Introduction to Neuroscience: Behavioral Neuroscience

Neuroethology,
Comparative Neuroscience,
Natural Neuroscience

Nachum Ulanovsky

Department of Neurobiology, Weizmann Institute of Science

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Principles of Neuroethology

Neuroethology seeks to understand the mechanisms by which the central nervous system controls the natural behavior of animals.

- **Focus on Natural behaviors:** Choosing to study a well-defined and reproducible yet natural behavior (either Innate or Learned behavior)
- **Need to study thoroughly the animal’s behavior, including in the field:** Neuroethology starts with a good understanding of Ethology.
- **If you study the animals in the lab, you need to keep them in conditions as natural as possible,** to avoid the occurrence of unnatural behaviors.
- **Krogh’s principle**
Krogh’s principle

“For such a large number of problems there will be some animal of choice or a few such animals on which it can be most conveniently studied. Many years ago when my teacher, Christian Bohr, was interested in the respiratory mechanism of the lung and devised the method of studying the exchange through each lung separately, he found that a certain kind of tortoise possessed a trachea dividing into the main bronchi high up in the neck, and we used to say as a laboratory joke that this animal had been created expressly for the purposes of respiration physiology. I have no doubt that there is quite a number of animals which are similarly "created" for special physiological purposes, but I am afraid that most of them are unknown to the men for whom they were "created," and we must apply to the zoologists to find them and lay our hands on them.” (Krogh, 1929)
Krogh’s principle and Neuroscience research

Studying the giant axon of the squid in order to understand mechanisms of action-potential generation

Q: Why was this species chosen?

A: Because of the huge size of its axon (~1 mm diameter), which allowed using macro-wires for recording electrical potentials - and doing voltage clamp.
Krogh’s principle and Neuroscience research

Studying the frog neuromuscular junction in order to understand the physiology of synaptic transmission

Q: Why was this species chosen?
A: Because of the size of this synapse (end-plate) and the simplicity of the reflex circuit involved.

Sir John Eccles
Nobel prize 1963

Sir Bernard Katz
Nobel prize 1970
Krogh’s principle and Neuroscience research

Studying the *Limulus* (horseshoe crab) retina in order to understand visual processing; discovery of the phenomenon of lateral inhibition

Q: Why was this species chosen?

A: Because horseshoe crabs have long optic nerves that can be physically *split* to record from individual nerve fibers; and the retina circuitry is *simple*: the compound eye has one photoreceptor under each ommatidium, which facilitates the study of lateral inhibition
Krogh’s principle and Neuroscience research

Studying the neurobiology of learning and memory in *Aplysia*

**Q:** Why was this species chosen?

**A:** Because of the **size** of its **identified** neurons; and not least importantly, because of the animal’s robust **behaviors** (e.g. sensitization; or classical conditioning of the gill withdrawal reflex)
Some commonly used animal models in Neuroscience: Past and Present (Not showing less common species)
Krogh’s principle vs. “standard animal models”

• **A corollary of Krogh’s Principle** – as viewed by Neuroethologists:
  You should choose the animal species that best fits your research question (fits either in terms of the animal’s behavior or for technical reasons) – i.e., choose well your animal model – rather than studying all the possible questions using just a few “standard animal model species” (e.g., mouse, drosophila).

• **Advantages of “Standard animal models”:** So much is known about their brains... Therefore, many people prefer this knowledge-base over Krogh’s principle. Additionally, there are very powerful experimental tools available for these animals (particularly molecular tools).

• **Discussion:** Pros ? Cons ? When would you favor Krogh’s principle and when favor a standard-model approach ?
Neuroethology has some additional historical traditions, which I find more problematic

- **Focus on “champion species”**

- **Neuroethology calls for studying the neural basis of natural behavior** – but oftentimes actually studies reduced preparations (with a few exceptions, most notably Bird Song)
Diversifying species vs. Diversifying behaviors

Model species

Non-standard

Artificial

Behaviors

Standard

Natural

Diversification along the species axis

Mainstream Neuroscience

Diversification along the behaviors axis

Comparative Systems Neuroscience

Neuroethology

Natural Neuroscience
Reasons for diversifying species

- **Comparative approach**: you can learn a lot by comparing across species

**V1**

![Cat V1: Columnar organization](image1)

![Rat V1: Salt-and-pepper organization](image2)

Based on Ohki et al 2005
Reasons for diversifying species

- Comparative approach: you can learn a lot by comparing across species

Hippocampus

Eliav et al., Cell (2018)
Reasons for diversifying species

• **Comparative approach:** you can learn a lot by comparing across species

**Hippocampus**

In rodents – 3 phenomena that are coupled together:

<table>
<thead>
<tr>
<th>Rodents</th>
<th>Bats</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓ Oscillations (theta)</td>
<td>X Oscillations (theta)</td>
</tr>
<tr>
<td>✓ Synchronization</td>
<td>✓ Synchronization</td>
</tr>
<tr>
<td>✓ Coding (of position)</td>
<td>✓ Coding (of position)</td>
</tr>
</tbody>
</table>

The comparative approach allows to identify what is invariant across species – and what is not.
Reasons for diversifying species

- **Comparative approach:** you can learn a lot by comparing across species. The comparative approach allows identifying mechanisms that generalize (or not) across species. Allows finding **invariant** computational principles.

- **Drawbacks of the pure-strain approach:** because of founder effects, mouse strains differ dramatically from each other and from wild mice.
Reasons for diversifying species

- **Comparative approach:** you can learn a lot by comparing across species.
- **Drawbacks of the pure-strain approach:** because of founder effects, mouse strains differ dramatically from each other and from wild mice.

**Dramatic differences in social behaviors**

Female attacks on intruder adult females (left) and on intruder alien pups (right).
- Wild females are much more aggressive.
- **Q:** Why was aggressiveness eliminated from laboratory females during the process of mouse domestication?
- **A:** To facilitate breeding.

Based on Chalfin et al 2014 (Tali Kimchi’s lab)
Reasons for diversifying species

- **Comparative approach:** you can learn a lot by comparing across species
- **Drawbacks of the pure-strain approach:** because of founder effects, mouse strains differ dramatically from each other and from wild mice

Dramatic differences in movement between BALB/c mice and wild mice

→ BALB/c is *not* a valid model for anxiety, as it is often considered!
Reasons for diversifying species

- **Comparative approach:** you can learn a lot by comparing across species. The comparative approach allows identifying mechanisms that generalize (or not) across species. Allows finding invariant computational principles.

- **Drawbacks of the pure-strain approach:** because of founder effects, mouse strains differ dramatically from each other and from wild mice.

- “Sanity check”: Does your finding from one species generalize to another? → Also for Medical research.

- **Krogh’s principle** → Different species offer unique opportunities to ask questions.

- **Certain behaviors are simply not present in standard models:** e.g. many Social behaviors.
  
  *Discuss:* Sentinels (meerkats), Altruism (bats), Theory of mind (primates), …

- **Diversity can allow identifying brain basis of specific behaviors** → e.g. Deer Mice (Hopi Hoekstra)

- **The Unknown Unknowns:** So many things were discovered in nonstandard species – who knows what may lie ahead?
Diversifying species vs. Diversifying behaviors

Claim:
Regardless of species used, it is important to study also natural behaviors – not just simple artificial controlled behaviors.
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Reasons for diversifying to more Natural Behaviors

• In a complex dynamical system like the brain you can’t isolate and ‘control’ individual factors – as they are all connected

Discuss:

The example of optogenetics: Even if you shut off /activate “only” neuronal subclass X, this affects also subclasses Y, Z, etc. – so you can’t claim that only subclass X is responsible for the behavior you observe.

Factors in the world that are connected to each other…

Behaviors that are connected to each other… (Example: Whisking & Sniffing)
Reasons for diversifying to more Natural Behaviors

• In a complex dynamical system like the brain you can’t isolate and ‘control’ individual factors – as they are all connected

• The brain and the world are reciprocally interacting

The example of active sensing.
Reasons for diversifying to more Natural Behaviors

- In a complex dynamical system like the brain you can’t isolate and ‘control’ individual factors – as they are all connected
- The brain and the world are reciprocally interacting

Active sensing

Sensory neurons care about natural stimulation (active sensing) vs. unnatural stimulation (passive)

Based on Ferezou et al. 2006
Reasons for diversifying to more Natural Behaviors

- In a complex dynamical system like the brain you can’t isolate and ‘control’ individual factors – as they are all connected
- The brain and the world are reciprocally interacting
- The brain responds dramatically to natural conditions
Reasons for diversifying to more Natural Behaviors

- In a complex dynamical system like the brain you can’t isolate and ‘control’ individual factors – as they are all connected
- The brain and the world are reciprocally interacting
- The brain responds dramatically to natural conditions
- Many behaviors are tightly coupled to each other, and you can’t isolate them naturally (e.g. whisking and sniffing)
- **Top-down effects in the brain:** Are eliminated in many controlled experiments, but exist in natural behaviors. Top down anatomical projections are massive in the cortex, and many studies showed strong top-down effects of expectation, prediction, attention, etc., on neuronal activity in lower areas.
Top down projections in the cortex are usually much stronger than the bottom-up projections.

Dorsal pathway:
“Where & How” = Space, Motion & Action

Ventral pathway:
“What” = Object recognition
Top down projections in the cortex are usually much stronger than the bottom-up projections.
Reasons for diversifying to more Natural Behaviors

• In a complex dynamical system like the brain you can’t isolate and ‘control’ individual factors – as they are all connected

• The brain and the world are reciprocally interacting

• The brain responds dramatically to natural conditions

• Many behaviors are tightly coupled to each other, and you can’t isolate them naturally (e.g. whisking and sniffing)

• **Top-down effects in the brain:** Are eliminated in many controlled experiments, but exist in natural behaviors

• **Evolution:** The brain has evolved to do specific behaviors – and therefore these natural behaviors should be our focus of research.

• **The problem of Unknown Unknowns**
Neural Basis of Behavior ... But which Behavior(s)?

Controlled laboratory experiments

“Controlled but Unnatural”

Natural behaviors

“Natural but uncontrolled”

Tube test in mice

Group hunting in lions & Communal defense in buffalo
Neural Basis of Behavior … But which Behavior(s) ?

- Head-fixed self stimulation
- Birdsong (zebra finch)
- Lion hunting
- 24/7 unconstrained behavior