

# What's so special about giant fibers?

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***Myelin: A new model for evolutionary innovation***

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What's so special about  
giant fibers?

*Giant fibers show us  
that **size matters.***

# Behavioral adaptation involves axon diameter.

## ***Benefit***

Larger axons increase speed and reliability of neural signaling.

## ***Compromise***

Smaller axons occupy less space and use less energy.

## ***Consequence***

Large axons evolve only where speed is critical.

## ***In vertebrates . . .***

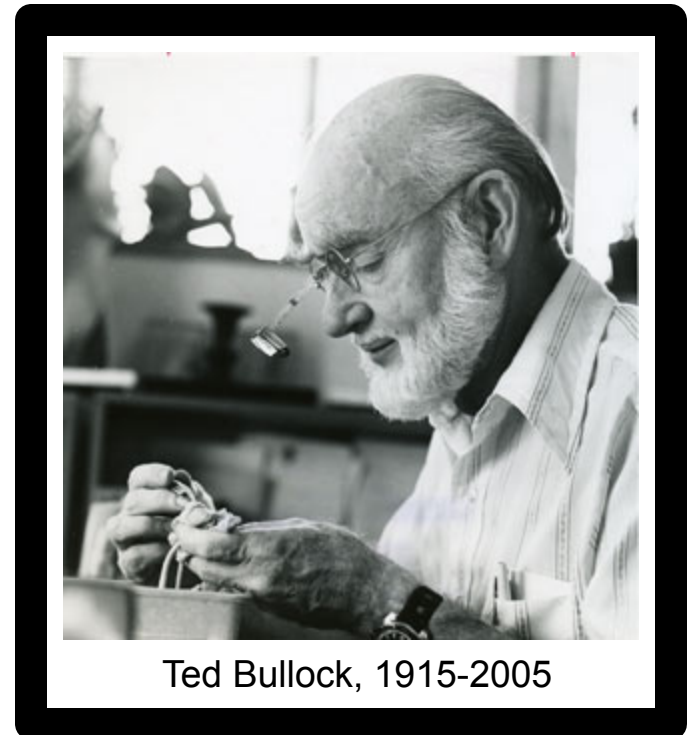
Axon diameter determines whether or not an axon is myelinated.

Axon diameter regulates the thickness of myelin.

See Michailov, G.V., et al. (2004) Axonal neuregulin-1 regulates myelin sheath thickness. *Science* 304: 700-703.

**Giant fibers are defined not by their absolute size but by the fact that they are far larger than the other fibers in the same animal.**

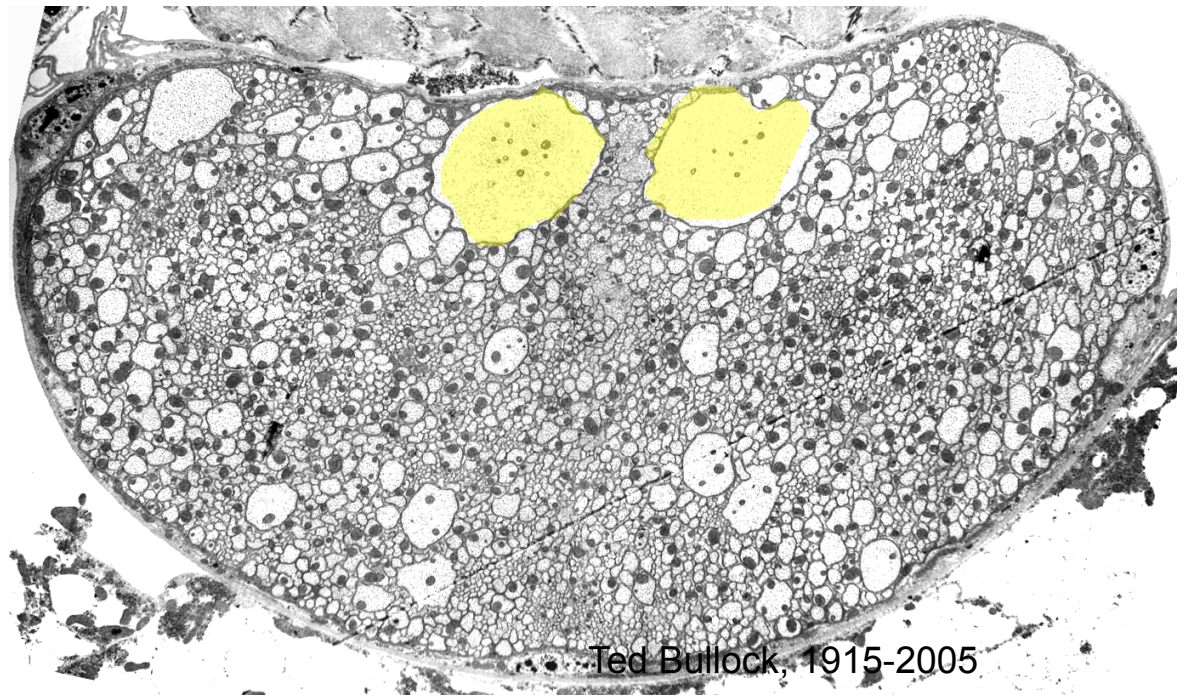
**Bullock & Horridge, 1965**  
*Structure and Function in the Nervous Systems of Invertebrates*



**Giant fibers are a conspicuous feature in the cervical connective of several flies (Diptera), such as *Drosophila melanogaster*.**

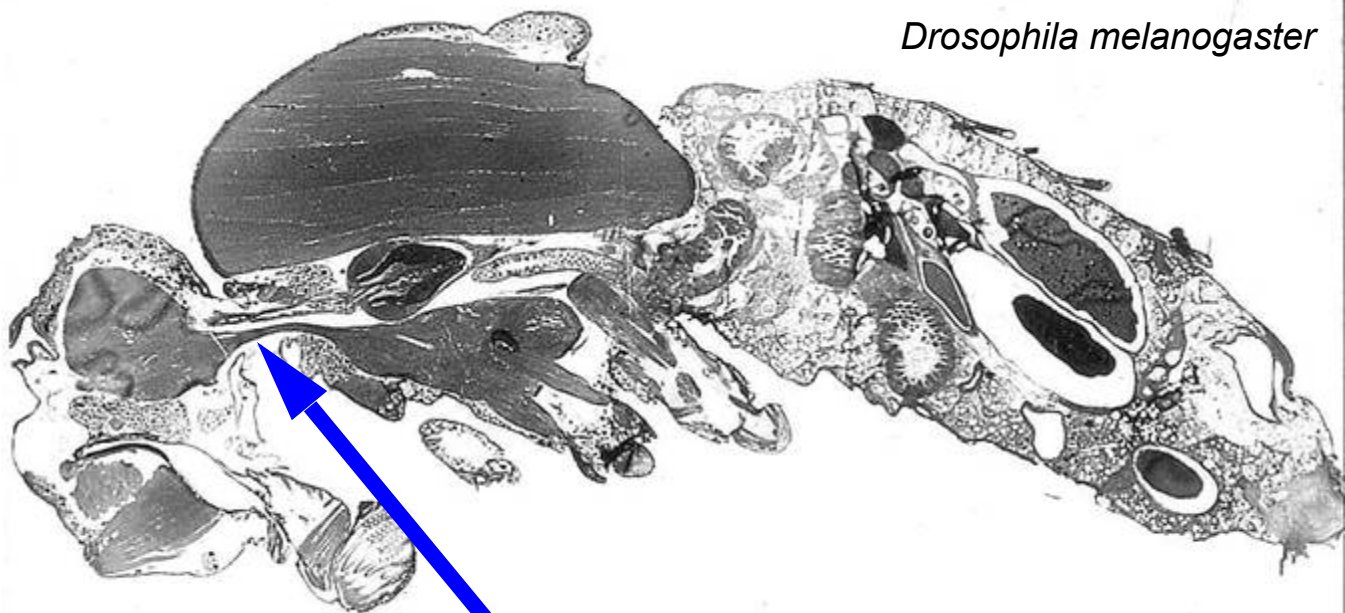


*Drosophila melanogaster*

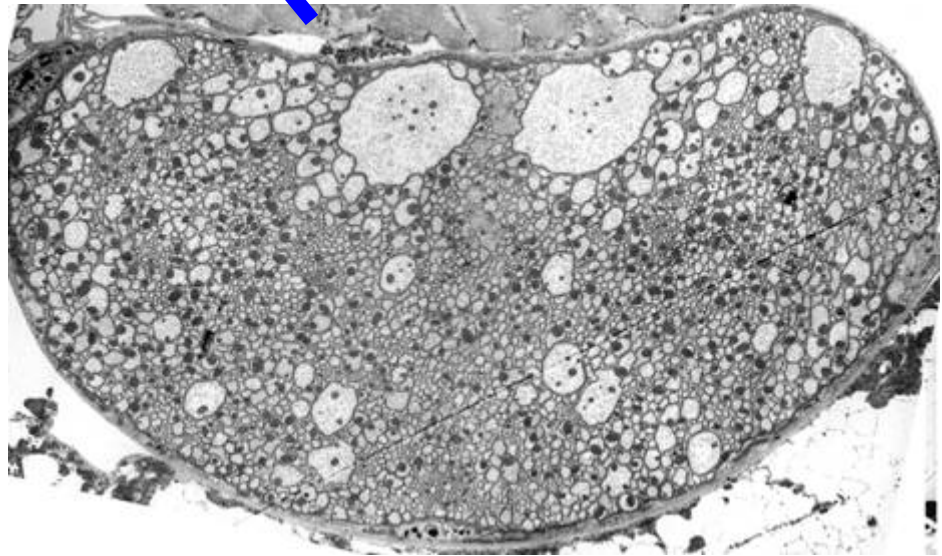


Ted Bullock, 1915-2005

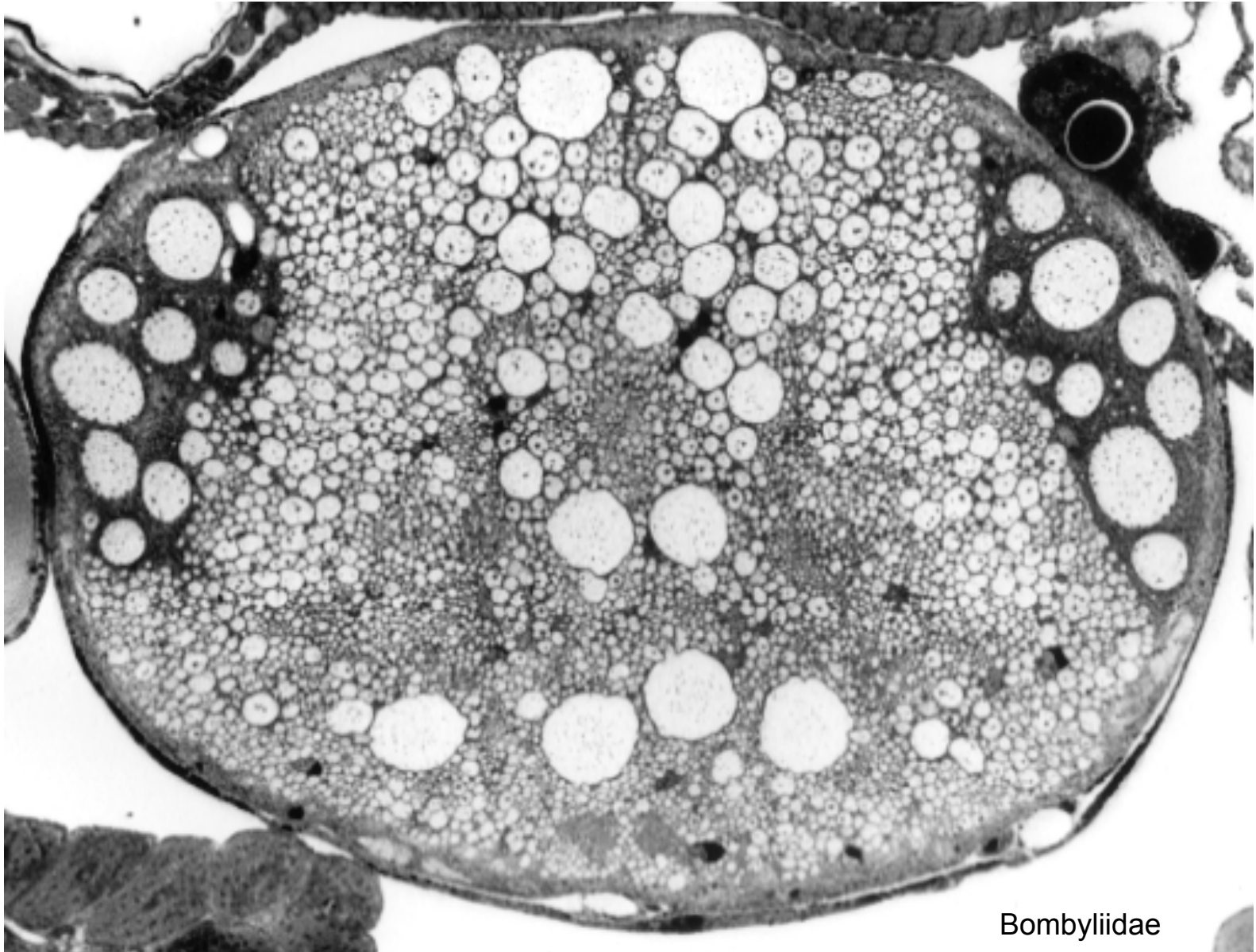
*Drosophila melanogaster*



cervical connective



**Cervical connective axons come in many sizes.**



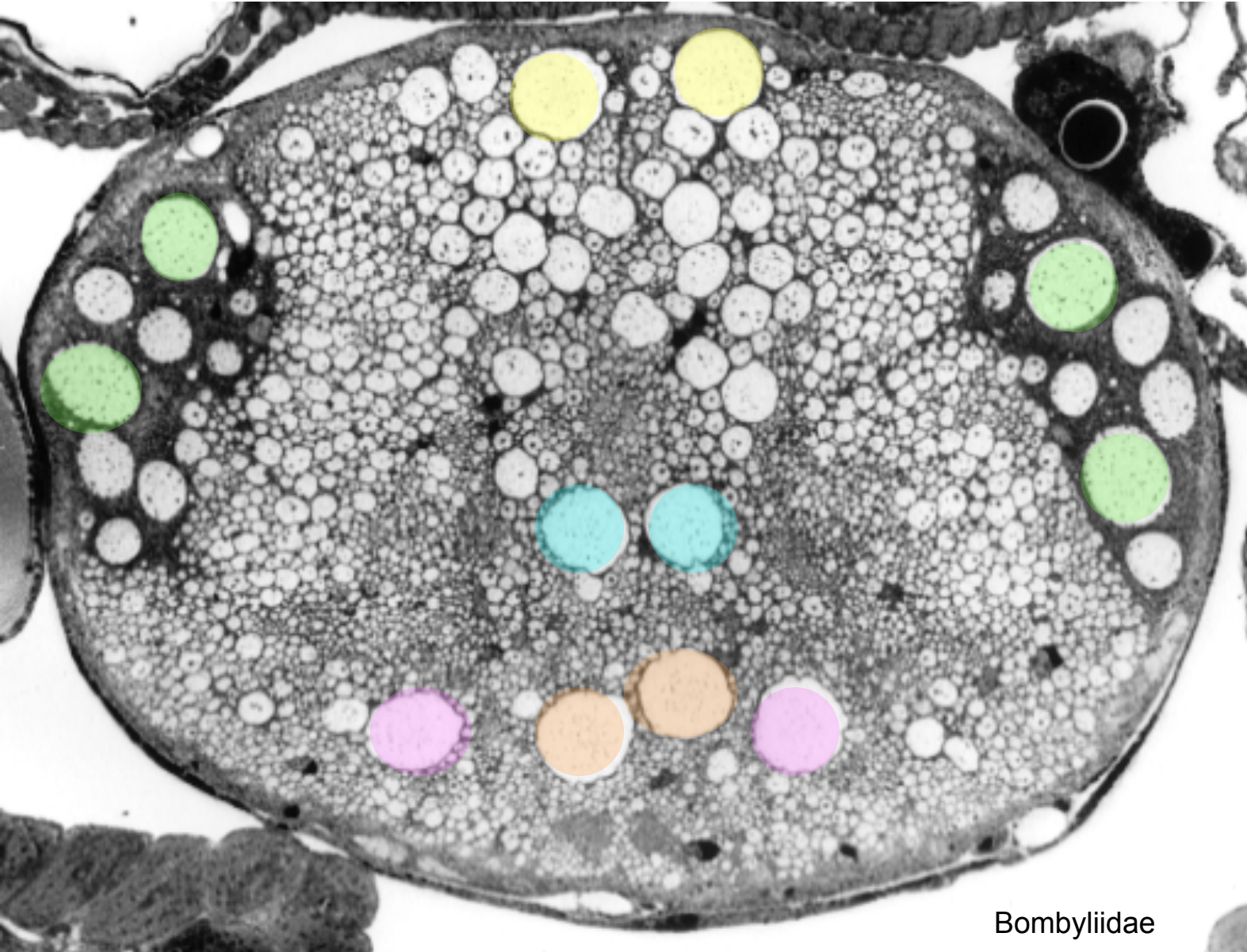
Bombyliidae



“Giantness” is relative.



Individual large axons are identifiable by position as well as size.

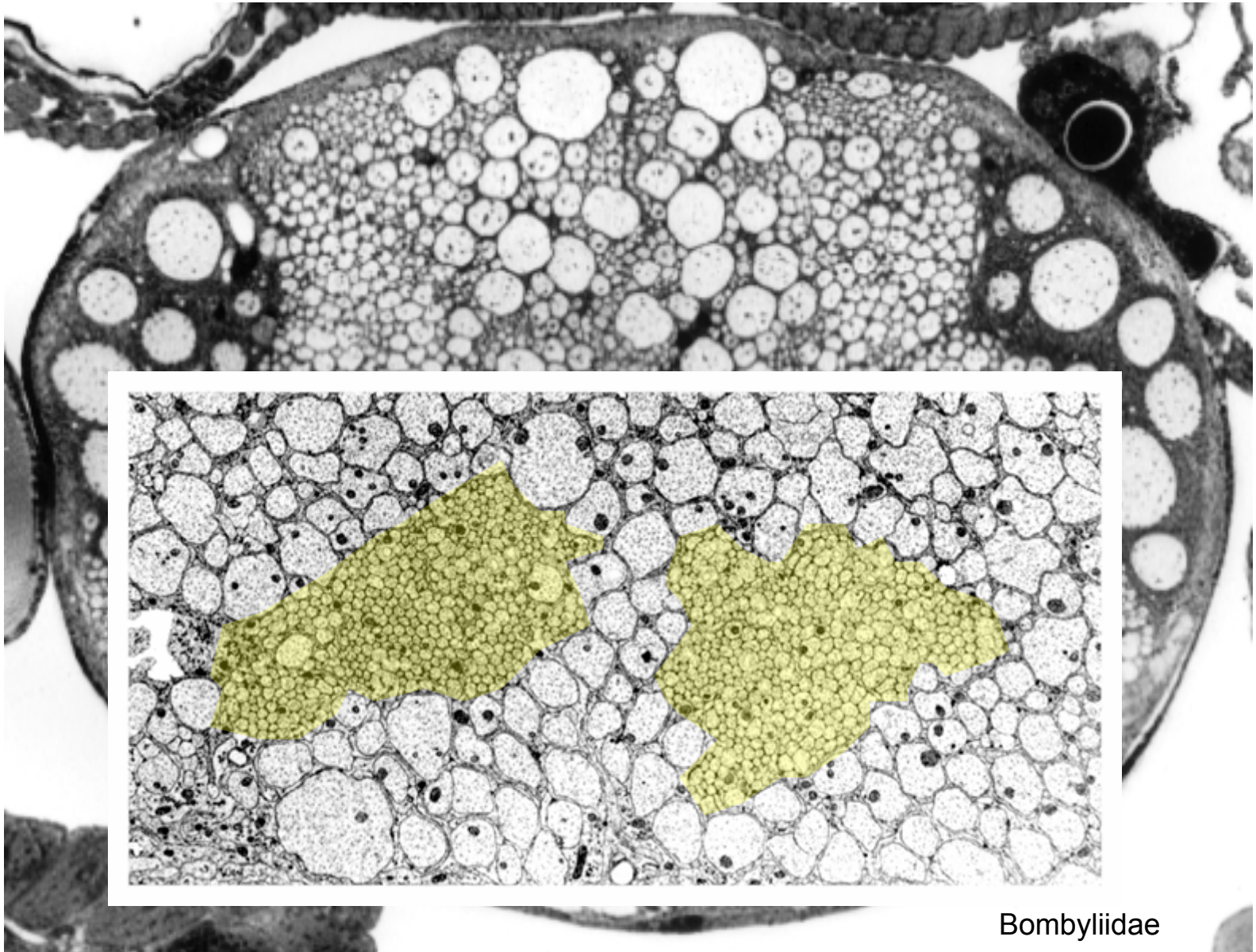


Even very small axons can be identified, at least as tracts.



Bombyliidae

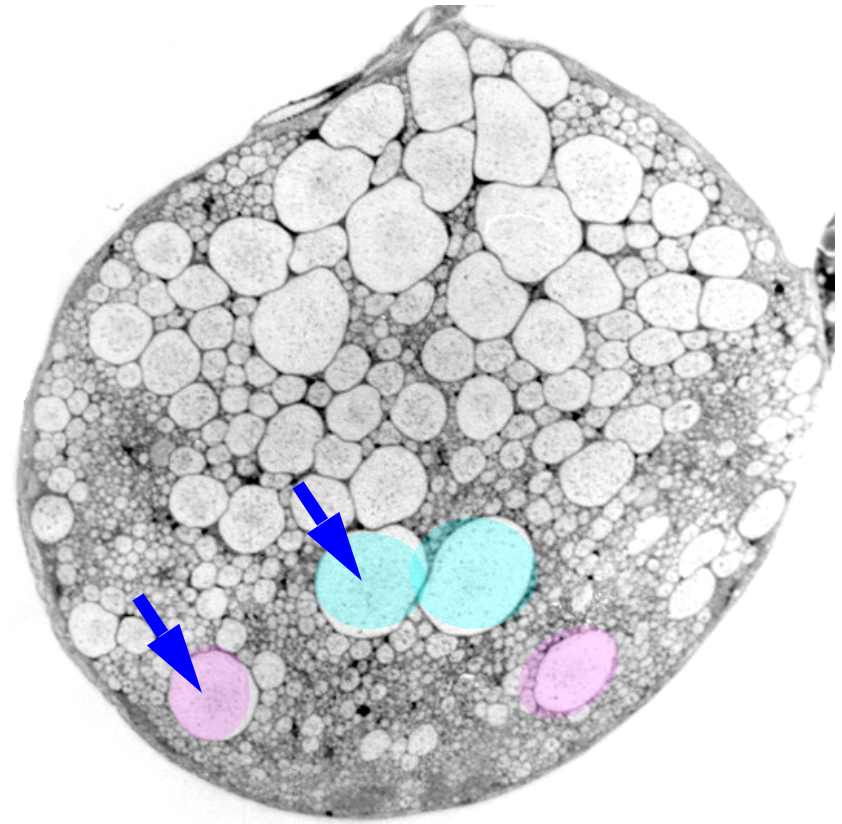
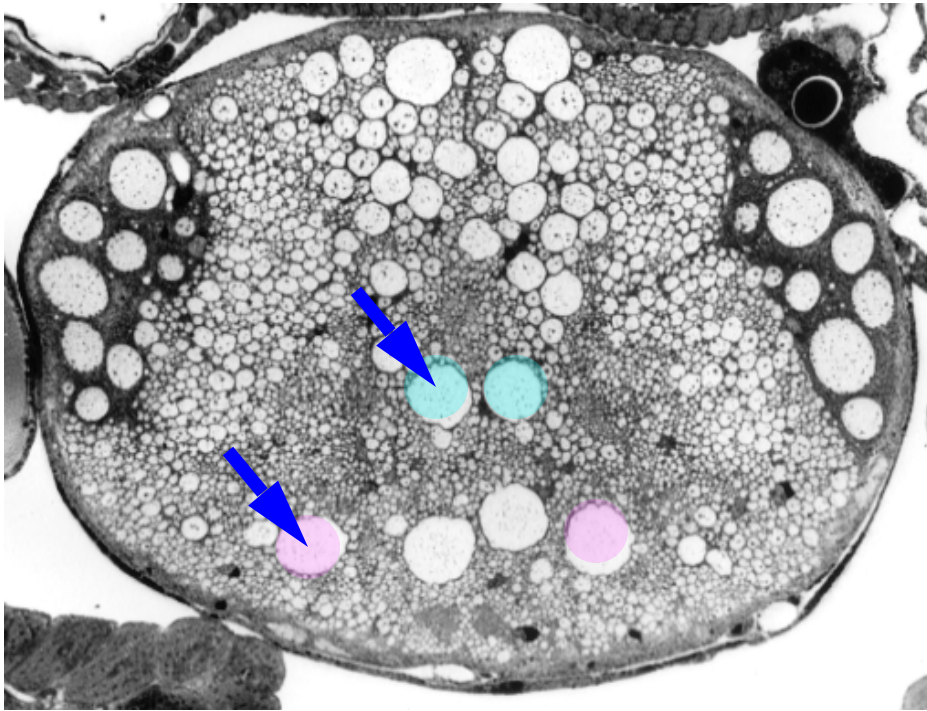
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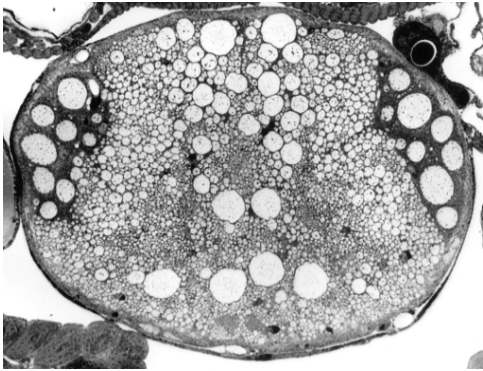
**Repeatedly in each group, we find that related species differ in respect to possession of giant fibers, which must therefore evolve rather readily.**

**Bullock & Horridge, 1965**  
*Structure and Function in the Nervous Systems of Invertebrates*

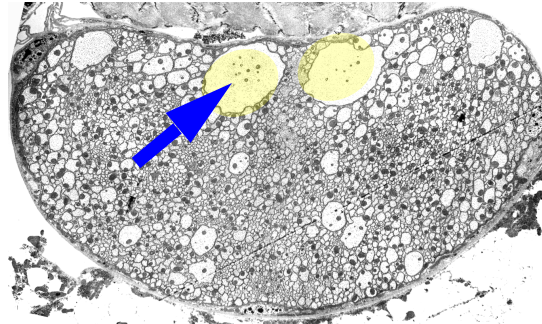
Repeatedly in each group, we find that related species differ **in their pattern of large and small axons**, which must therefore evolve rather readily.



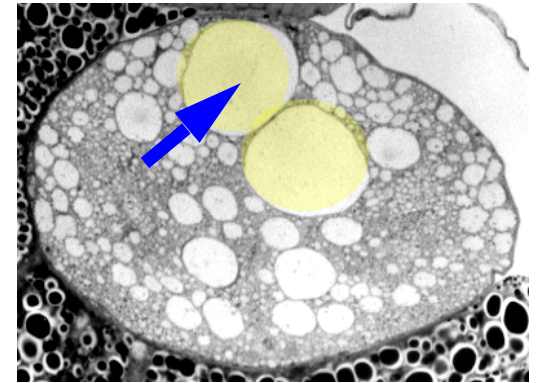
... more variation in the pattern of large and small axons.



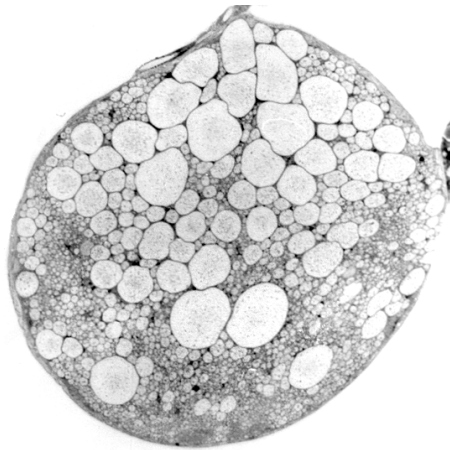
Bombyliidae



Drosophilidae



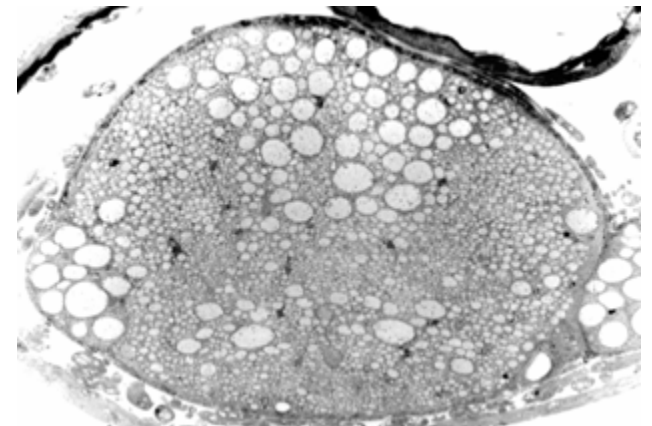
Lauxaniidae



Bombyliidae

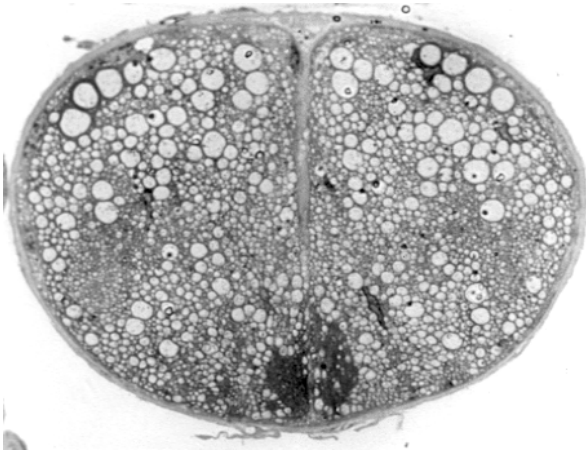


Sphaeroceridae

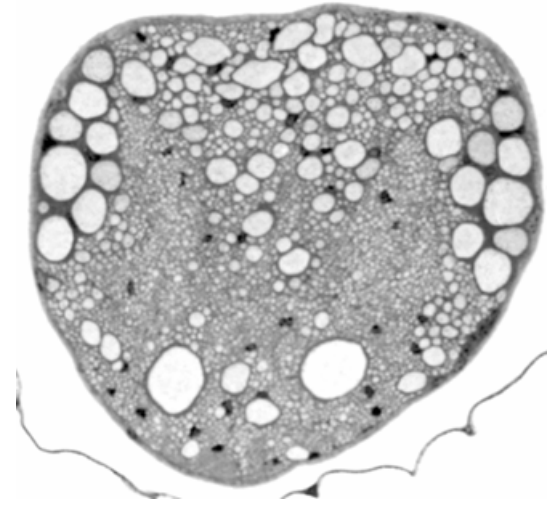


Tachinidae

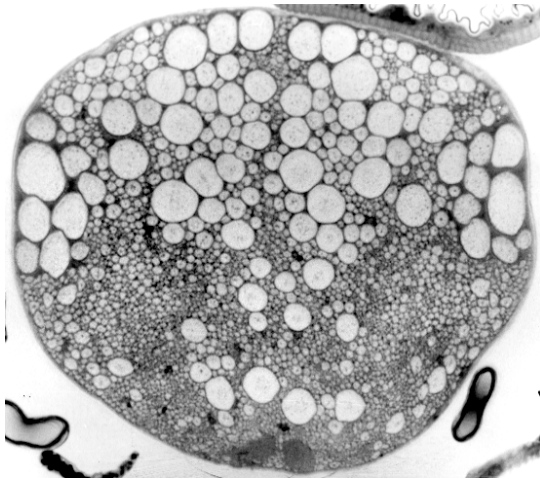
Axon size displays remarkable evolutionary flexibility.



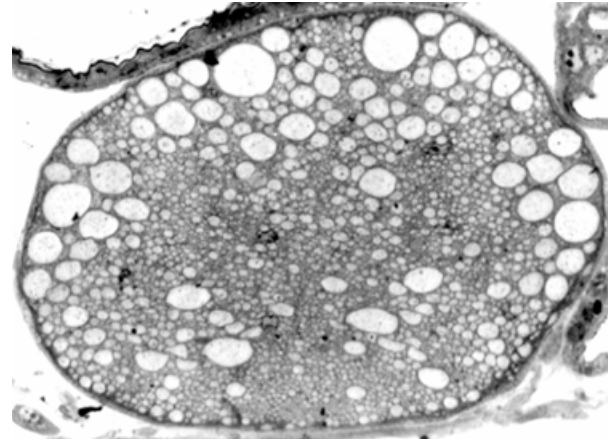
Tipulidae



Tabanidae

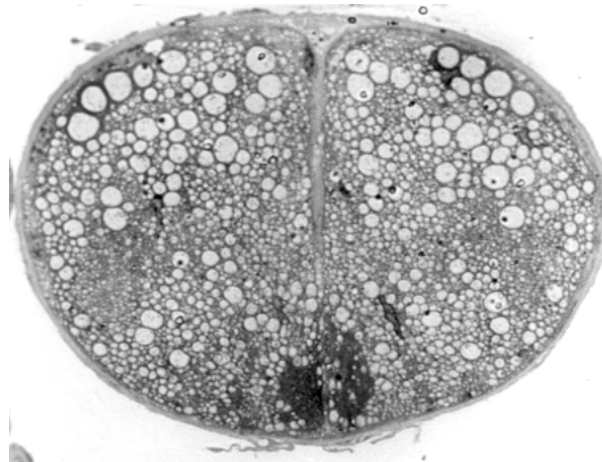
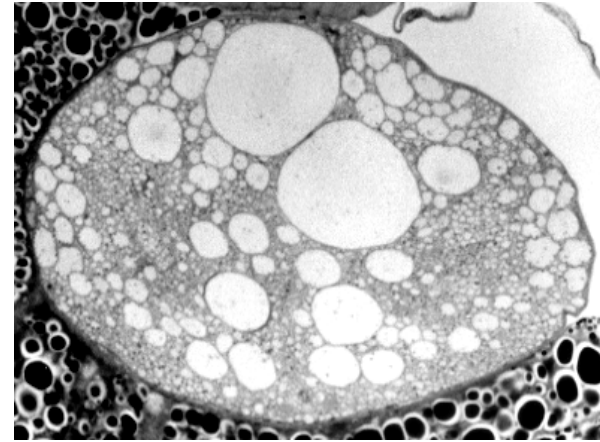
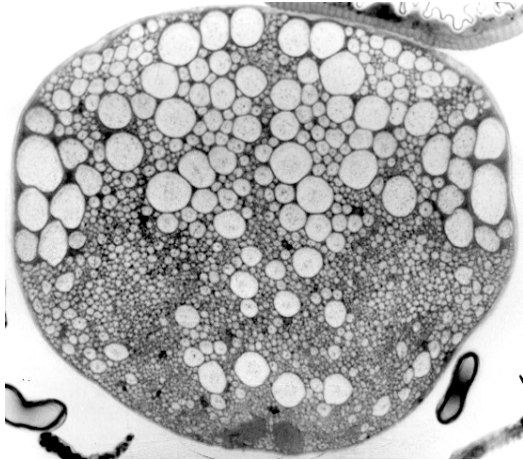


Syrphidae



Sarcophagidae

# Evolutionary flexibility raises several questions.





# Three evolutionary questions

## 1. **Natural selection**

What selective advantage is provided by the trait?

## 2. **Phylogeny**

When (and how often) did a trait evolve, and what condition preceded it?

## 3. **Variation**

What kinds of mutation enable the trait to be advantageously modified?

## **Selection** -- Phylogeny -- Variation

1. What selective advantage is provided by differentiated axon diameters?

We believe that axon size is adaptively related to behavioral quickness, balanced against other economic constraints.

## Selection -- **Phylogeny** -- Variation

1. What selective advantage is provided by differentiated axon diameters?
2. What has been the evolutionary history of differentiated axon diameters?

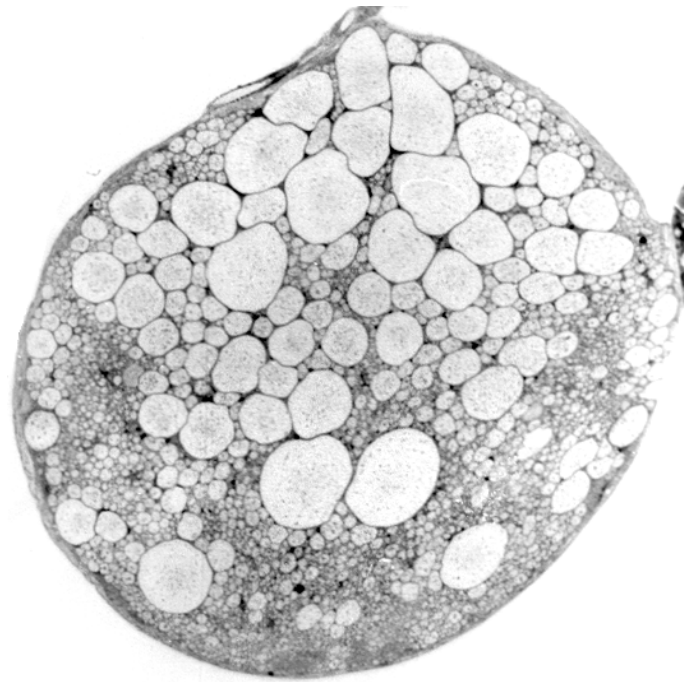
Differing axon size distributions have evolved independently many times.

# Selection -- Phylogeny -- **Variation**

1. What selective advantage is provided by differentiated axon diameters?
2. What has been the evolutionary history of differentiated axon diameters?
3. How does mutation adjust the pattern of differentiated axon diameters?

**This is the challenging, unanswered question!**

# What is so special about giant fibers?

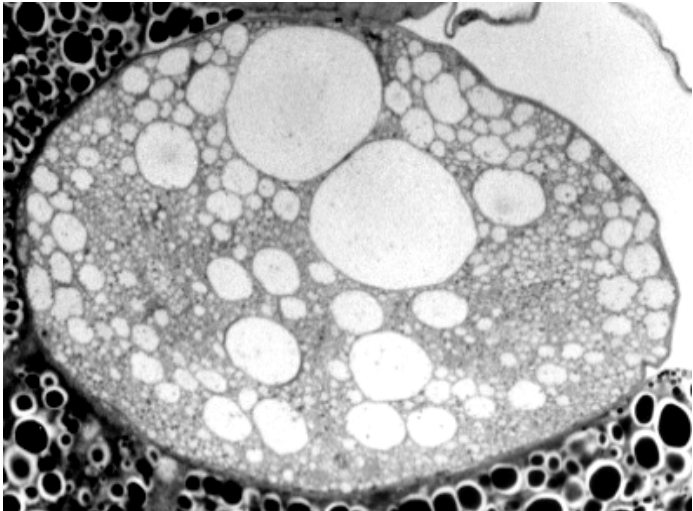
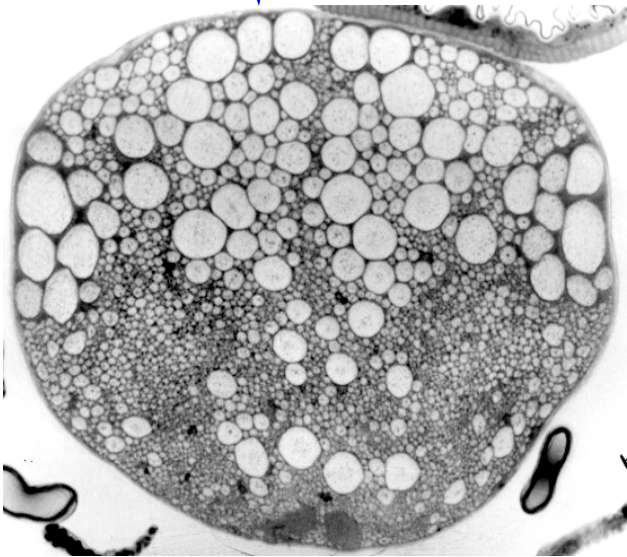
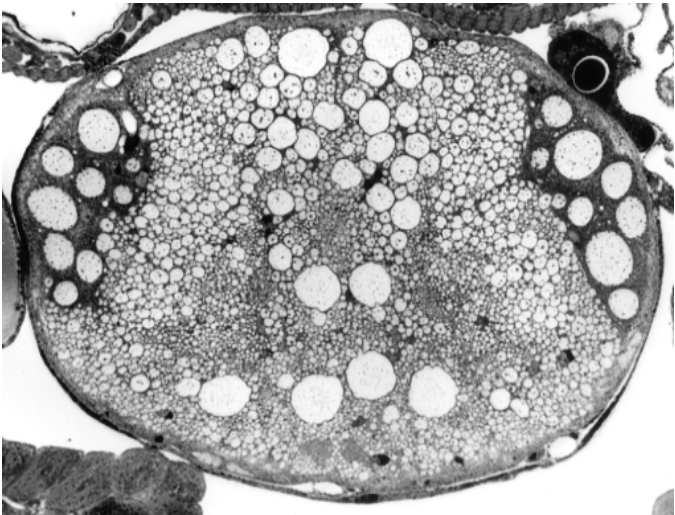
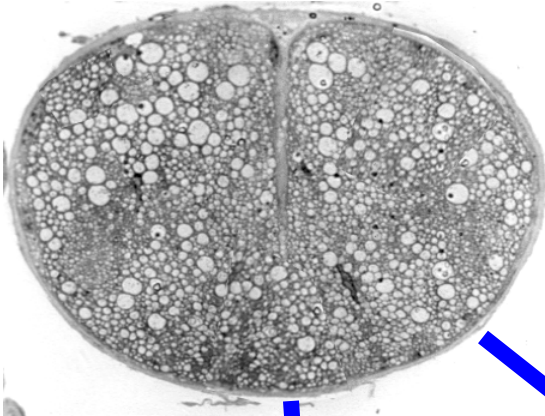


# What's so special about giant fibers?

*Giant fibers are significant not just because they are exceptionally large . . .*

Giant fibers are exemplars of the wonderfully fine detail available for evolutionary plasticity of individual cells.

(hypothetical ancestral state)



***Charles Darwin:***

What the devil determines each particular variation?

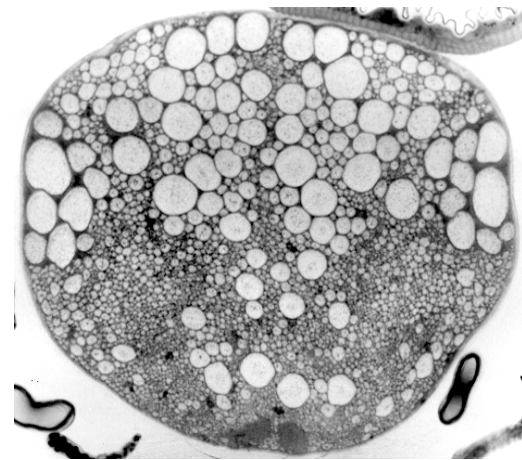
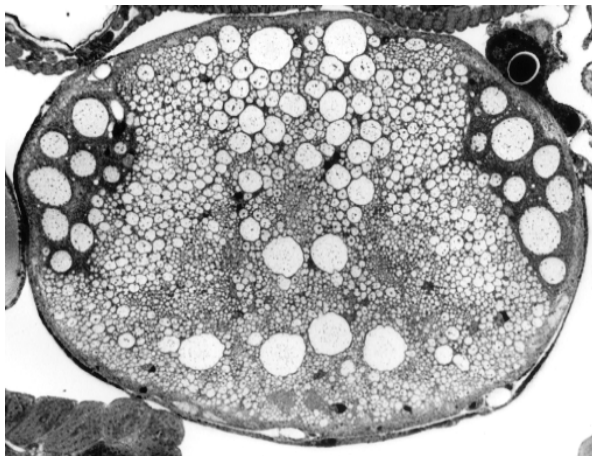
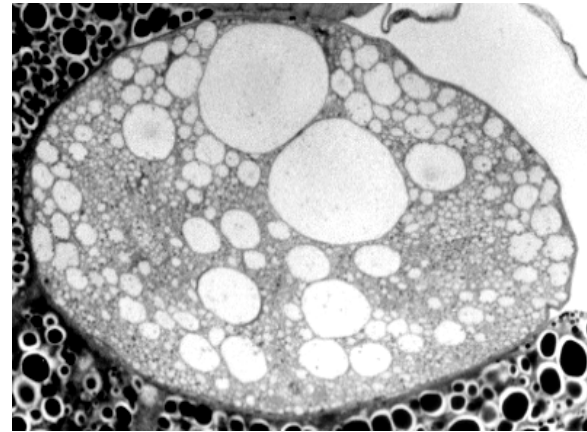
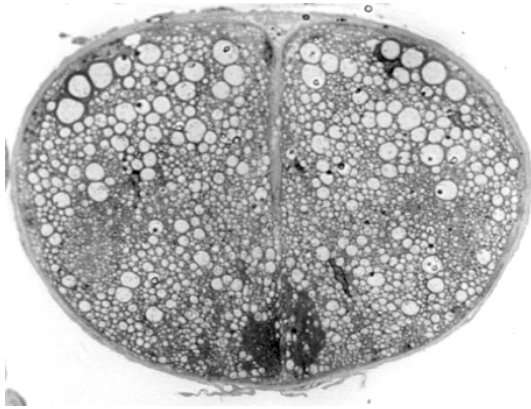
What makes a tuft of feathers come on a cocks head,  
or moss on a moss rose?

letter to T.H. Huxley  
Nov. 25, 1859





What the devil determines the particular size for each individual axon? What makes giant fibers come in a fly's neck?

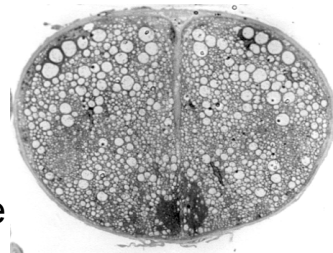


How does the genome tell particular axons what their individual sizes should be?

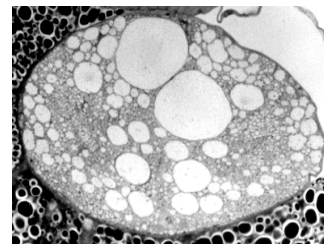
How does DNA specify precise parameters of axonal growth?

How are *individual* axons genetically differentiated from one another?

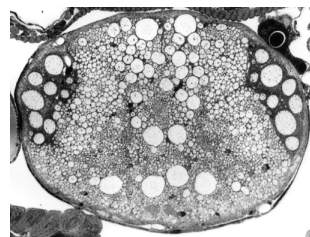
How is this specification and differentiation adjusted by mutation?



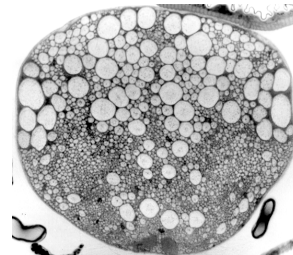
Tipulidae



Lauxaniidae



Bombyliidae



Syrphidae

# How does this apply to myelin?

How does mutation adaptively “tune” the signaling relationship between myelin-forming cells and their associated axons?

How does mutation specify the identities of particular axons destined for myelination?



Answers to such questions may tell us not just about myelin, but about evolution itself.

**Copepod axons:** Davis, et al. (1999) *Nature* **398**: 571.

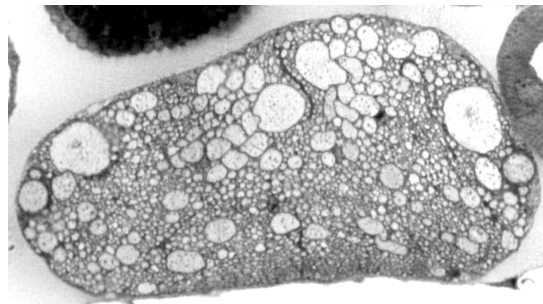
## ***Charles Darwin again:***

A grand and almost untrodden field of inquiry will be opened,  
on the causes and laws of variation . . .

Origin of Species, 1859

Can we find ***protocols*** for mutation, which can facilitate the  
evolutionary adjustment of adaptive traits, such as size and  
myelination for individual nerve cells?

See: Doyle, Csete & Caporale (2006)  
in ***The Implicit Genome***.



Ephyridae

**God in his wisdom made the fly  
And then forgot to tell us why.**

Ogden Nash



*Flies were made so one and all  
To contemplate the mystery  
Of many axons great and small  
Evolved in such diversity.*

DGK

## REFERENCES

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Doyle, J., Csete, M., & Caporale, L. (2006) An engineering perspective: The implicit protocols. In: *The Implicit Genome*, L. Caporale, ed. Oxford Univ. Press, New York.

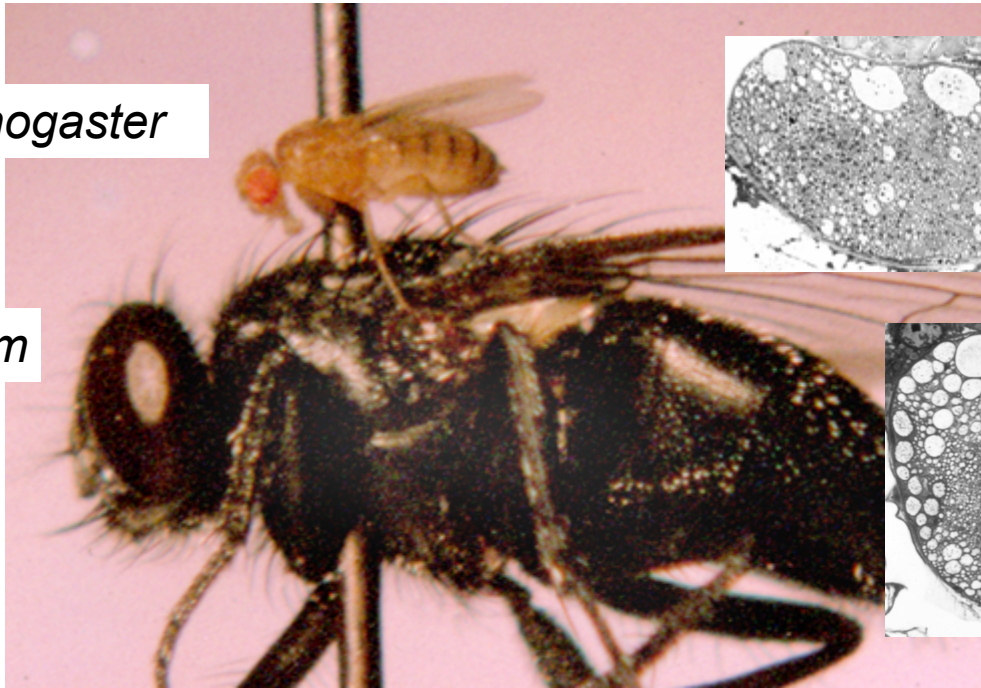
## ACKNOWLEDGMENTS

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Technical assistance was provided by J. Bozzola, M. Doran, N. Kammlade, S. Sharif, and R. Venezia.

Most fly identifications were provided by entomologists cooperating with the Systematic Entomology Laboratory of the Agricultural Research Service, USDA.

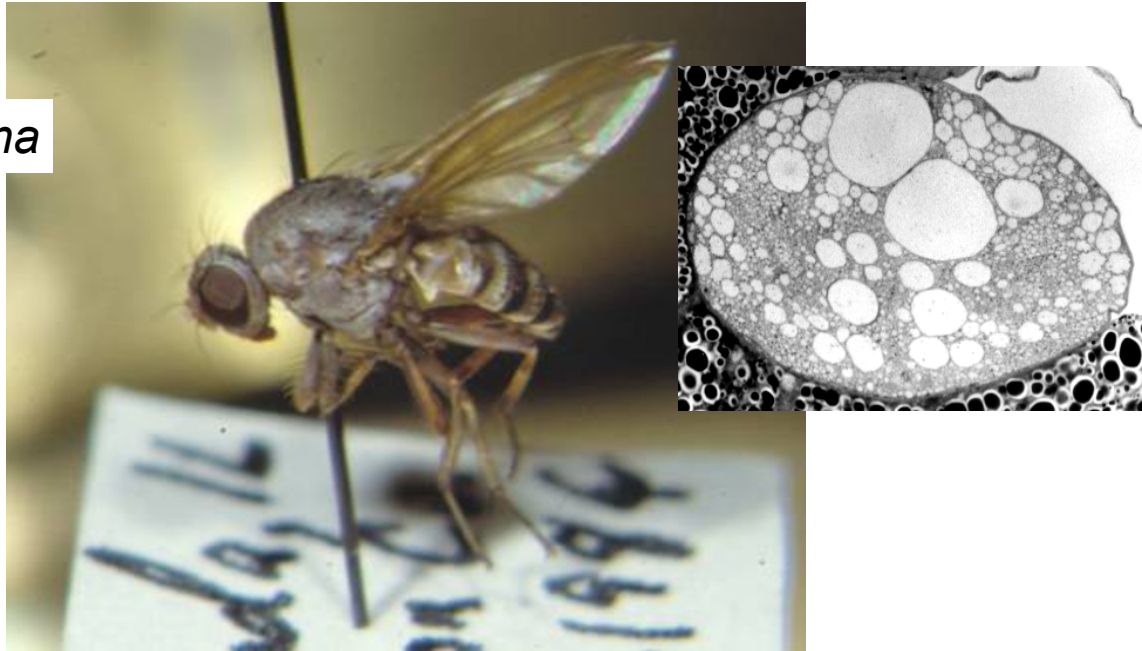
*Drosophila melanogaster*



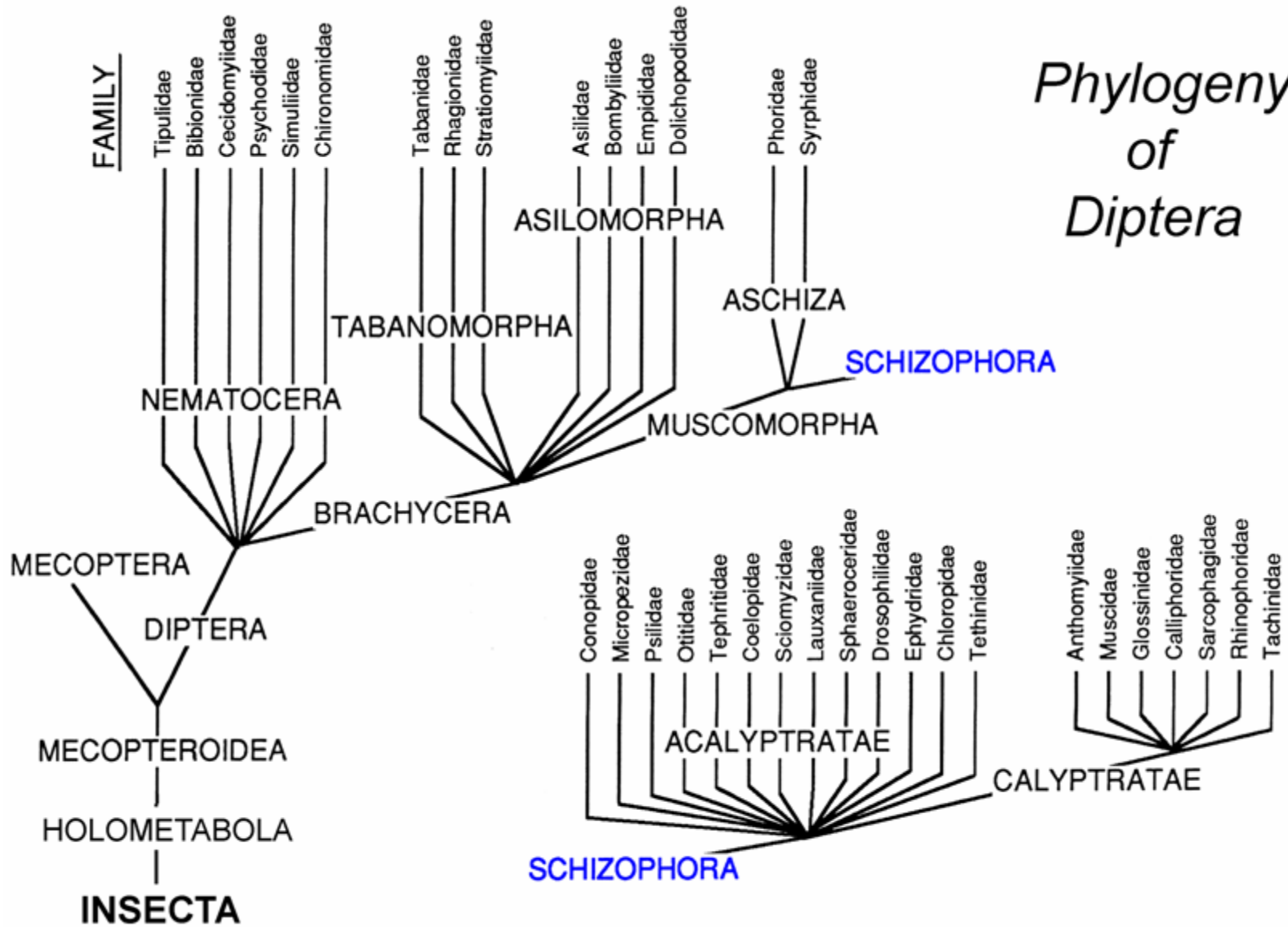
*Muscina pascuorum*



*Minettia magna*



# Phylogeny of Diptera





*Ochthera* sp.  
Ephydridae

