Computation in olfactory neuronal networks beyond synchronization

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Overview

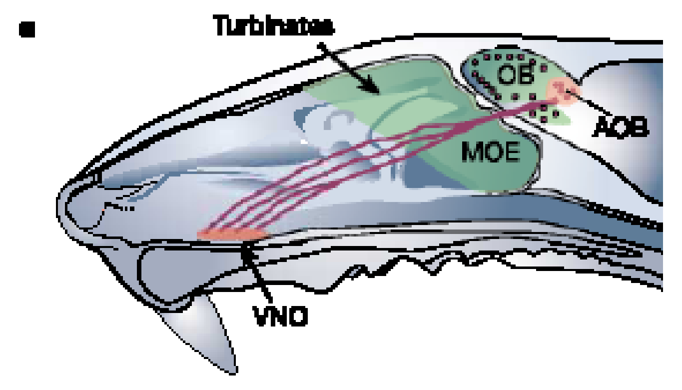
- The problem: olfactory coding
- The Lempel-Ziv-distance between spike trains
- Neuronal clustering in the olfactory system:
    - Experimental procedure
    - Data analysis
    - Results
- An explanatory framework
- Open questions

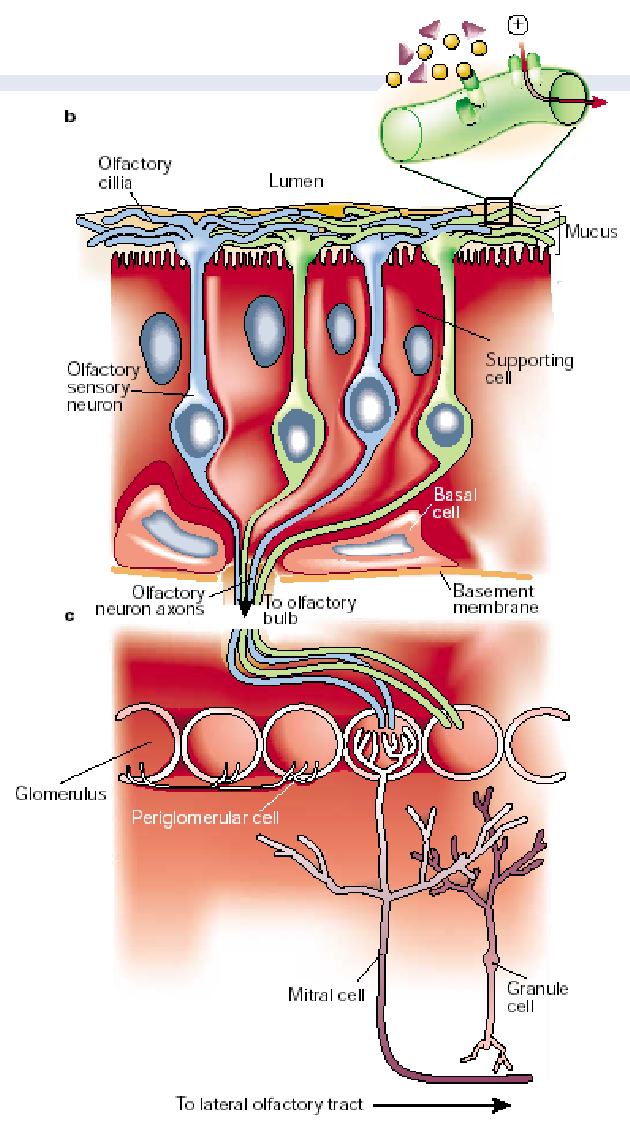
Olfaction

Odor is a **chemical sense**, differing from senses which process physical input (photon density / air pressure / particle velocity).

A major distinction is the **synthetic property** of olfaction: the ability to assign a specific identity to a great number of component mixtures.

Olfactory computation refers to the problem of how specific ordors lead to a specific activation of the output neurons (mitral cells) given the boundary condition of neuronal connectivity in the olfactory bulb.





Firestein, Nature, 2001

Odor encoding by neuronal clusters

Understanding olfactory coding requires the **analysis of functional clustering** within a neuronal network of an olfactory sensor when confronted by a specific odour.

The most frequently applied criterion determining membership of a specific neuron to such a cluster is whether the activity of that neuron is **synchronised** with the other neurons in the cluster:

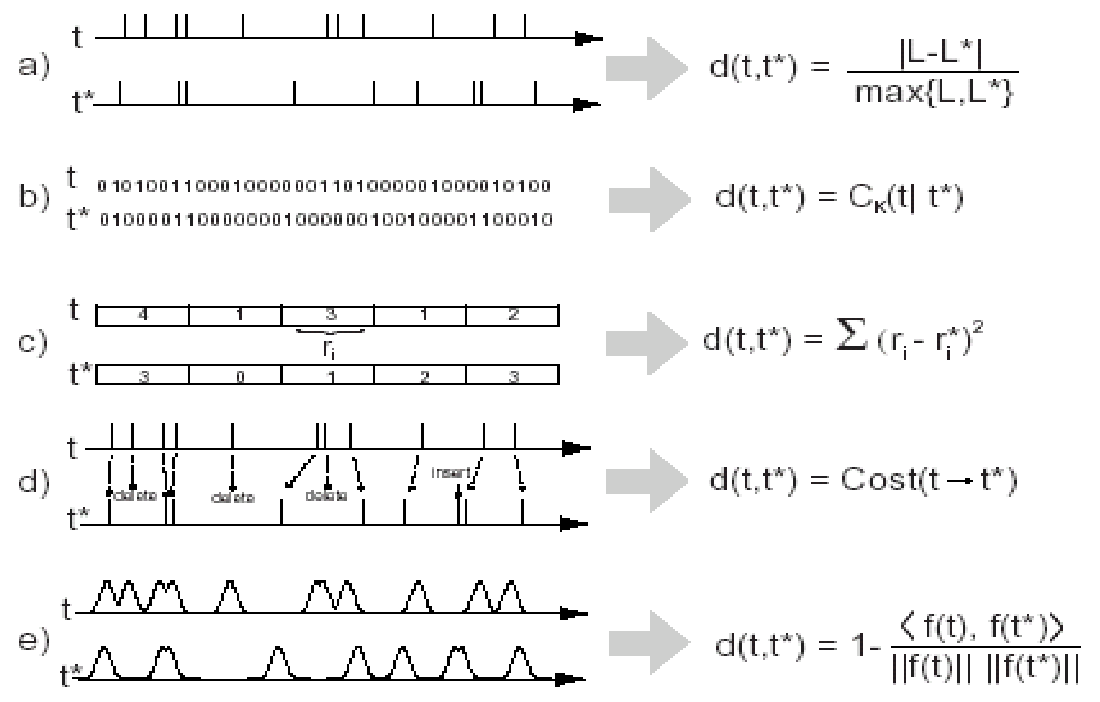
- Support in invertebrates (e.g. bees)
- Unclear situation in vertebrates
- Is synchronization the correct marker of a computation?
- How is synchronized activity decoded by higher areas?

We address this question using **alternative criteria for neuronal population identification** based on the Lempel-Ziv distance (LZ-distance) of spike trains and the sequential superparamagnetic clustering paradigm.

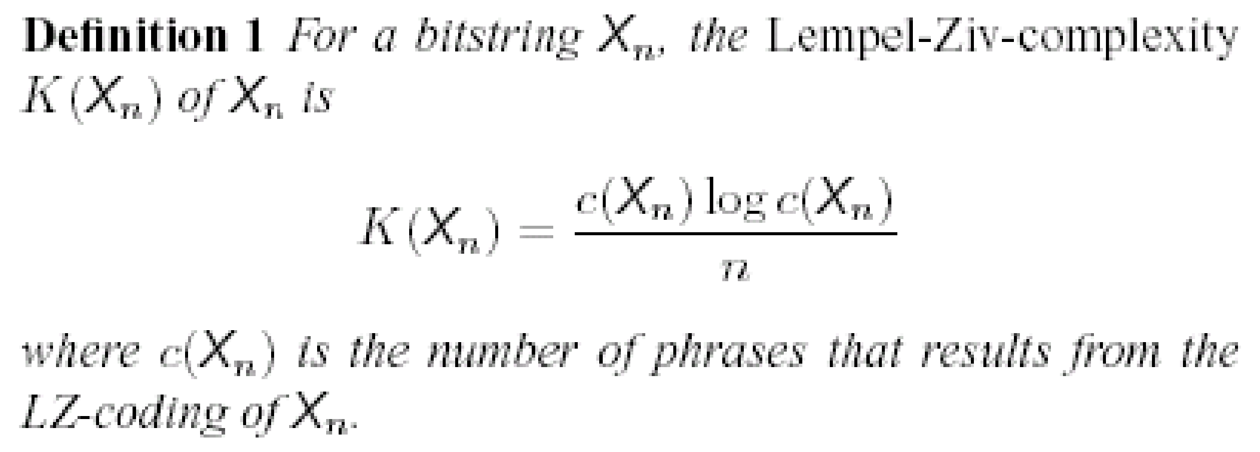
Spike train distance measures

The empirical determination of neuronal clusters requires:

- A measure (distance) defining the „closeness“ within a cluster (we compare the LZ-distance with the C-distance (coincident firing))
- A clustering algorithm (unbiased).



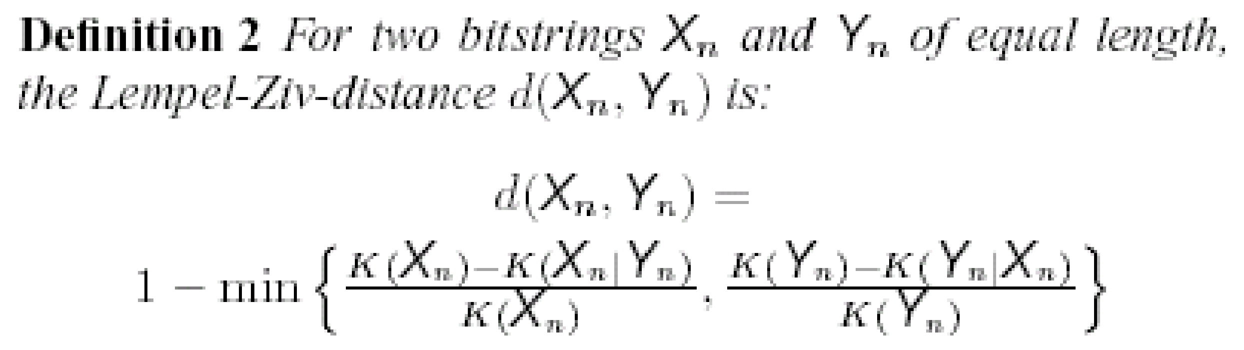
The Lempel-Ziv-distance (1)



Definition 1 *For a bitstring* X_n, *the* Lempel-Ziv-complexity $K(X_n)$ *of* X_n *is*

$$K(X_n) = \frac{c(X_n)\log c(X_n)}{n}$$

where $c(X_n)$ *is the number of phrases that results from the LZ-coding of* X_n.

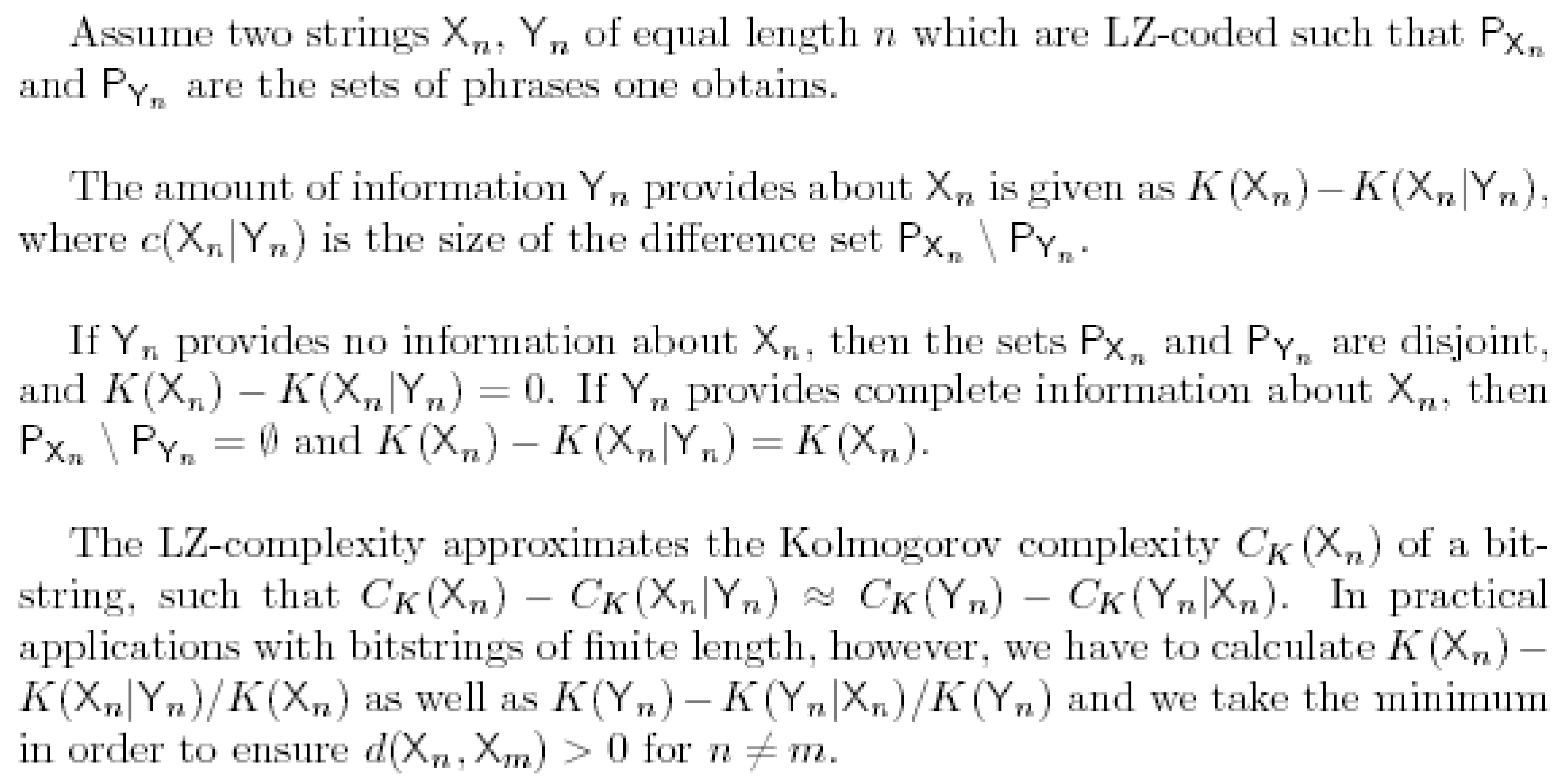


Definition 2 *For two bitstrings* X_n *and* Y_n *of equal length, the Lempel-Ziv-distance* $d(X_n, Y_n)$ *is:*

$$d(X_n, Y_n) =$$

$$1 - \min\left\{\frac{K(X_n) - K(X_n|Y_n)}{K(X_n)}, \frac{K(Y_n) - K(Y_n|X_n)}{K(Y_n)}\right\}$$

The Lempel-Ziv-distance (2)



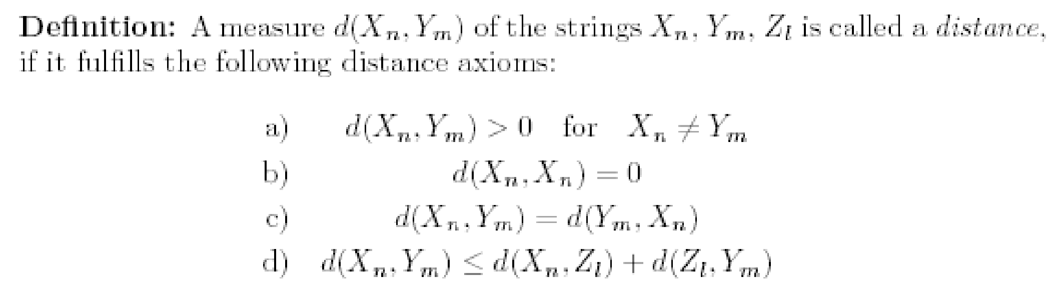
Assume two strings X_n, Y_n of equal length n which are LZ-coded such that $\mathsf{P}_{\mathsf{X}_n}$ and $\mathsf{P}_{\mathsf{Y}_n}$ are the sets of phrases one obtains.

The amount of information Y_n provides about X_n is given as $K(\mathsf{X}_n) - K(\mathsf{X}_n|\mathsf{Y}_n)$, where $c(\mathsf{X}_n|\mathsf{Y}_n)$ is the size of the difference set $\mathsf{P}_{\mathsf{X}_n} \setminus \mathsf{P}_{\mathsf{Y}_n}$.

If Y_n provides no information about X_n, then the sets $\mathsf{P}_{\mathsf{X}_n}$ and $\mathsf{P}_{\mathsf{Y}_n}$ are disjoint, and $K(\mathsf{X}_n) - K(\mathsf{X}_n|\mathsf{Y}_n) = 0$. If Y_n provides complete information about X_n, then $\mathsf{P}_{\mathsf{X}_n} \setminus \mathsf{P}_{\mathsf{Y}_n} = \emptyset$ and $K(\mathsf{X}_n) - K(\mathsf{X}_n|\mathsf{Y}_n) = K(\mathsf{X}_n)$.

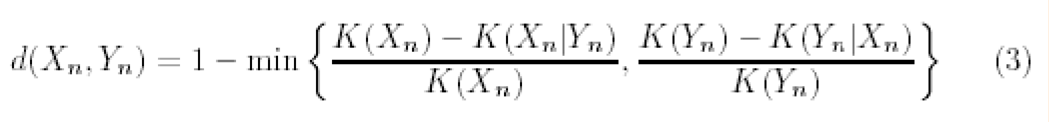
The LZ-complexity approximates the Kolmogorov complexity $C_K(\mathsf{X}_n)$ of a bitstring, such that $C_K(\mathsf{X}_n) - C_K(\mathsf{X}_n|\mathsf{Y}_n) \approx C_K(\mathsf{Y}_n) - C_K(\mathsf{Y}_n|\mathsf{X}_n)$. In practical applications with bitstrings of finite length, however, we have to calculate $K(\mathsf{X}_n) - K(\mathsf{X}_n|\mathsf{Y}_n)/K(\mathsf{X}_n)$ as well as $K(\mathsf{Y}_n) - K(\mathsf{Y}_n|\mathsf{X}_n)/K(\mathsf{Y}_n)$ and we take the minimum in order to ensure $d(\mathsf{X}_n, \mathsf{X}_m) > 0$ for $n \neq m$.

The Lempel-Ziv-distance (3)

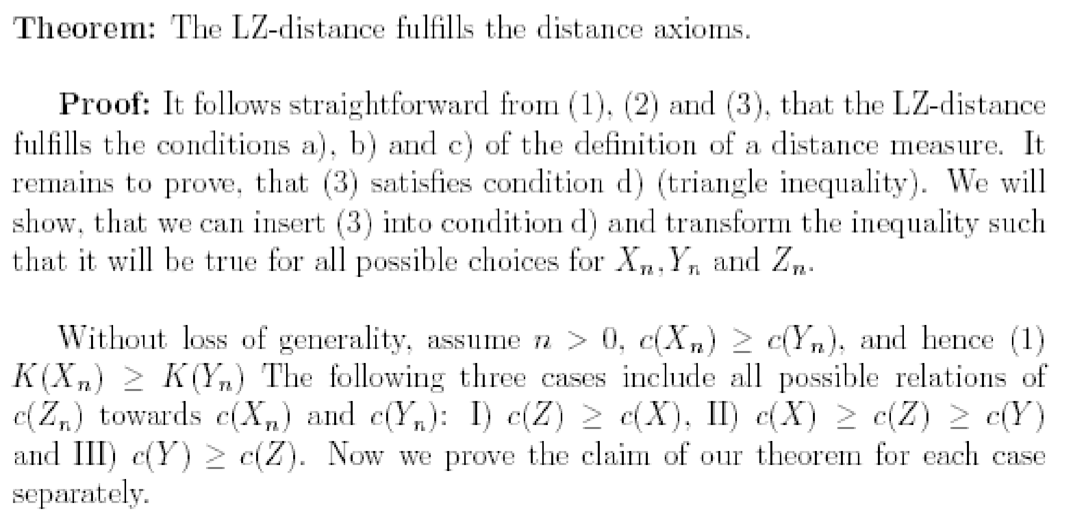


Definition: A measure $d(X_n, Y_m)$ of the strings X_n, Y_m, Z_l is called a *distance*, if it fulfills the following distance axioms:

$$\begin{array}{ll} \text{a)} & d(X_n, Y_m) > 0 \quad \text{for} \quad X_n \neq Y_m \\ \text{b)} & d(X_n, X_n) = 0 \\ \text{c)} & d(X_n, Y_m) = d(Y_m, X_n) \\ \text{d)} & d(X_n, Y_m) \leq d(X_n, Z_l) + d(Z_l, Y_m) \end{array}$$



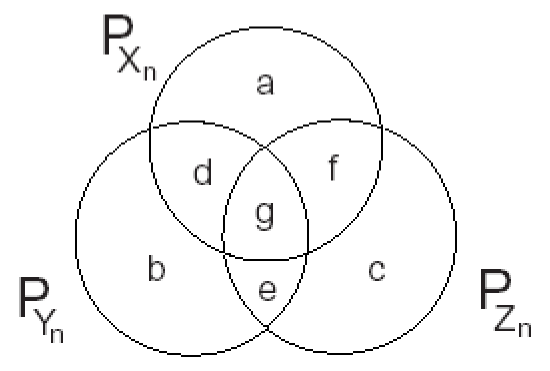
$$d(X_n, Y_n) = 1 - \min\left\{\frac{K(X_n) - K(X_n|Y_n)}{K(X_n)}, \frac{K(Y_n) - K(Y_n|X_n)}{K(Y_n)}\right\} \qquad (3)$$

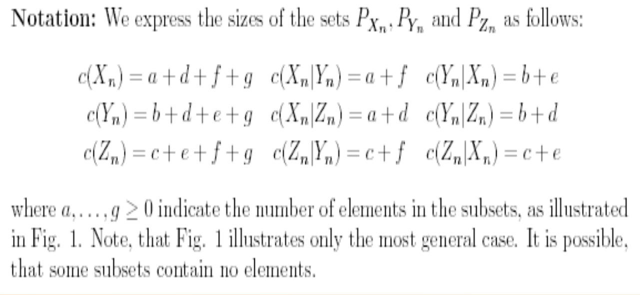


Theorem: The LZ-distance fulfills the distance axioms.

Proof: It follows straightforward from (1), (2) and (3), that the LZ-distance fulfills the conditions a), b) and c) of the definition of a distance measure. It remains to prove, that (3) satisfies condition d) (triangle inequality). We will show, that we can insert (3) into condition d) and transform the inequality such that it will be true for all possible choices for X_n, Y_n and Z_n.

Without loss of generality, assume $n > 0$, $c(X_n) \geq c(Y_n)$, and hence (1) $K(X_n) \geq K(Y_n)$ The following three cases include all possible relations of $c(Z_n)$ towards $c(X_n)$ and $c(Y_n)$: I) $c(Z) \geq c(X)$, II) $c(X) \geq c(Z) \geq c(Y)$ and III) $c(Y) \geq c(Z)$. Now we prove the claim of our theorem for each case separately.





Notation: We express the sizes of the sets P_{X_n}, P_{Y_n} and P_{Z_n} as follows:

$$\begin{array}{lll} c(X_n) = a+d+f+g & c(X_n|Y_n) = a+f & c(Y_n|X_n) = b+e \\ c(Y_n) = b+d+e+g & c(X_n|Z_n) = a+d & c(Y_n|Z_n) = b+d \\ c(Z_n) = c+e+f+g & c(Z_n|Y_n) = c+f & c(Z_n|X_n) = c+e \end{array}$$

where $a, \ldots, g \geq 0$ indicate the number of elements in the subsets, as illustrated in Fig. 1. Note, that Fig. 1 illustrates only the most general case. It is possible, that some subsets contain no elements.

Experimental Procedure

Neuronal activity of anaesthetised rats was sampled by means of a electrode array positioned in the olfactory bulb (30 electrodes).

The activity was sampled in the 10s period before odor onset (pre) and the 10s period of odor presentation (during).

Individual neurons were discriminated from multiple neuron activity using a Kohonen network to cluster principle components derived from the action potential waveforms allowing discrimination of activity from 1-6 neurons at each active site.

Data: - 40-54 neurons in total obtained in two animals
- 40 „pre-stimulus“ spike trains per neuron.
- 40 „during-stimulus“ spike trains per neuron.

Data analysis (1)

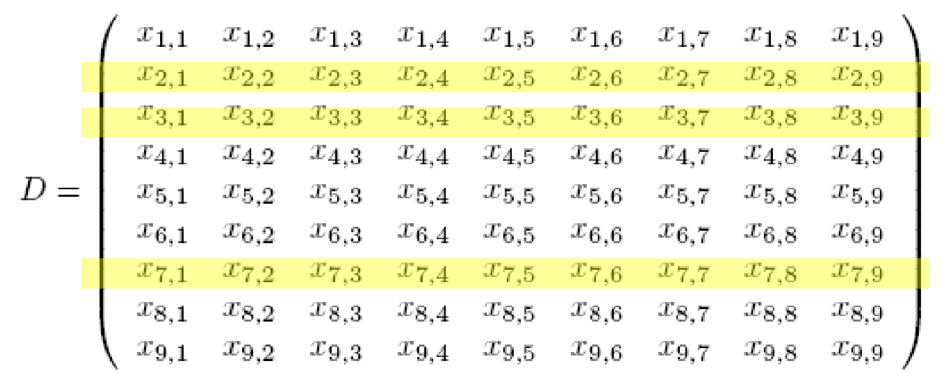
The analysis has been performed in a three-step procedure:

1) The **number of clusters** of neurons in each of the 40 periods of recording (pre and during), using both the LZ-distance and the C-distance, was determined.

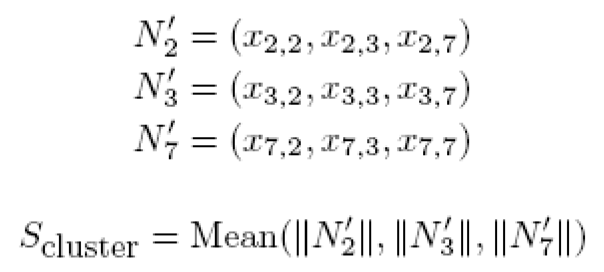
2) To **quantify the mean interactions of each neuron** with each other neuron in the during-stimulus period compared to the pre-stimulus period, we assigned to each neuron a vector $\mathbf{N}_i = (x_1, \ldots, x_{40})$, whose components indicate the number of times the specified neuron finds itself in a cluster with another neuron. By using the normalized dot product for each pair $\mathbf{N}_i$ and $\mathbf{N}_j$ we obtain the distance matrix **D**. Clustering with this distance measure provides “clusters among partners”, the **degree of interrelation of neurons within the network, averaged over all trials**.

Data analysis (2)

3) We identify those neurons that remain in the same “cluster among partners” for both pre and during stimulus (almost all neurons keep their partners). For each group identified in this way we reduce **D** as follows (example):



$$D = \begin{pmatrix} x_{1,1} & x_{1,2} & x_{1,3} & x_{1,4} & x_{1,5} & x_{1,6} & x_{1,7} & x_{1,8} & x_{1,9} \\ x_{2,1} & x_{2,2} & x_{2,3} & x_{2,4} & x_{2,5} & x_{2,6} & x_{2,7} & x_{2,8} & x_{2,9} \\ x_{3,1} & x_{3,2} & x_{3,3} & x_{3,4} & x_{3,5} & x_{3,6} & x_{3,7} & x_{3,8} & x_{3,9} \\ x_{4,1} & x_{4,2} & x_{4,3} & x_{4,4} & x_{4,5} & x_{4,6} & x_{4,7} & x_{4,8} & x_{4,9} \\ x_{5,1} & x_{5,2} & x_{5,3} & x_{5,4} & x_{5,5} & x_{5,6} & x_{5,7} & x_{5,8} & x_{5,9} \\ x_{6,1} & x_{6,2} & x_{6,3} & x_{6,4} & x_{6,5} & x_{6,6} & x_{6,7} & x_{6,8} & x_{6,9} \\ x_{7,1} & x_{7,2} & x_{7,3} & x_{7,4} & x_{7,5} & x_{7,6} & x_{7,7} & x_{7,8} & x_{7,9} \\ x_{8,1} & x_{8,2} & x_{8,3} & x_{8,4} & x_{8,5} & x_{8,6} & x_{8,7} & x_{8,8} & x_{8,9} \\ x_{9,1} & x_{9,2} & x_{9,3} & x_{9,4} & x_{9,5} & x_{9,6} & x_{9,7} & x_{9,8} & x_{9,9} \end{pmatrix}$$



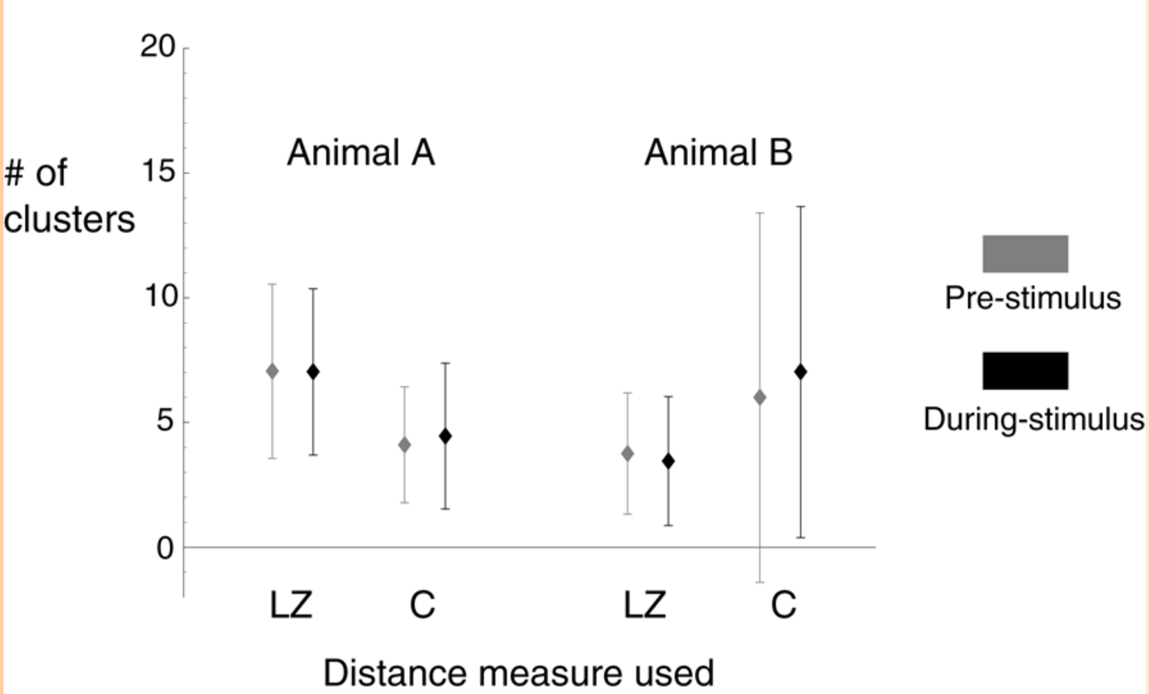
$$N'_2 = (x_{2,2}, x_{2,3}, x_{2,7})$$
$$N'_3 = (x_{3,2}, x_{3,3}, x_{3,7})$$
$$N'_7 = (x_{7,2}, x_{7,3}, x_{7,7})$$

$$S_{\text{cluster}} = \text{Mean}(\|N'_2\|, \|N'_3\|, \|N'_7\|)$$

This is performed for both the pre and during stimulus condition. We receive in this way the stability of each cluster in either condition.

Results (1)

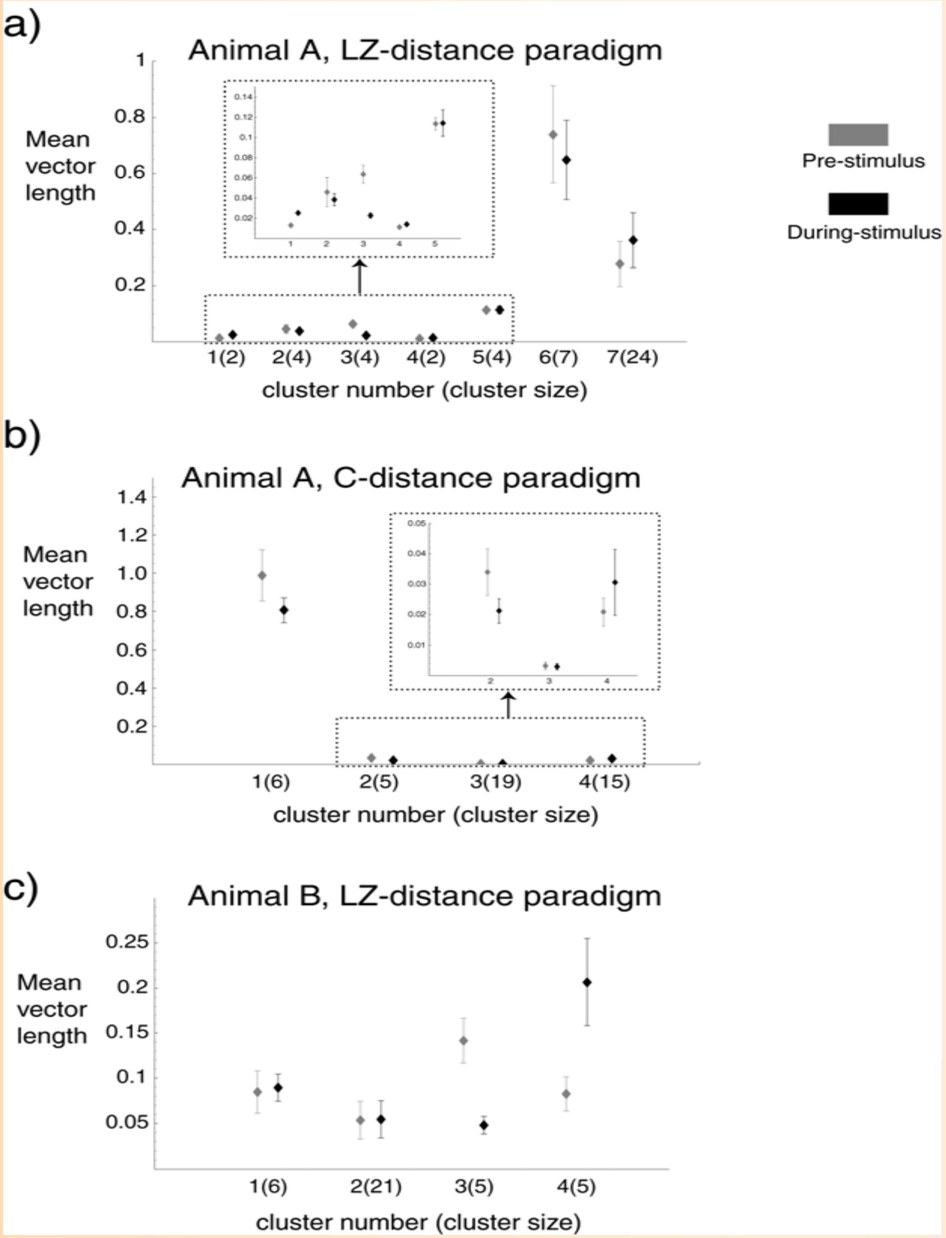
We find that the number of clusters emerging on stimulus presentation does not *per se* indicate whether the network is in a pre stimulus or a during stimulus condition, using both distance measures for clustering (special case: animal B using the C-distance).



Results (2)

But if the *mean behavior* of the network is investigated, we find clear differences between pre and during stimulus for some clusters: stabilization and de-stabilisation effects.

Both stabilization and de-stabilisation effects are more pronounced in the LZ-paradigm compared to the C-paradigm.



Interpretation of the result

We find that – using both distance measures – neurons tend to be in the same clusters independent of the presence or absence of an odor, presumably reflecting the underlying neuronal connectivity that remains unchanged during short timescales.

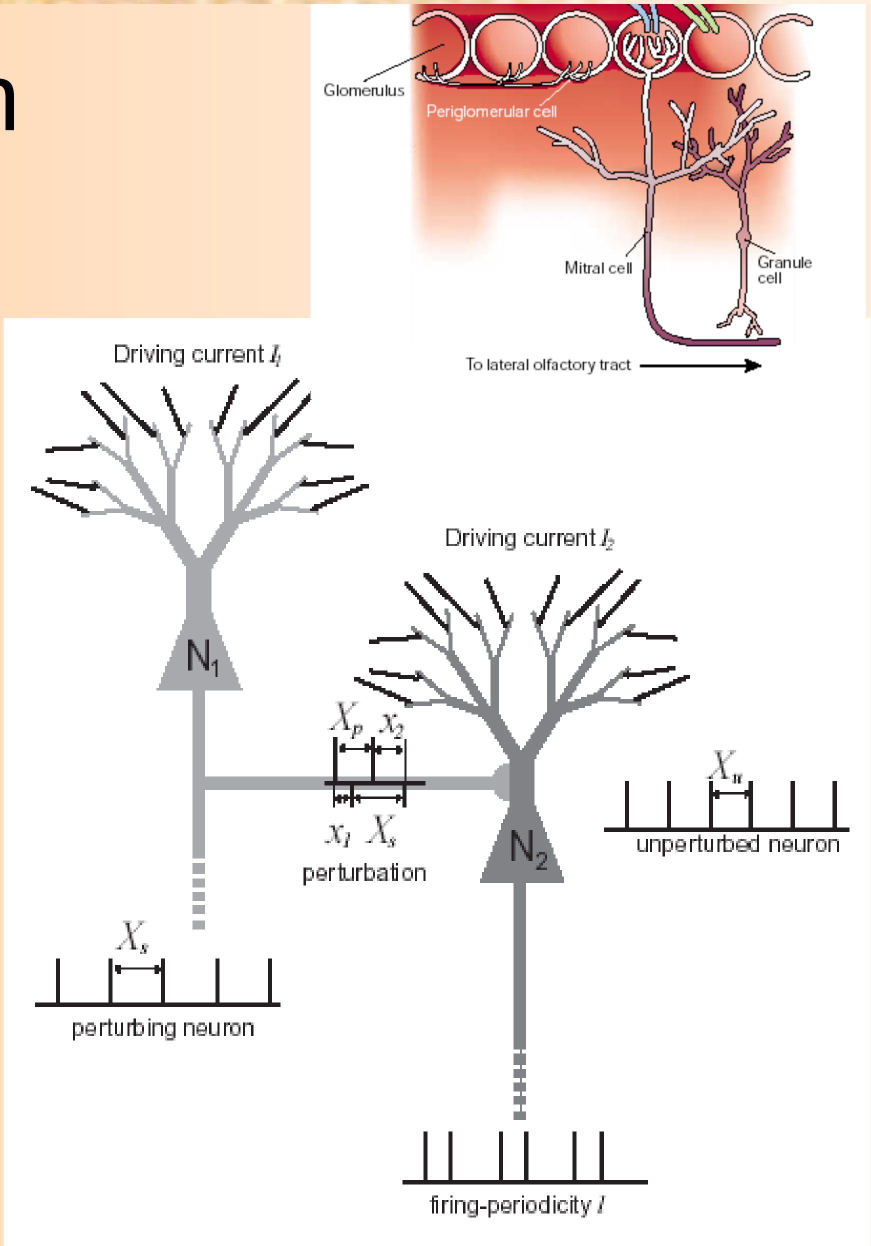
However, the stability of some clusters measured in the Lempel-Ziv paradigm changes significantly when an odor is presented to the olfactory neuronal network – an effect that is much less present in the synchronization paradigm. This functional change presumably reflects neuronal computations performed by the neurons due to odor presentation, reflected by changes in neuronal pattern firing.

This indicates that neuronal clustering using the Lempel-Ziv distance may be a better approach to understand the computation performed in an olfactory neuronal network compared to synchronization.

A possible explanation

The generic scheme of the „Stoop-model“ of neuronal computation:

- In a quasi-stationary state, most neurons show limit-cycle behavior.
- Coupling of limit cycles leads to the phenomenon of locking: currents are encoded in firing-periodicities.
- The neuroanatomy in the olfactory bulb is consistent with this scheme.
- Similar inputs lead to groups of neurons with similar (but not necessarily synchronous) patterns.
- Spontaneous activity (pre-stimulus) would lead to less stable firing patterns.



Problems and open questions

The following shortfalls and problems should be considered:

1) Is the **spike sorting** good enough?
2) In data obtained by multi-electrode array recordings, there is a **bias against synchronous firing**, as coincident spikes are not distinguished. This may affect the C-distance-analysis.
3) What is the effect of the neuronal clusters detected in the LZ-paradigm on **higher areas** along the olfactory information pathway?