# Descending Networks Transform Command Signals into Population Motor Control

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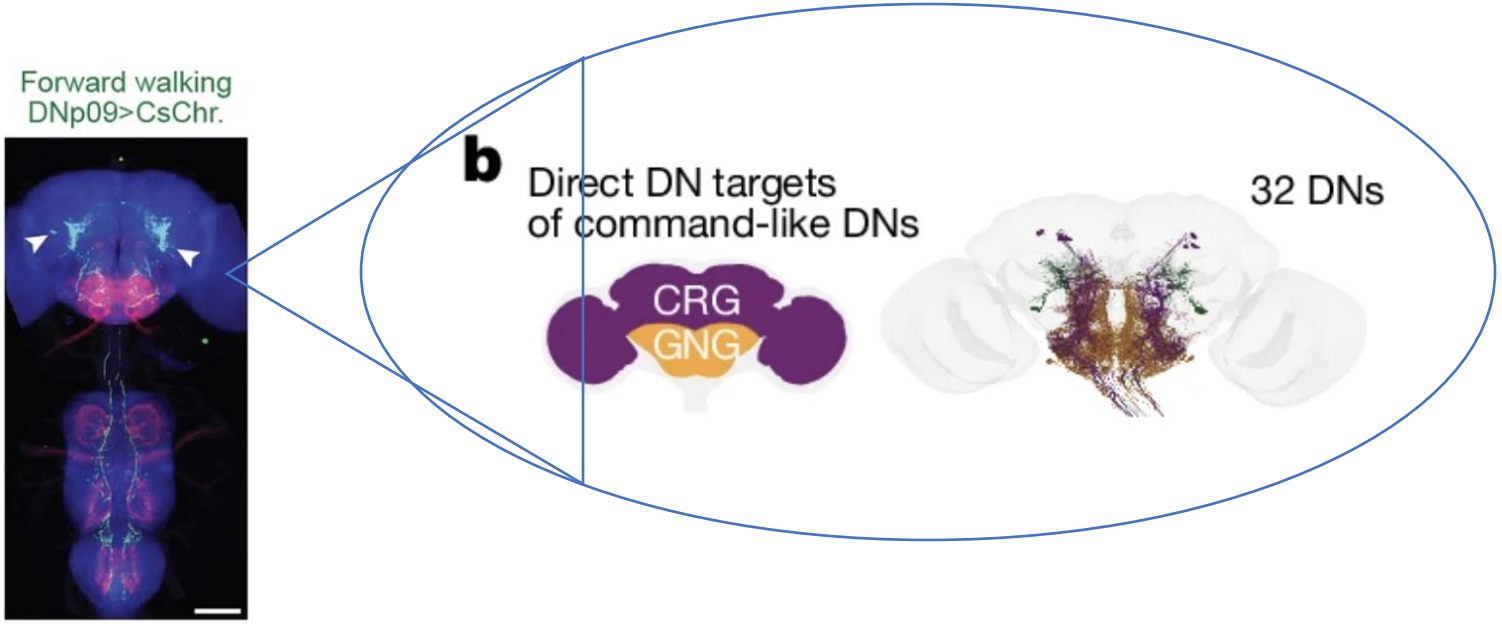
**Jonas Braun**
**Femke Hurtak**
**Sibo Wang-Chen**
**Pavan Ramdya**

# How does the descending neurons (DNs) convert movement instructions to actions?




*A **descending neuron (DN)** is a type of neuron that transmits motor-related signals from the brain to downstream motor circuits in the spinal cord (in vertebrates) or the ventral nerve cord (VNC, in invertebrates).*

# Agenda

- Background
- From comDNs to DN populations.
- ComDNs recruit Addition DNs
- Behavioural requirement of DN recruitment
- Network size predicts behavioral necessity
- Network clusters correlate with behaviour

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- ❑ **Background**
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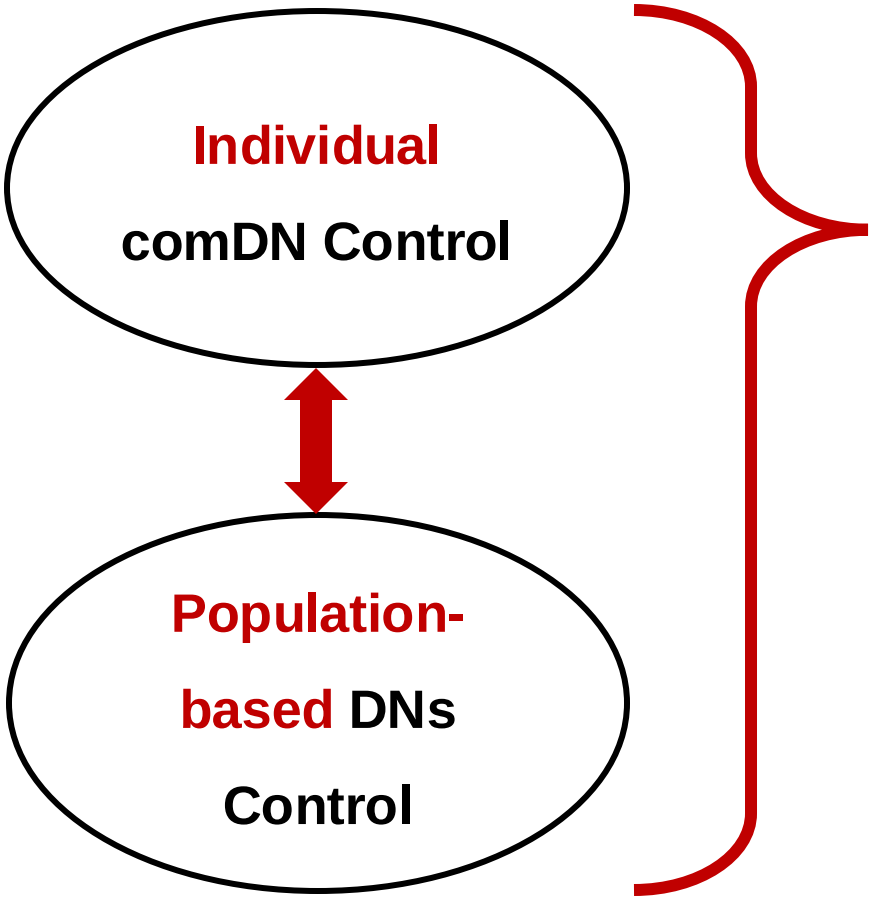
# Background

| | Before this paper | This paper |
|---|---|---|
| **Individual comDN Control** | **Despite numerous DNs in the fly brain, activating of pairs of 'command-like' DNs (comDNs) can drive a complete behavior.**<br>- Activate comDNs to induce forwards walking, grooming, backwards walking, escape, egg-laying, and courtship. | **DN control relies on multiple DN classes working together as a network.**<br>- Act as neuromodulatory units beyond simple movement control.<br>- Represent individual DNs as single dimensions of a broader control signal. |
| **Population-based DNs Control** | **Co-activating multiple DNs is more effective than a single DN in triggering actions like take-off.**<br>- Observe widespread DN co-activation during walking, with 15 DNs modulating wing beat amplitude and improving take-off likelihood. | |

## 2 Conflict Models




## 2 Unified Scenarios

**Hyp 1) comDNs may be privileged in that they can recruit additional DN populations to drive complete behaviours.**

**Hyp 2) comDNs and non-comDNs may connect to different motor circuits, with some capable of generating complete behaviors and others not.**

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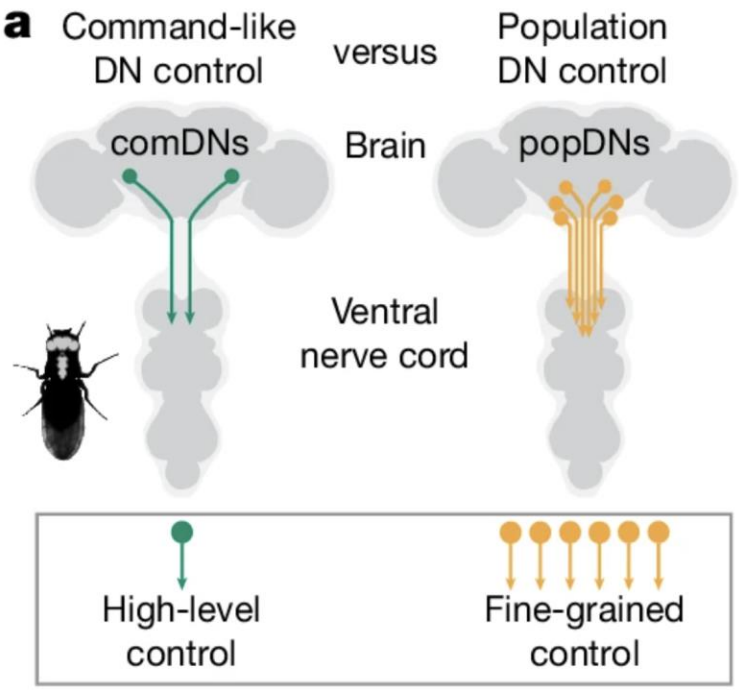
# From comDNs to DN populations

**Individual comDN Control**

Small sets of neurons that send high-level motor commands directly to motor circuits.

**Population-based DNs Control**

Co-activating multiple DNs is more effective than a single DN in triggering actions like take-off.

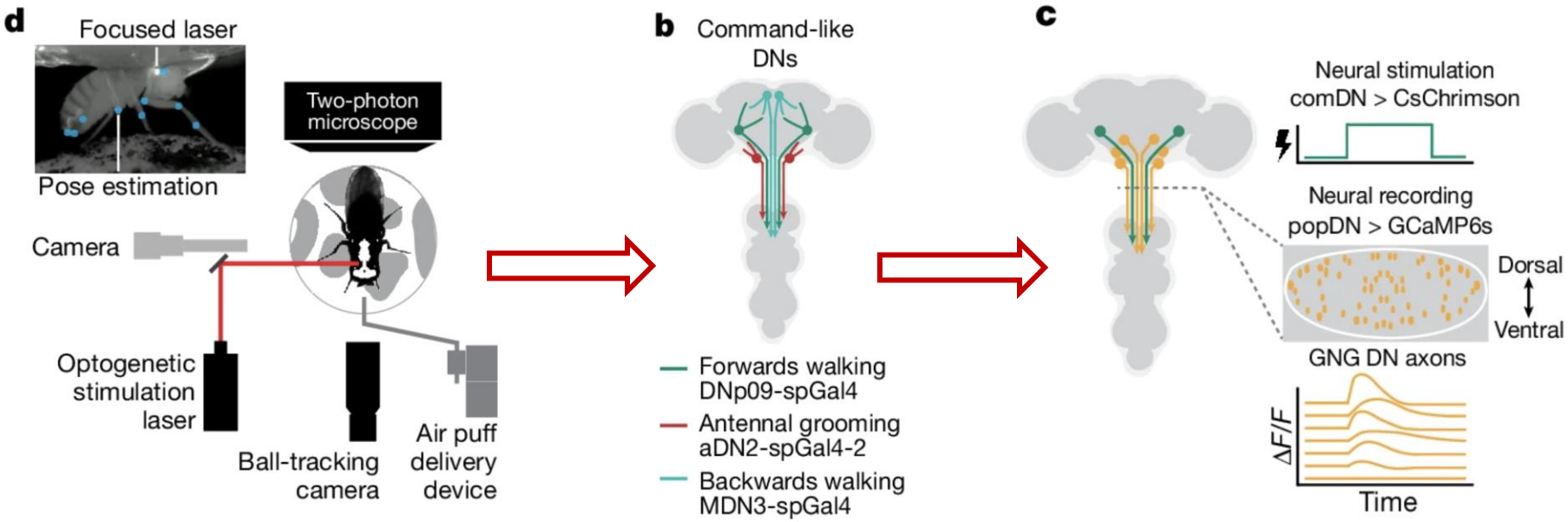


# From comDNs to DN populations

How do DNs coordinate movement in the Drosophila?

- **Optogenetics** → Used to **stimulate** comDNs and trigger behaviors.
- **Two-Photon Microscopy** → Used to **record** which DNs were recruited.

**Experimental Approach**



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# ComDNs recruit additional DNs

**Experimental Validation:** Do comDNs recruit additional DNs in the GNG?

- **Approach:** Open-Loop Optogenetic Stimulation.

# Behind the scenes

## Optogenetic Stimulation:

- **Permits the Selective Activation of comDNs by Red-Light Stimulation. -- Through CsChrimson usage.**

- **The neurons can be activated through the emission of red-light.**

- **Optogenetics were used to stimulate three well-characterized comDNs:**
  - **DNp09 – For Forward Walking**
  - **ADN2 – For Antennal Grooming**
  - **MDN – For Backward Walking**

## Two-Photon Imaging:

**Used to record the activity of DNs in the GNG through a calcium indicator. -- Fluorescent = Activated**

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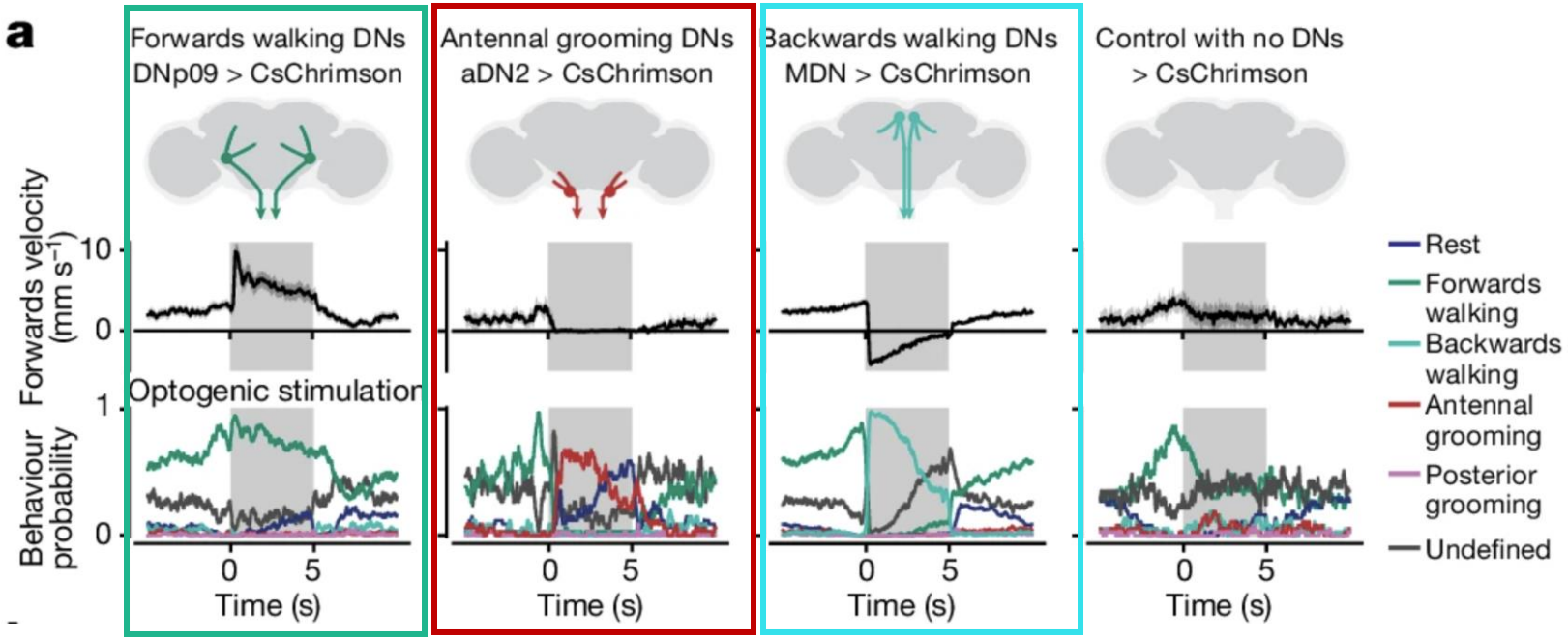

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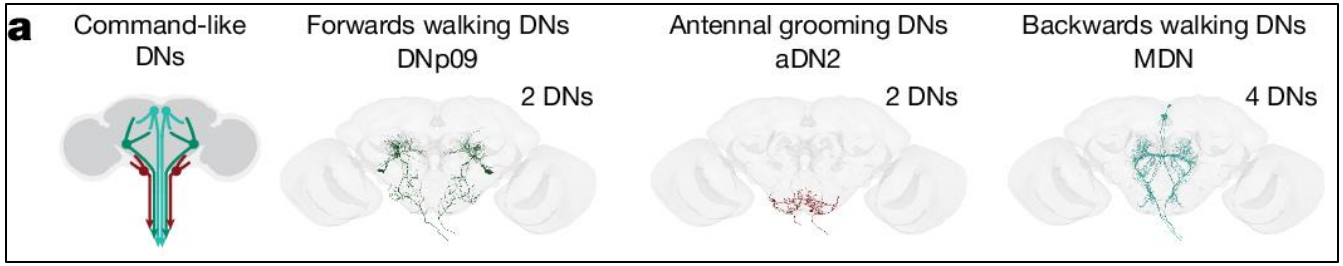
# How do comDNs connect to other DNs?

2 Circuit Mechanisms

- direct, monosynaptic excitatory connections
- indirectly via local interneurons

**Each comDN has direct, monosynaptic connections to other DNs**

**Three sets of comDNs in the female adult fly brain connectome**




**direct, monosynaptic connections between comDNs & downstream DNs**

**The location and morphologies of DNs directly targeted by comDNs.**

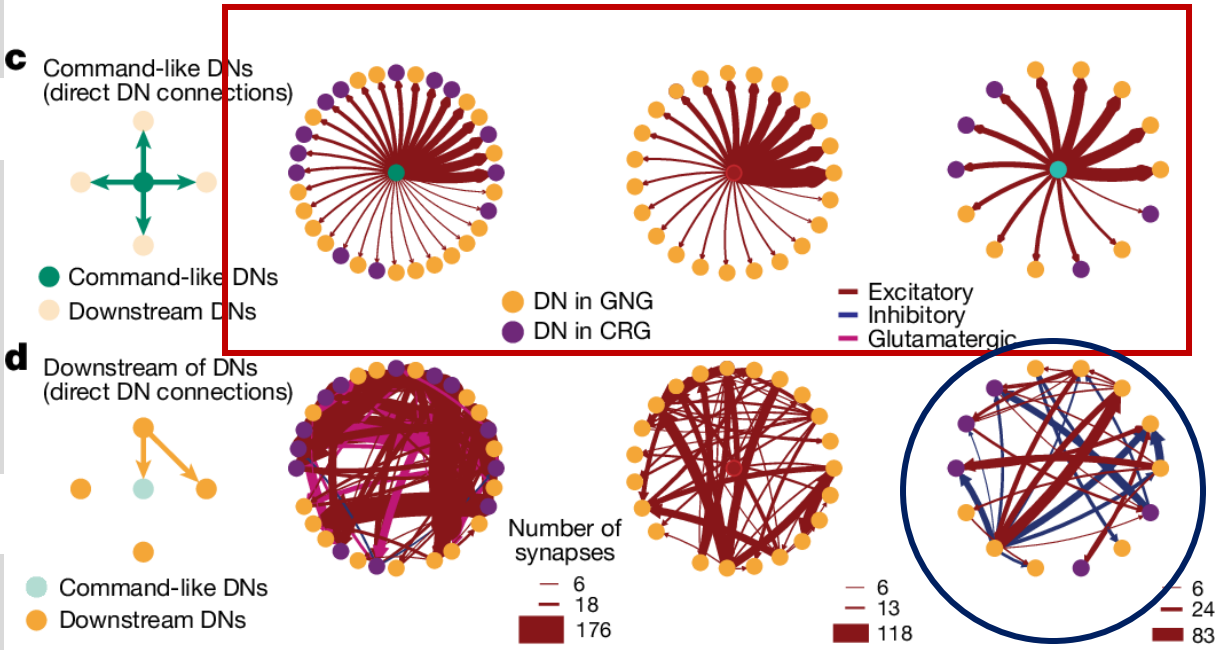
# How do comDNs connect to downstream DNs and influence neural network dynamics?

1. ComDNs probably form **excitatory connections** with downstream DNs

2. These connections are **predominantly feedforward with only sparse feedback connections**

3. Among downstream DNs, there is **strong recurrent connectivity**, with some inhibitory interactions.

**1. Almost all red arrows (excitatory connection)**




**3. Blue arrows represent the recurrent connections.**

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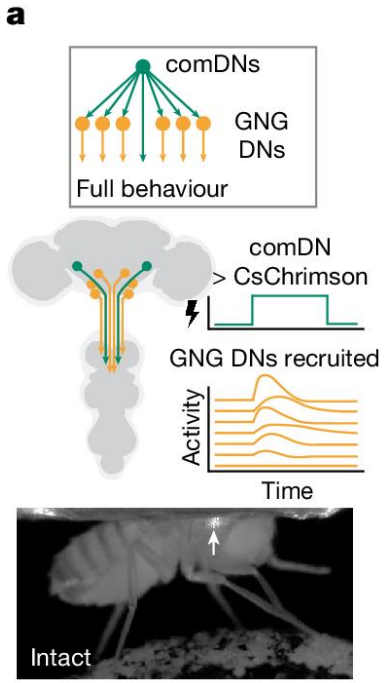
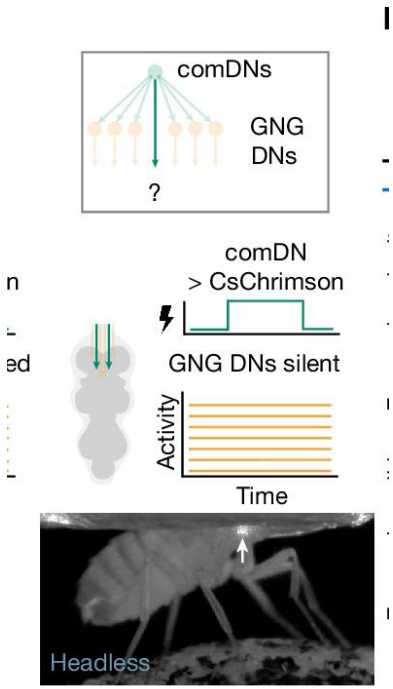
# Which behaviors require DN recruitment? —— Experiment

Method —— **Decapitation(Headless) Experiment**

- Flies remained alive and exhibited behaviors for hours.



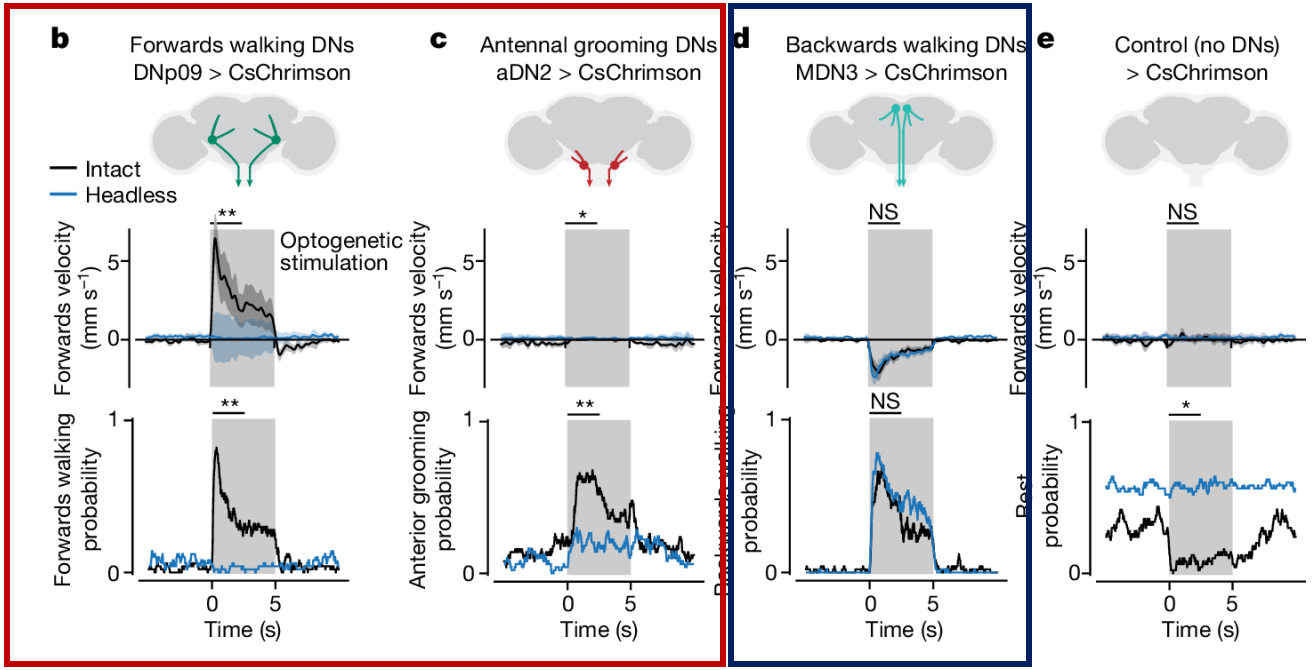

**Intact Flies:**

- comDN activation (green) recruits other DNs (orange).
- Leads to complete behaviour execution.

**Headless Flies:**

- comDN axons (green) remain active in the VNC.
- Other DNs (orange) in the brain stay silent.

# Which behaviors require DN recruitment? —— Result

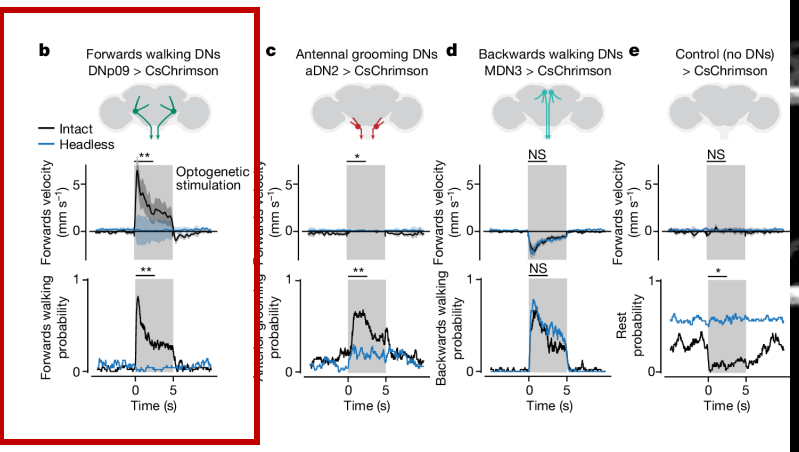


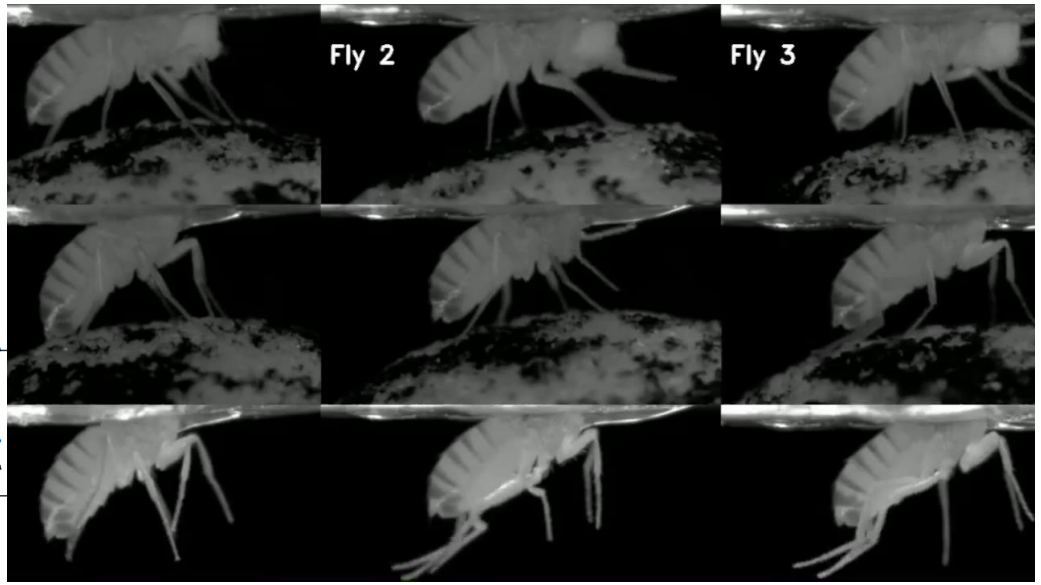

- **DNp09 failed to elicit forwards walking, but induced abdominal contraction**
- **aDN2 failed to elicit antennal, but triggered front leg approach**

- **MDN activation in headless flies still drives backwards walking.**

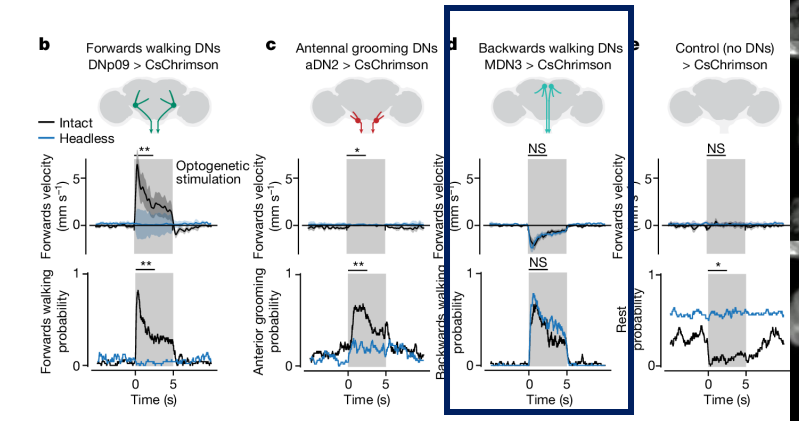
# Behavior requires & does not require DN recruitment

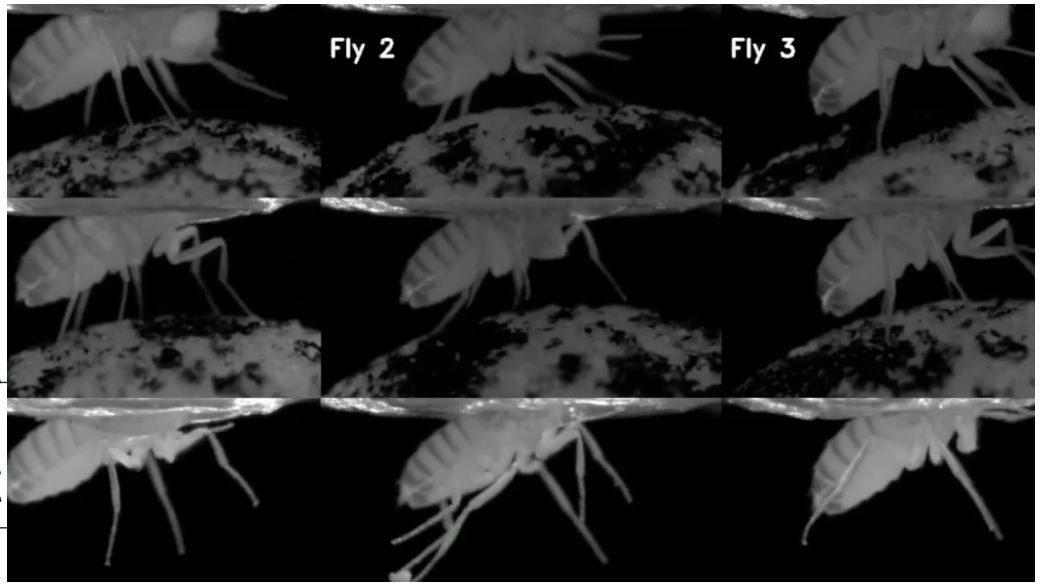
## DNp09 ✗ forwards walking



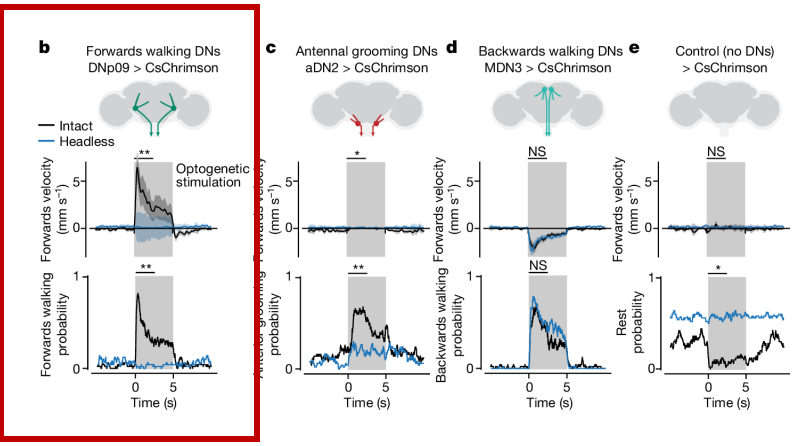

## MDN ✓ backwards walking

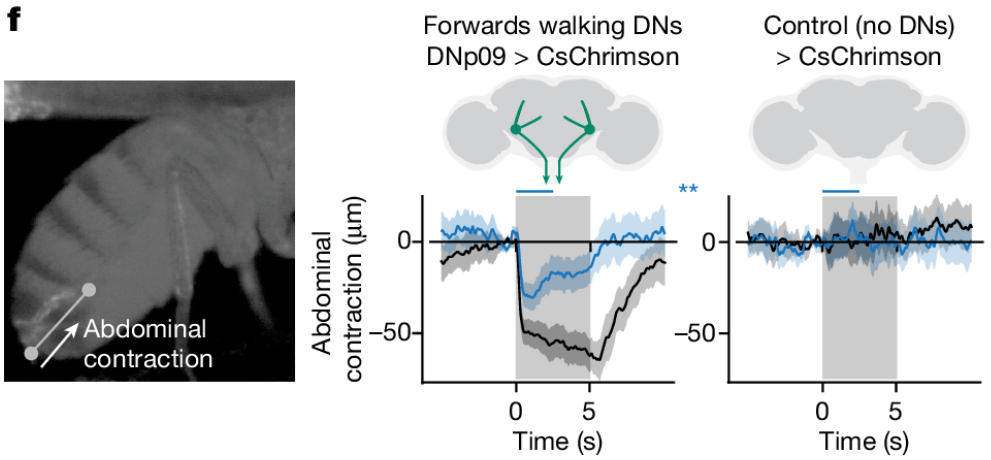


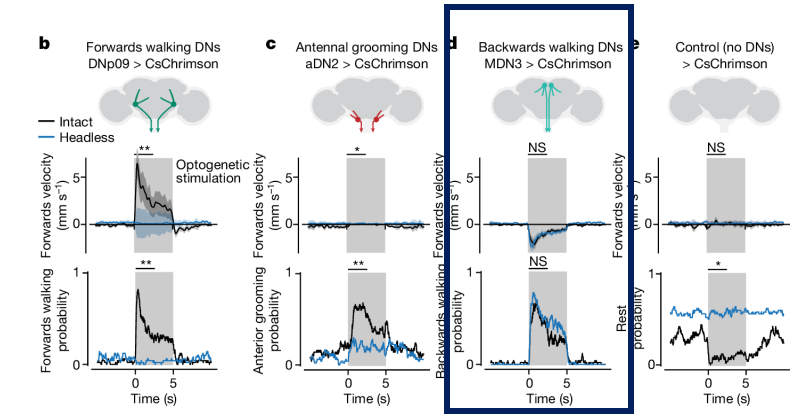
# Even behaviors requiring DN recruitment can still partially execute upon stimulation

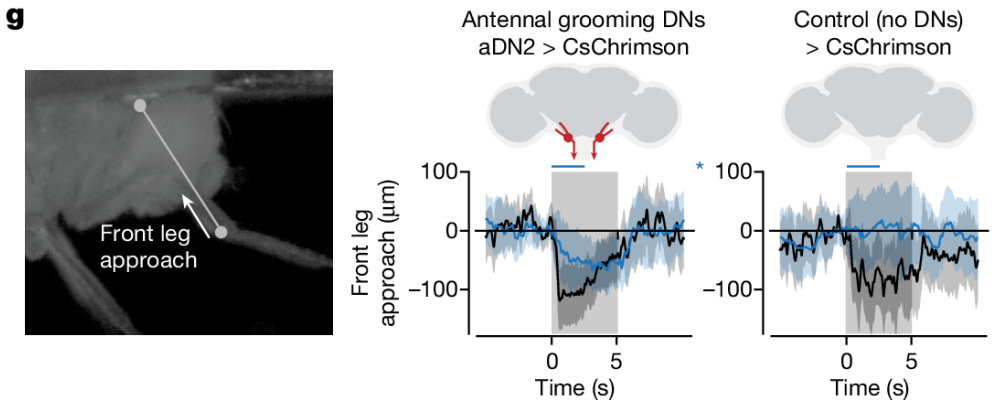
## DNp09 ✅ abdominal contraction




## aDN2 ✅ front leg approach



# DN Recruitment is Essential for Specific Behaviors

**Key Findings:**

- comDNs alone can activate in headless flies.
- Differences in behaviour between intact and headless flies stem from the **inability to recruit additional downstream DNs**.
- comDNs require DN recruitment for some behaviours (forwards walking, antennal grooming) but not others (backwards walking).

**Conclusion:**

These results suggest **multiple modes of DN behavioural control.**

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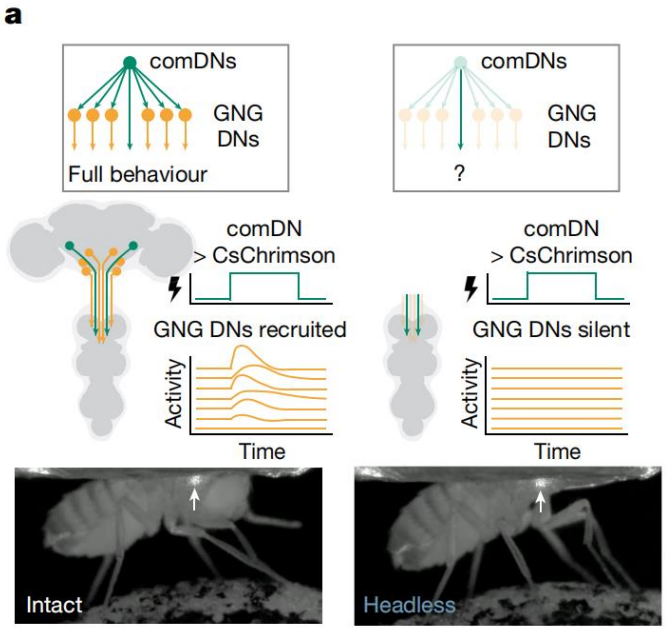
# Is recruitment necessary?

Design experiments to confirm:

- **How is the number of downstream DNs correlated with the necessity of additional recruitment?**

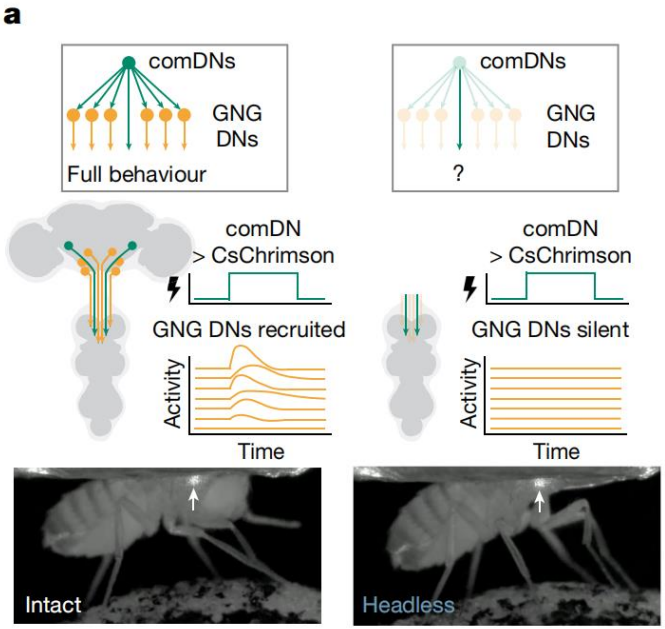



Experiment design

# Experiment Logic:

A. **Fact: Recruitment happens in the brain.** Once DNs reach the VNC, their axons mostly terminate on local motor circuits rather than on other DNs.
B. **If additional recruitment is needed for DNs to activate certain behavior, then blocking recruitment will block the behavior.**

**A+B: If additional recruitment is needed, removing the brain will block the behavior.**

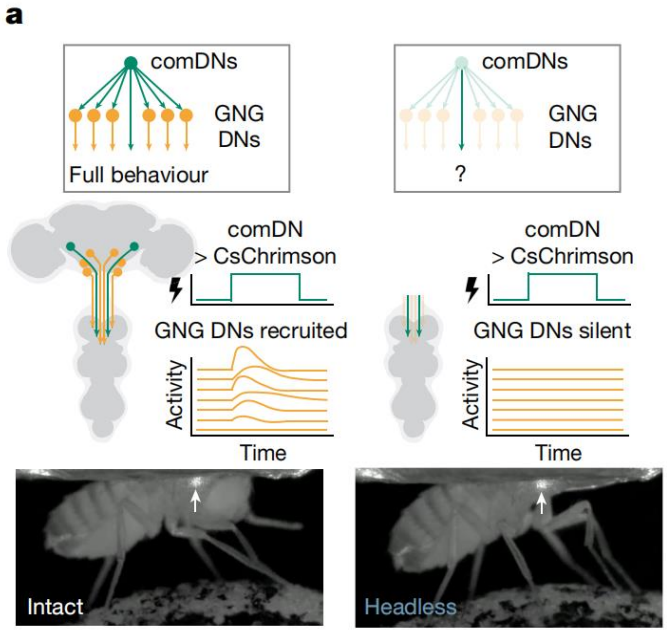



Experiment design

# Network Size Predicts Behavioral Necessity

Experiment results:

- DNs with **many connections** lost their function in headless animals (e.g., DNp09, aDN2).
- DNs with **few or no connections** retained their function (e.g., MDN, DNg14).

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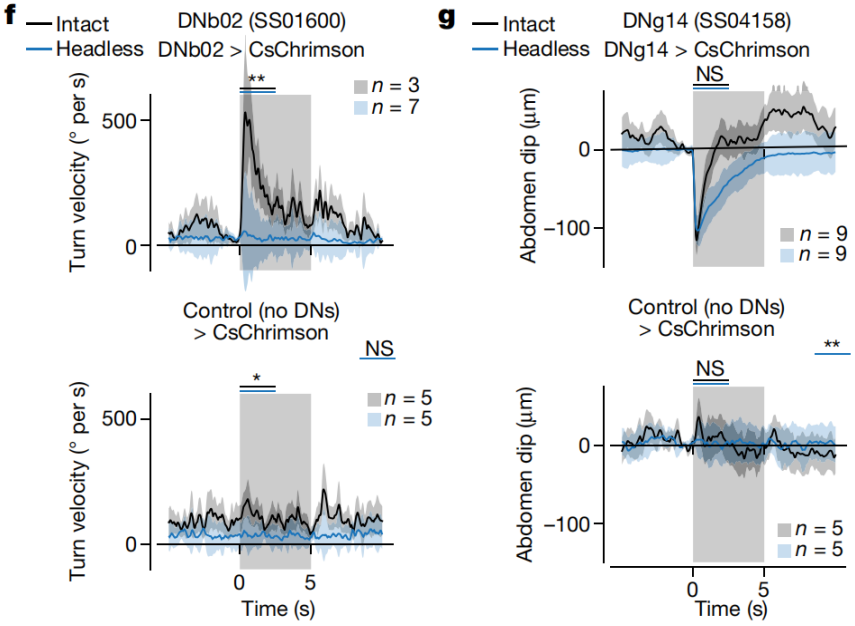
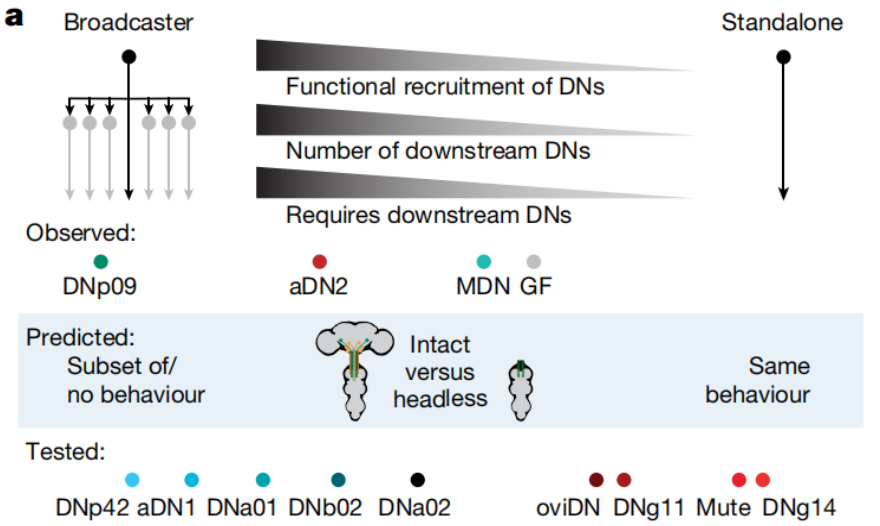


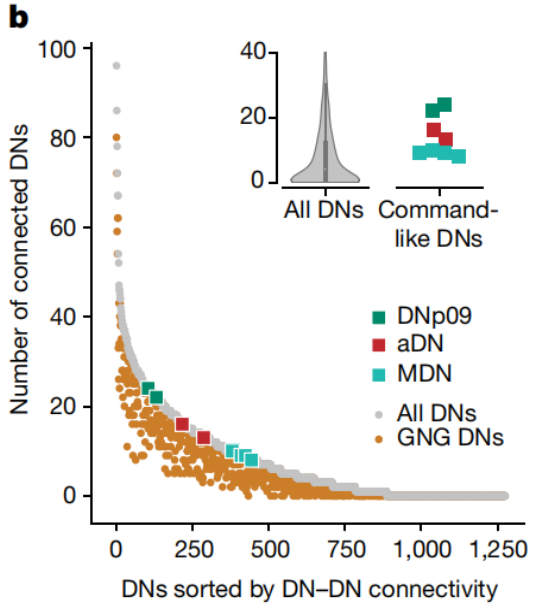

Experiment results

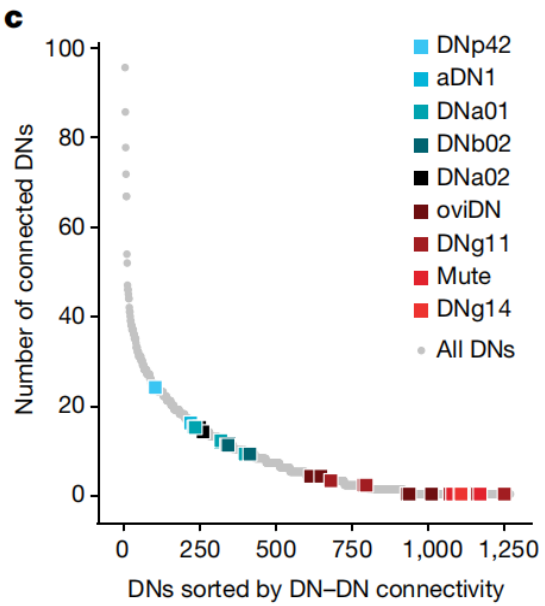
# Network Size Predicts Behavioral Necessity

Experiment results:

- There is a spectrum of DN network connectivity. **DNs with more connection is more likely to rely on the recruitment mechanism.**



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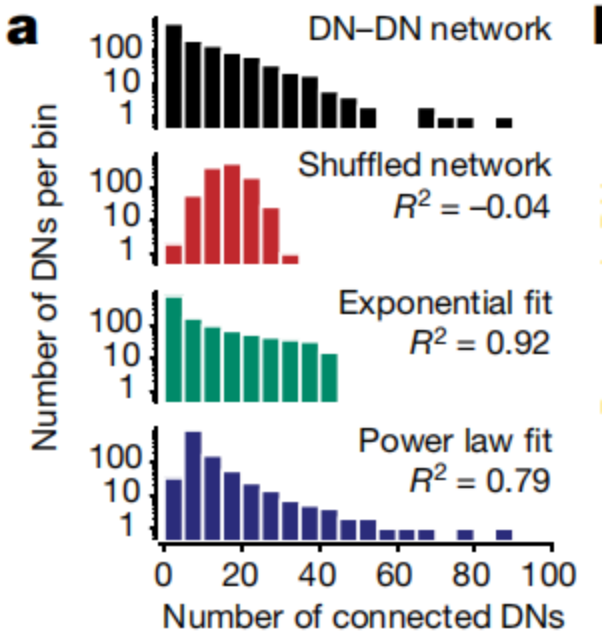
- ❑ **Network clusters correlate with behaviour**

# How is the DN Network Organized?

Possibilities:

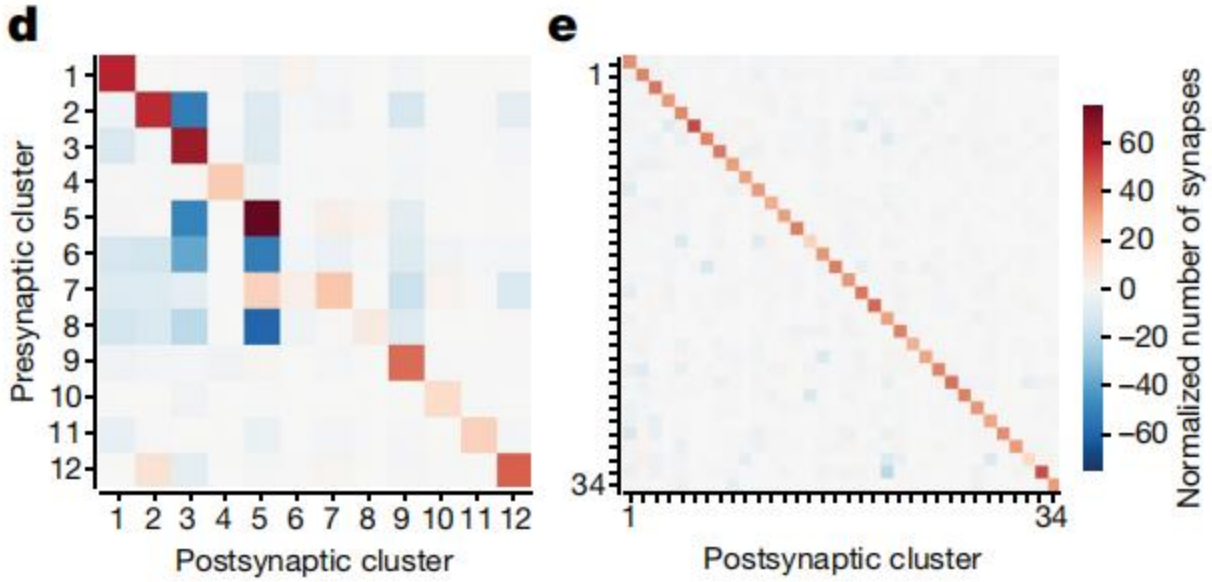
1. Random connection laws
2. Some strange connection laws (If so, which law? Why this law?)

# DN Connection is NOT Random




Degrees of vertices for different networks

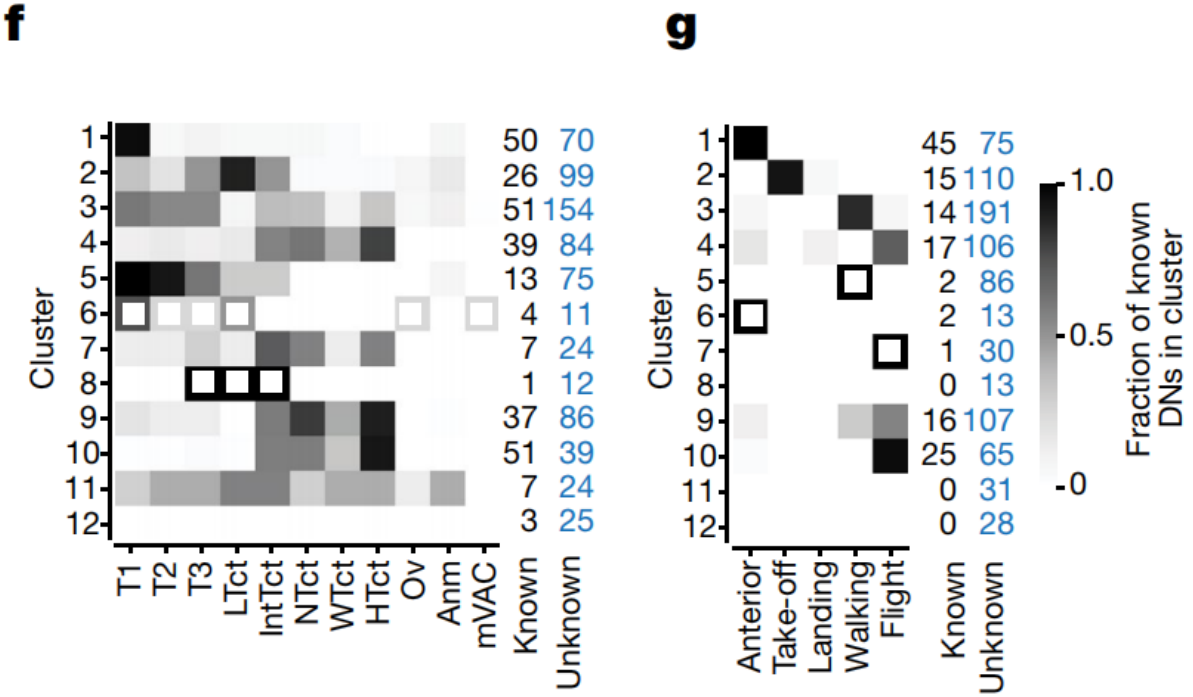
# Louvain Method Detects DN Clusters




Clusters found by Louvain Method for DN-DN network (d) and random network (e)

# Binding DN Clusters to Behaviors

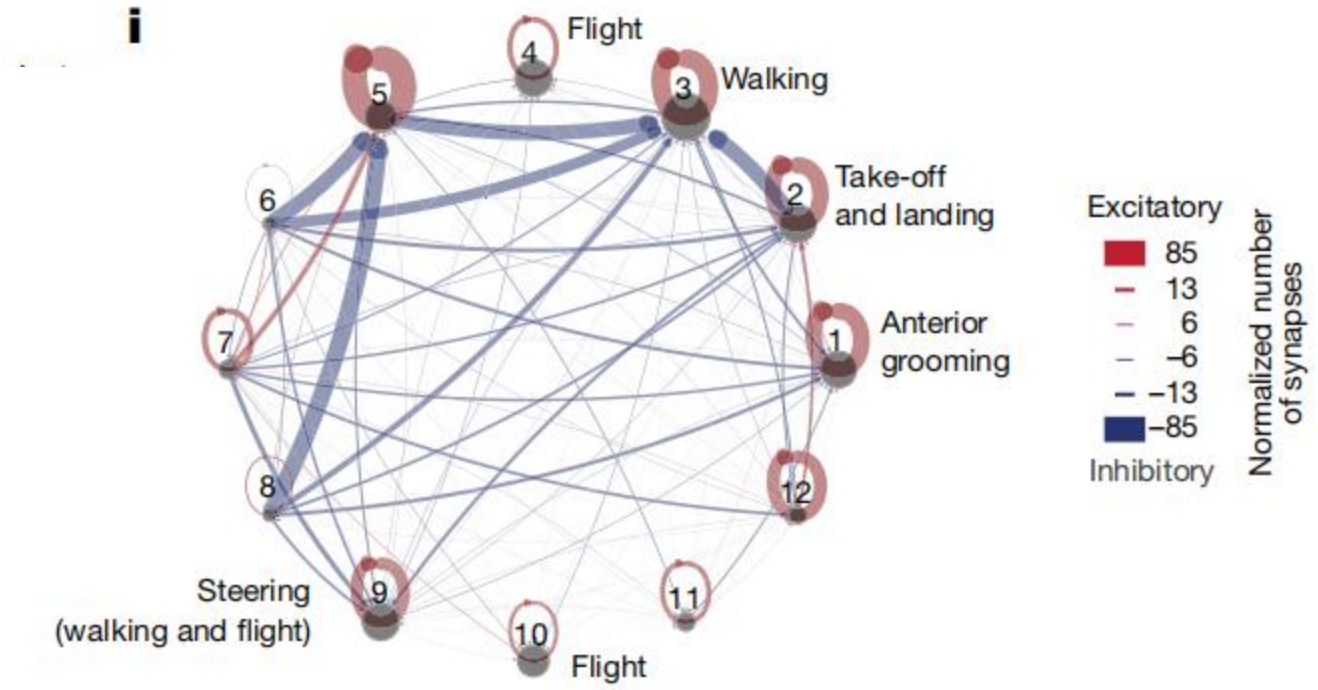
1. We already know the related behavior of some DNs, we can use this information to label DN clusters.




Labeling clusters with known DNs

# Connection Laws & Implications

1. **Excitatory connections** dominate **within** DN clusters, suggesting that neurons within a cluster work together to drive specific behaviors.
2. **Inhibitory connections** dominate **between** clusters, which likely helps in behaviour selection by suppressing conflicting movements.




Connection within and between clusters

# Main Takeaways

#1 ComDNs do not work alone, they recruit DN networks.

#2: Different DNs have different roles in motor control.

#3: DN networks are behaviorally specialized.

#4: The above findings extend beyond flies.