Sensory coding in neural assemblies: examples from the olfactory and auditory systems

UE Neural Networks
6/12/2016
Brice Bathellier
CNRS CR1, Group leader
UNIC, Gif sur Yvette
Content of the course

A. Understanding perception: key concepts about sensory coding
B. Coding in the olfactory system: extracting the code without input parametrization
C. Coding in the auditory cortex: beyond simple (linear) models
Perception: two problematics

• Detecting
  - Peripheral systems
  - Conversion of physical quantities into nervous impulses
  - Many evident technical analogies

• Discriminating, interpreting, identifying, linking to actions
  - Central sensory systems
  - Segmentation of sensory scenes
  - Technical analogies are scarce
Different types of sensory receptors...

- Photon transducers (e.g. retina, circadian neurons) based on opsin protein.

- Mechanical transducers: (e.g. skin, whiskers follicles, inner ear) force-gated channels + amplification systems

- Chemical detectors: (e.g. nasal epithelium, taste buds), G-proteins-coupled receptors or ion channels

- Other senses: magnetic (some birds, fish, insects), electric (some fishes),...
... but one formalism: the sensory « image »

Activity of cell $i \Rightarrow v_i(t)$

The ensemble is described by a sensory vector

$$\vec{V}(t) = \begin{pmatrix} v_1(t) \\ v_2(t) \\ \vdots \\ v_i(t) \end{pmatrix}$$
What is perceiving?
Mathematical formalism

Receptors

\[ \vec{V} \]
Sensory input vector

Perceptual representations

\[ \vec{F}(\vec{V}) \]
Sensory representation vector
Classical pitfall, to perceive is not « copying » the sensory inputs inside the brain. It is NOT simply about transmitting information.

\[
\vec{F}(\vec{V}) \neq \vec{V}
\]

Descartes (1596 - 1650) remarked that the brain receives an image that is « upside-down » and people started to think about how the brain could flip it up.
To perceive is to decide about the presence of global structures

- Perception is about creating a meaningful scene composed of many perceptual attributes (objects & action/motion)
  
- Thus perception is not necessarily univocal.
- It may depend on context
Another striking exemple of visual illusion

Old or young lady

German postcard, 19th century
What is perceiving?
Mathematical formalism

Receptors (retina)

Detection of a face

Detection of the eyes, mouth...

Sensory input vectors

Vector of perceptual attributes

$\vec{V}(t)$

$\vec{F} \left( \vec{V}(t) \right)$
How to separate attributes?
The «ancestral model»: the perceptron

\( \vec{w} \cdot \vec{V} = \sum_{i} w_i V_i > 0 \)
How to separate attributes?

A simple model: the perceptron
(Rosenblatt 1957)

\[ \mathbf{w} \cdot \mathbf{V} = \sum_i w_i V_i > 0 \]

\[ \mathbf{w} \cdot \mathbf{V} = 0 \]
The optimal hyperplane is well defined, if it exists (Linear Support Vector Machine).

If there is no optimal hyperplane (the usual case), **non-linear transformations** are in fact necessary to make the problem « linearly separable ».

But it is hard to find the right function...
Combining attributes for elaborate perception

Deep learning

“Face”

LeCun et al. Nature 2015
Sensory systems have also multiple stages

Exemple the early auditory system

Multiple stages in cortex too, in particular in more complex brains (primates, humans)
Questions for neurophysiology of perception

• What are the representations? What type of attribute are encoded at each stage?
• What are the transformations implemented from one processing stage to the next? What are the underlying computations and circuits?
• What is the code? Firing rates or more complex aspects of the neuronal discharges in a neuron and across a population?
• Do the representations explain the structure of perception?

We need to explore large neuronal networks
We need appropriate maths
We need large neuronal samples. Why?

- Sensory representations even in flies or mice involve a large number of neurons ($10^3$ to $>10^8$): we need to avoid sampling biases.

- Single neurons are often unreliable: so we will have a better idea of the general principles by finding regularities in large ensembles.

- Exploration of coding principles based on coincident activation of certain sets of neurons.
Available techniques for massive parallel recordings

• Multi-channel electrodes
  – Traditionally few 10’s of neurons, going towards 100’s or 1000’s (massively parallel approaches)
  – Good temporal precision (< 1ms)
  – Spatial mapping difficult and neuronal type identification only through optogenetics

• Two-photon imaging
  – Traditionally few 100’s going towards 1000’s or 10000’s
  – Good spatial mapping and easy identification of cell types with genetic markers
  – Poor temporal resolution (> 100ms)
How do we think about representations?

• The receptive field concept.
  – The subset of stimuli for which a neuron is responding

• The representation is defined as the combination of receptive fields from different neurons.
  – Identifying receptive fields
  – Quantifying their distribution

Problem: the number of possible stimuli is infinite!
How do we think about representations?

- Receptive field models (linear)

\[
\begin{align*}
r(x, y) &= \iiint_{all \, u \, \text{and} \, v} h(x-u, y-v)s(u, v)dudv \\
r(t) &= \iiint_{all \, f \, \text{and} \, u} h(t-u, f)s(u, f)dfdu
\end{align*}
\]
Limits of current receptive field models

• Works only if you can parameterize the input space: not always possible (e.g. chemical senses)

• Suppose linearity.
  – This is a major problem as perception is in essence non-linear (deep networks are also highly non-linear)
  – Attempt to address non-linearities by including second order non-linear terms, but this is only a local description (local expansion).
Overview

Part 1: Exploring odor coding in the mouse olfactory system without receptive fields.
  – Observations
  – Understanding the neural code without parametrization of the input

  – Capturing non-linearities at the population scale.
  – Techniques to go beyond linear receptive?
  – Techniques to link representations with perception.
Organization of inputs to the olfactory bulb

Smell
Visualizing olfactory input maps

Dorsal surface of the bulb

Activity map

Images from Bathellier et al. 2007
Similar map from one mouse to another

Images from Bathellier et al. 2008
Visualizing olfactory input maps: synaptopHfluorin

Images from Bathellier et al. 2007
Different maps for different odors

Images from Bathellier et al. 2007

Amyl acetate 10 %

Methyl benzoate 20 %

Methyl benzoate 1 %
The independent receptor channels are cross-modulated through a dense interneuronal network.
Accessing the olfactory bulb output layer

Bathellier et al. 2008
A dense representation of odor

101 neurons recorded in olfactory bulb

Most cells are affected by the presence of an odor. Many cells respond to more than two very different odors.

So what makes the specificity?
Temporal modulation of olfactory bulb activity

Neuron 1
Amyl acetate

Odor Inhalation
320 ms

Respiration

Neurone 5
Amyl acetate

Odor Inhalation
320 ms

Neurone 6
Amyl acetate
Visualization of single cell activity
Diversity of responses across cells

Complexity on slow and fast time scales

No obvious coding principle at single cell level
Representing the activity of a neuronal population over time

Neurone #

Neurone 1
Neurone 2
Neurone 3
Neurone 4

::

Neurone 101

Vecteur

\[ t_1 \quad t_2 \quad t_3 \quad t_4 \quad t_n \]
Visualizing vector time series

101 dimensions

Principal Components

3 components \rightarrow 3D space

Dimensionality reduction

Vector $\Leftrightarrow$ point in space
Slow time scale dynamics

(Time bin = 1 breathing cycle, i.e. 312 ms)

Velocity = Vect(t_{n+1}) - Vect(t_n)

Time to FP: ~ 1s
Fast population vector dynamics

(8 bins per breathing cycle)
Different trajectories for different odors and concentration

**G**

- **Amyl Acetate**
  - (2 concentrations)
  - AA (10 %)
  - AA (20 %)

- **Ethyl Butyrate**
  - (1 concentration)
  - EB (20 %)

**H**

- **Amyl Acetate**
  - (5 concentrations)
  - AA: 20 %
  - AA: 10 %
  - AA: 5 %
  - AA: 2 %
  - AA: 1 %
What is the code?
Three possible ways of reading out the neural activity

Temporal coding
(t₁,t₂,t₃)

Rate coding (high resolution)
t₁ or t₂ or t₃

Rate coding (low resolution)
t₁ + t₂ + t₃

Vectors

Time

Concatenated trajectory

OR

Single point of the trajectory

OR

Average vector
(or cumulative spike count)
Linear classifier analysis of the response vector

\[ \vec{V} \]

\[ \vec{W} \]

Vector dimension 2

Vector dimension 1

S1

S2

S3
Temporal information is mainly redundant.

![Graph showing % correct vs. time for different cycles and resolution rates.](chart.png)

- **1st cycle**
- **2nd cycle**

- Temporal
- Rate: high resolution
- Rate: low resolution

The graph shows that the temporal information is mainly redundant with high and low resolution rates. The significance level is indicated by the red dashed line at $P = 0.05$. The $\chi^2$ test is used to determine significance.
In the behaving mouse, the first inhalation is sufficient to discriminate odors.

Odor classification success based on OB neural population recordings (SVM)

Cury et al. 2010
Neural population coding in the olfactory bulb

- Population activity is highly dynamic
- The ensemble of mitral cell generate complex trajectories developing on slower and faster time scales
- The temporal details (full trajectory) of these dynamics are not necessarily essential to predict the odor presented to the animal: there are multiple ways of decoding them.
Overview

• Part 1: Exploring odor coding in the mouse olfactory system without receptive fields.
  – Observations
  – Understanding the neural code without parametrization of the input

• Part 2: Population coding of sounds in the mouse auditory cortex.
  – Capturing non-linearities at the population scale.
  – Techniques to go beyond linear receptive?
  – Techniques to link representations with perception.
What is audition?

Interpretation of pressure waves from the environment
Transduction in the cochlea: frequency decomposition

- Inner ear

Mecano-electric transduction

Traveling wave on the basilar membrane
The cochlea computes the spectrogram of the sounds = extract the frequency pattern
How does the brain encode frequency patterns?

Classically the auditory system codes for frequency...

... but it is much more complex than that.
How does the cortex encode frequency patterns?

Perception discretize the environment into meaningful tokens.

- The code should be about classes of patterns
- One should also observe invariances with respect to certain parameters (e.g. amplitude)

Perceptual objects and categories are discrete representations of the environment.
Possible scenarios for auditory representations in cortex

- **Discrete = categories**
- **Sparse (?)**
- **Continuous = linear**
2-photon calcium imaging *in vivo* in the mouse auditory cortex

*In vivo* 2-photon imaging in layers 2/3 under light isofluorane anesthesia

![Image of calcium dye (OGB1-AM)](Image)

![Diagram of craniotomy, skull, and cortex](Image)

![Image of Auditory cortex imaged area](Image)

![Graph of Extracellular voltage and ΔF/F](Image)

![Graph of Deconvolution and Firing rate](Image)
Recording activity patterns for a large set of sounds

Pure tones

Complex sounds

Cell number

Time (s)

Firing rate

0 80 (AP/s)
Construction of response vectors

Time (s)

Cell number

Trial #

2 kHz  4 kHz  8 kHz  16 kHz  32 kHz  64 kHz

Firing rate

0  50 (AP/s)

AP/s

0
Clustering analysis of local population responses in auditory cortex

Response vectors for each sound

Measure of similarity (correlation)

Average correlations

Hierarchical clustering to find categories of patterns
Local populations represent sounds with only few reliable response modes. Example I (~80%)
Local populations represent sounds with only few reliable response modes. Example II (~20%)

Bathellier et al. 2012
Non-linear transitions suggesting competition between response modes.
Discriminability of sounds by a global neuronal population of the auditory cortex

Space of neuronal activity

Global population: 4674 neurons from 74 pooled populations, 14 mice

Decomposition along $n$ activity templates ($n =$ number of modes)

$$\vec{R} = \sum_{i=1}^{n} \alpha_i \vec{m}_i + \vec{r}$$
Do auditory cortex representations match sound perception in the mouse?
Spontaneous categorization of sounds by behaving mice discriminating a pair of sounds
Categorization of sounds by global cortical representations

Space of neuronal activity

Activity of cell 1 vs Activity of cell 2

Trained linear classifier (Support Vector Machine)

Global population vector

Population 1

Population 2

Population N

Probability of choosing sound 2

14 mice, 74 pop., 4734 neurons
Global codes can predict generalization behavior

Behavior
- Sound 2 = S+ (n = 6)
- Sound 2 = S- (n = 6)
- Balanced group (mean ± SD, n = 12)

SVM Prediction
- Pooled dataset (4734 neurons 74 populations, 14 mice)

Lyubov Ushakova
Global codes can predict generalization behavior

Red line: behavioral replicate
Summary

• The auditory cortex is non-linear.

• Existence of local response modes with attractor-like (category forming) properties in the auditory cortex.

• Local response modes form a basis set for representation and discrimination of many sounds.

• The sound representation generated by local responses modes matches the perceptual space of mice.

What is encoded in these non-linear categories?
Perceiving a sound is about recognizing a spectral and temporal pattern in a spectrogram.
Temporal features are important for sound identification.
Humans perceive ascending sounds as more loud

Collaboration with P. Sucini’s team IRCAM (Paris)

P. Sucini et al. 2007
1/ Are up- and down-ramps represented with unequal saliency in auditory cortex?
2/ How does the brain build divergent percepts from time-symmetric intensity profile?
GCAMP6-based 2-photon calcium imaging in mouse auditory cortex

We can now record up to ~1200 neurons in parallel over a 1x1 mm region
Automated cell detection and deconvolution

Deconvolution + neuropil correction

Roland, Deneux, Bathellier*, Fleischmann*, Elife 2017
Strong difference in cortical saliency symmetry of cortical responses to ramps: a strongly non-linear effect

4088 neurons
15 recordings
5 mice

Deneux et al., Nature Communications 2016
Neither linear nor adaptation models can explain the asymmetry

Property of all linear filters (e.g. STRF): the integral of the output is invariant through time reversal

=> The linear approximation is also very bad for global population activity
Do mice also perceive up-ramps louder?
Comparing saliency of up- and down-ramps using associative learning speed

Classical conditioning: More salient stimuli are learnt faster.
Ascending ramps are more salient than descending ramps
What is the source of the asymmetry? Are the representations diverging like in perception?

Activity of >4000 neurons

Alexandre Kempf
Multiple population patterns emerge during an intensity ramp
Clustering reveals complex functional cell types

Deneux et al., Nature Communications 2016

More functional cell types prefer up-ramps

Down ramp prefering
The different cell types are clustered in space.
Modeling the asymmetry of cortical responses

What are the minimal mathematical operations that can explain the observed cortical responses?

Non-linear input scaling

Linear filters = functional connections
Modeling the asymmetry of cortical responses
Multilayer architectures build more divergent representations
Conclusions

• Up- and down-ramps produce asymmetric population responses in mouse auditory cortex, which matches the observed saliency asymmetry, and could explain our divergent percepts.

• This could be useful for detecting approaching threats.

• This asymmetry result from complex nonlinearities of the auditory system, which bias representations towards features of the up-ramp. Multilayer architectures can account for these effects (but not classical receptive field or LN models).

Kernel > non-linearity > Kernel >... = Deep learning architecture
THE END

Thanks!
The olfactory cortex

In humans

In mice

Olfactory cortex is mainly constituted of the piriform cortex
A three layer cortex
No spatial organisation in piriform cortex

Stettler et al 2009
Cortical representations may be plastic and represent also the behavioral significance of odors. When A and A' have the same signification, piriform cortex responses are more similar.

Chapuis et al. 2011