable mechanism, then we can test whether it is suitable to operate in synchrony with the constraints provided by the remaining features of the system.

We can try to solve the system using trial and error method as we did in Steps I, II, III (see pages 2 and 3) in the example of the system of linear equations and arrive at the solution. The following findings provide precise descriptions how the basic principle of operation of the system should be taking place.

1. Convergence of inputs - Postsynaptic potentials (PSPs) attenuate as they propagate towards the neuronal cell body. PSPs also mix with other PSPs arriving from other spines to the dendrite. Hence, an ideal location for a learning change with specificity is at the spine head. To satisfy these requirements, there are only three possibilities.

a) Inputs from associatively learned stimuli arrive at the adjacent spines of one neuron

b) Inputs from associatively learned stimuli arrive at any spines of one neuron

c) Inputs from associatively learned stimuli arrive at the spines of different neurons; but they interact by removing the insulation provided by the extracellular matrix between these spines.

Conditions 1a) and 1b) are not possible because no electrical cables are present between the spines for providing specificity. Moreover, mean inter-spine diameter is more than mean spine head diameter making condition 1a) not possible through the extracellular matrix space. There are no electric cables with insulations between spines of a dendritic branch, making conditions 1a) and 1b) not possible. Hence, the only condition that can satisfy the requirements is condition 1c).

- 2. Conditioning paradigm in associative learning necessitates two associatively learned sensory inputs to propagate to (or activate) each other's' output neurons for generating their corresponding output functions. Hence, the associative learning mechanism is expected to get connected to separate output neurons. This can match with only condition 1c). To explain 1c), it is necessary to explain the interaction between abutted spines that belong to different neurons. This interacting mechanism should be reversible (to explain its ability to remain only for a short duration to explain working memory), stabilizable (to explain its ability to remain only for a long duration to explain a spectrum of short-term and long-term memories).
- 3. Memory in response to one of the associatively learned stimuli is a first-person internal sensation and can be viewed as a cue-induced hallucination. Cue stimulus is expected to trick the interacting spine to hallucinate that it is receiving an input from the environment through the latter's presynaptic terminal (**Ref. 1**). A pre-condition or an ideal plot or background condition for this to occur is continuous depolarization of the postsynaptic terminal by its presynaptic terminal. (Continuous quantal release of neurotransmitter molecules even during sleep and the absence of toxins on Earth that can completely block this quantal release guarantees the maintenance of background state. Furthermore, intermittent activation of the synapses during day by different internal and external stimuli & possible activation of the synapses during sleep during altering wave patterns of oscillating extracellular potentials also help to maintain the background state). So, the cue stimulus should get inserted into an intermediate path at the location of convergence for tricking the path of the second stimulus to generate a hallucination that it is receiving sensory stimulus from the second stimulus. The expected unitary internal sensations generated should be able to get integrated to generate the system effect of memory of the associatively learned second item.
- 4. The cue-induced retrieval of memory should take place in association with the vector components contributing to the oscillating extracellular potentials. It should have at least two vector components that will be activating at nearly perpendicular directions. Synaptic transmission between neurons of two neuronal orders can provide the component. Interaction between spines that belong to different neurons of the same neuronal order is expected to produce a second component perpendicular to the direction of synaptic transmission.
- 5. Since no cellular or molecular changes were observed during memory retrieval, memory is generated by a passive reactivation of learning-generated change. So the cue stimulus should reactivate the learning change occurred between spines that belong to different neurons.
- 6. Learning and memory retrieval take place in millisecond time-scales. This has to be a mechanism generated spontaneously by the energy contained in the depolarization. So this should be occurring through a mechanism taking place concurrent with the propagation of depolarization along the membranes. We can exclude all delayed events as candidate mechanisms.

The six conditions 1 to 6 that we used to solve the nervous system inform that the system can operate to function only through an inter-neuronal inter-spine interaction (**Ref.2**). It also provides an auxiliary condition that can generate internal sensations without motor actions when inter-spine interaction takes place between spines that belong to different dendritic branches of a single neuron.

References

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