C. elegans optogenetics

A freshman laboratory experience

Justin Bois

BE 159, Jan 27, 2020

The Manchurian Candidate, United Artists, 1962

How optogenetics works

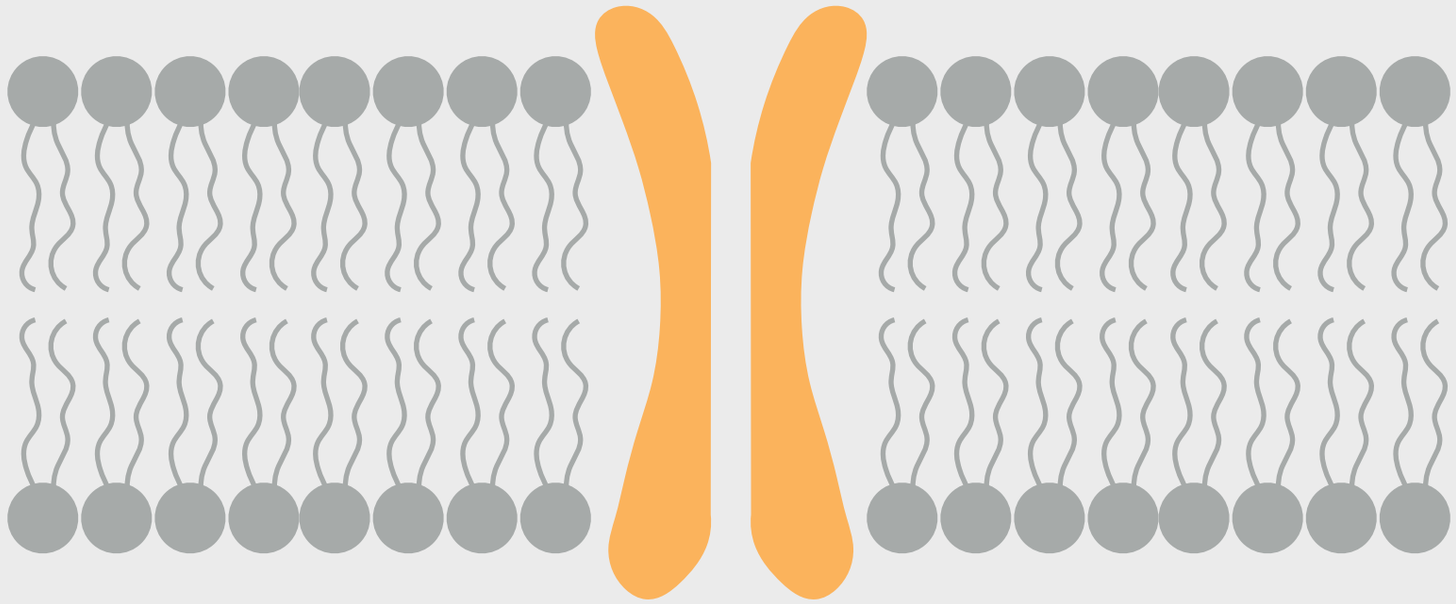
Our central research question on neural networks

Statistical analysis

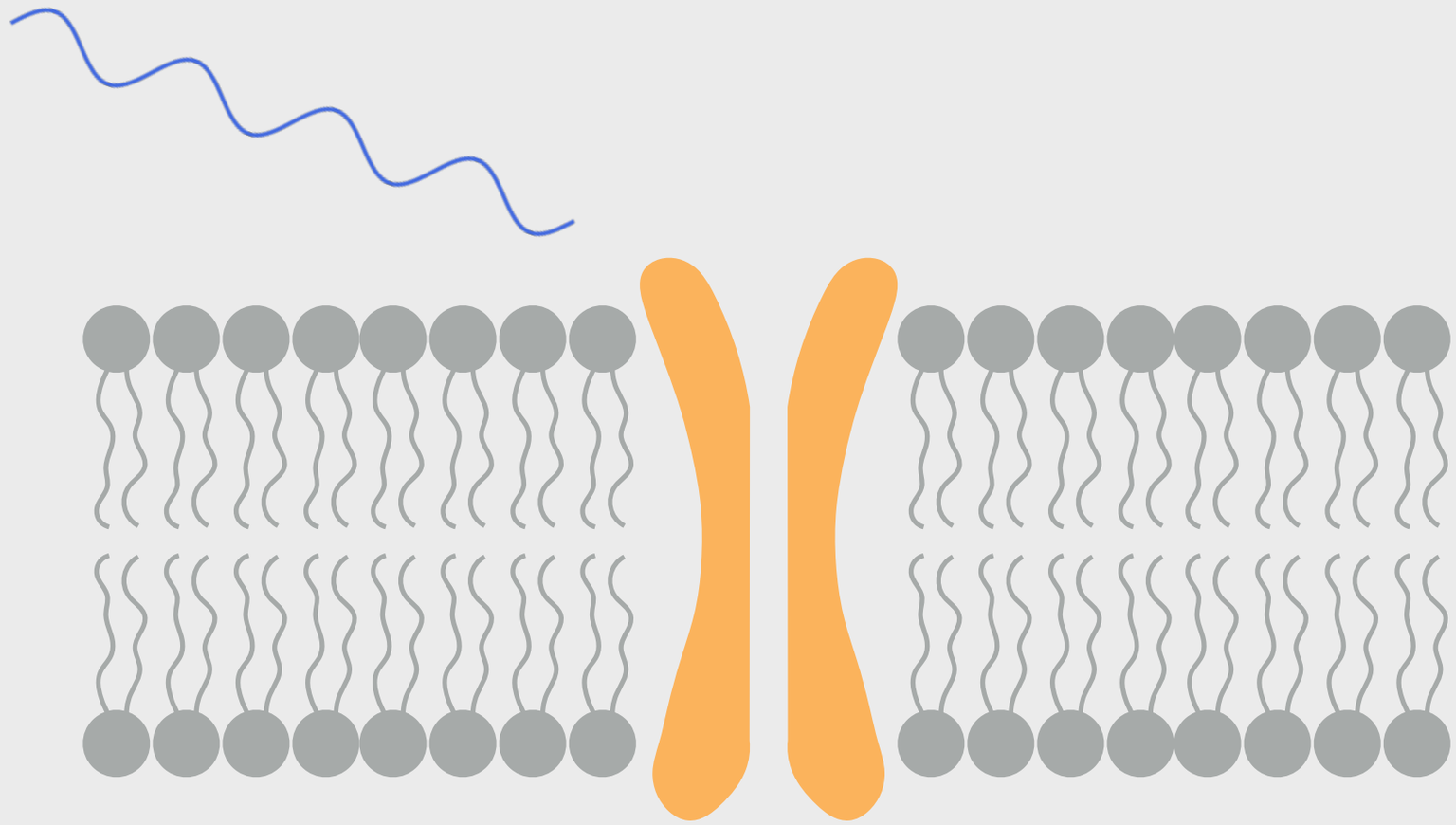
Chlamydomonas has an eyespot with Channelrhodopsin

Image: Wolfgang Bettighofer

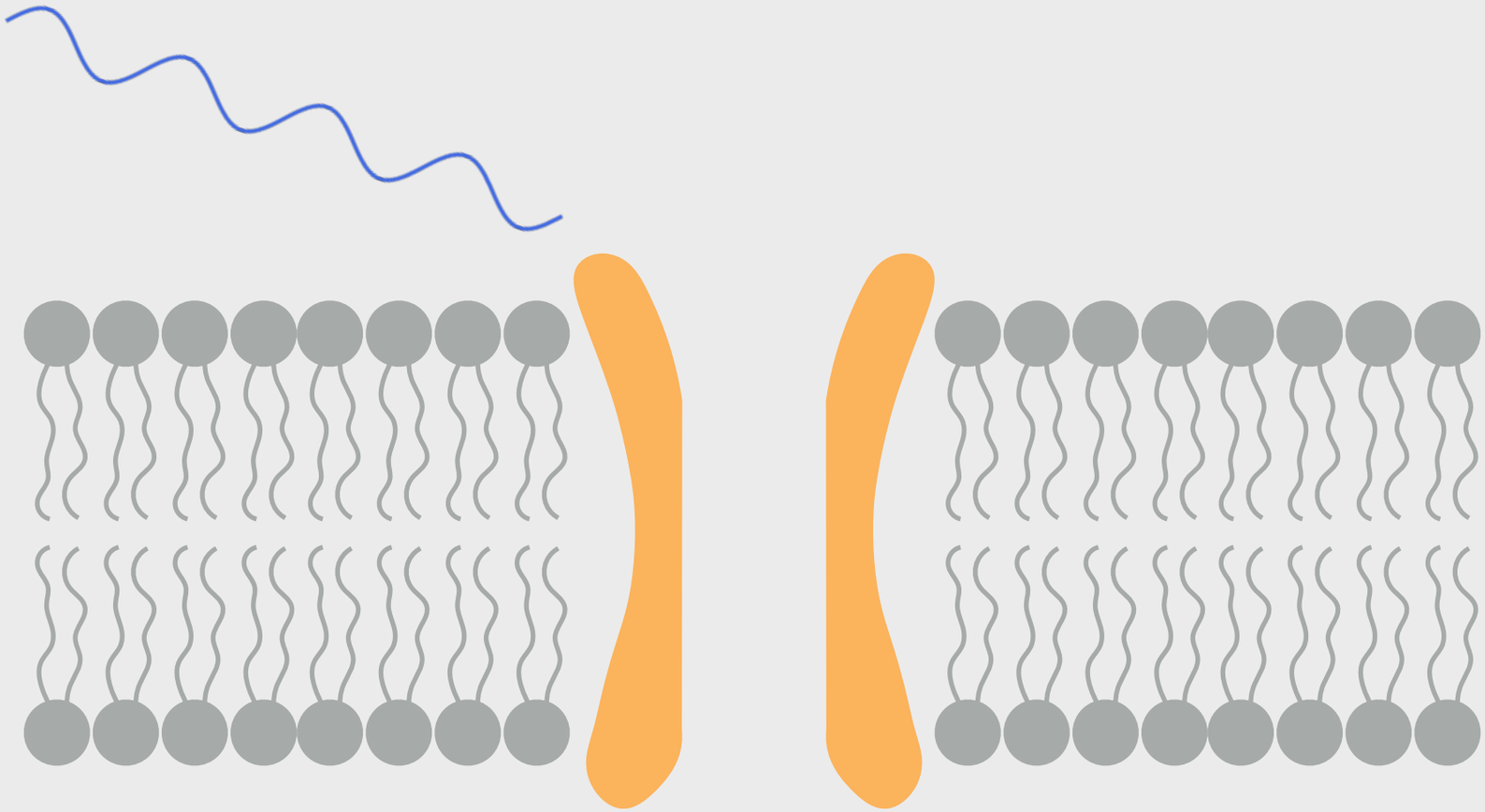
Channelrhodopsin is an optically-activated ion channel



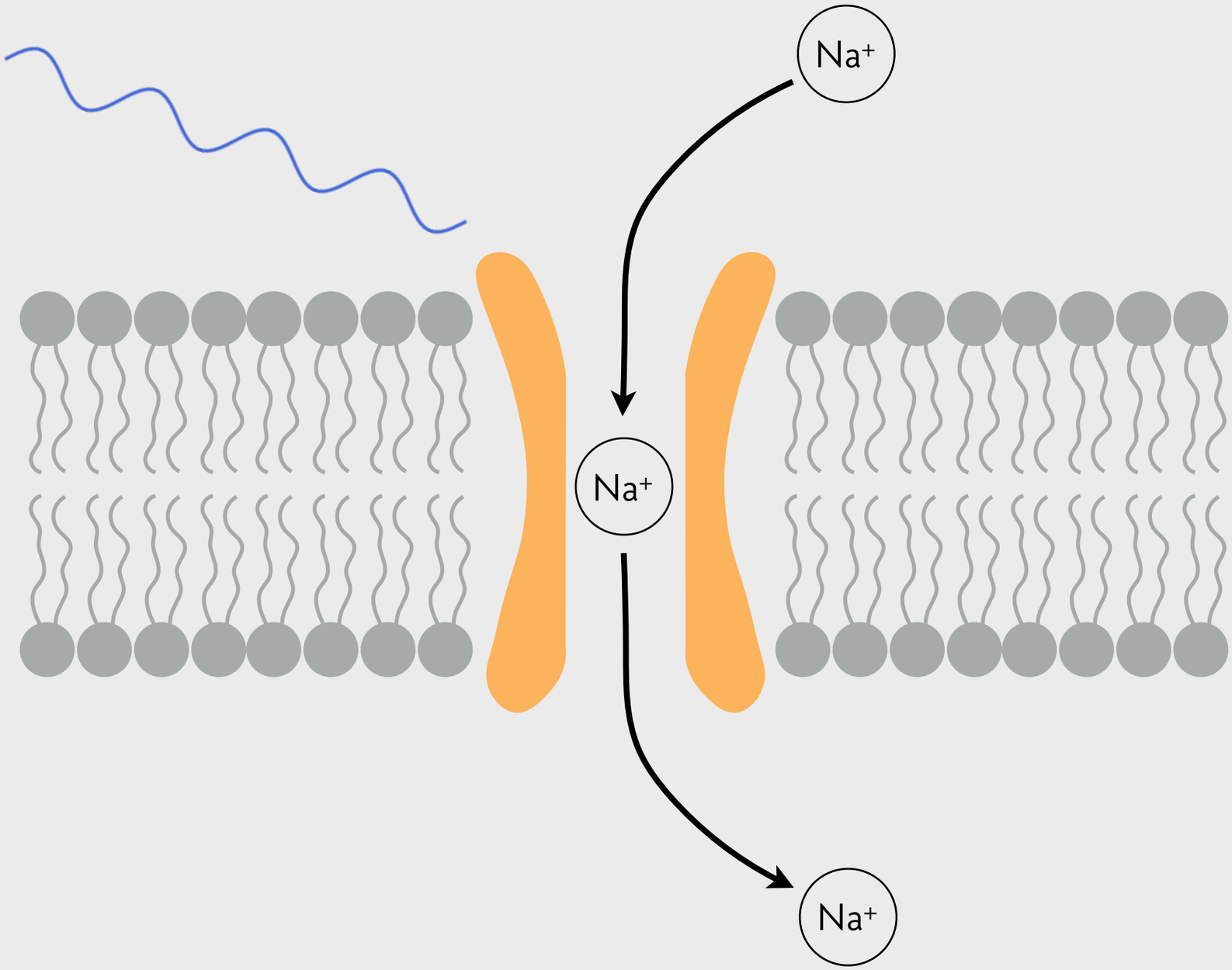
Channelrhodopsin is an optically-activated ion channel



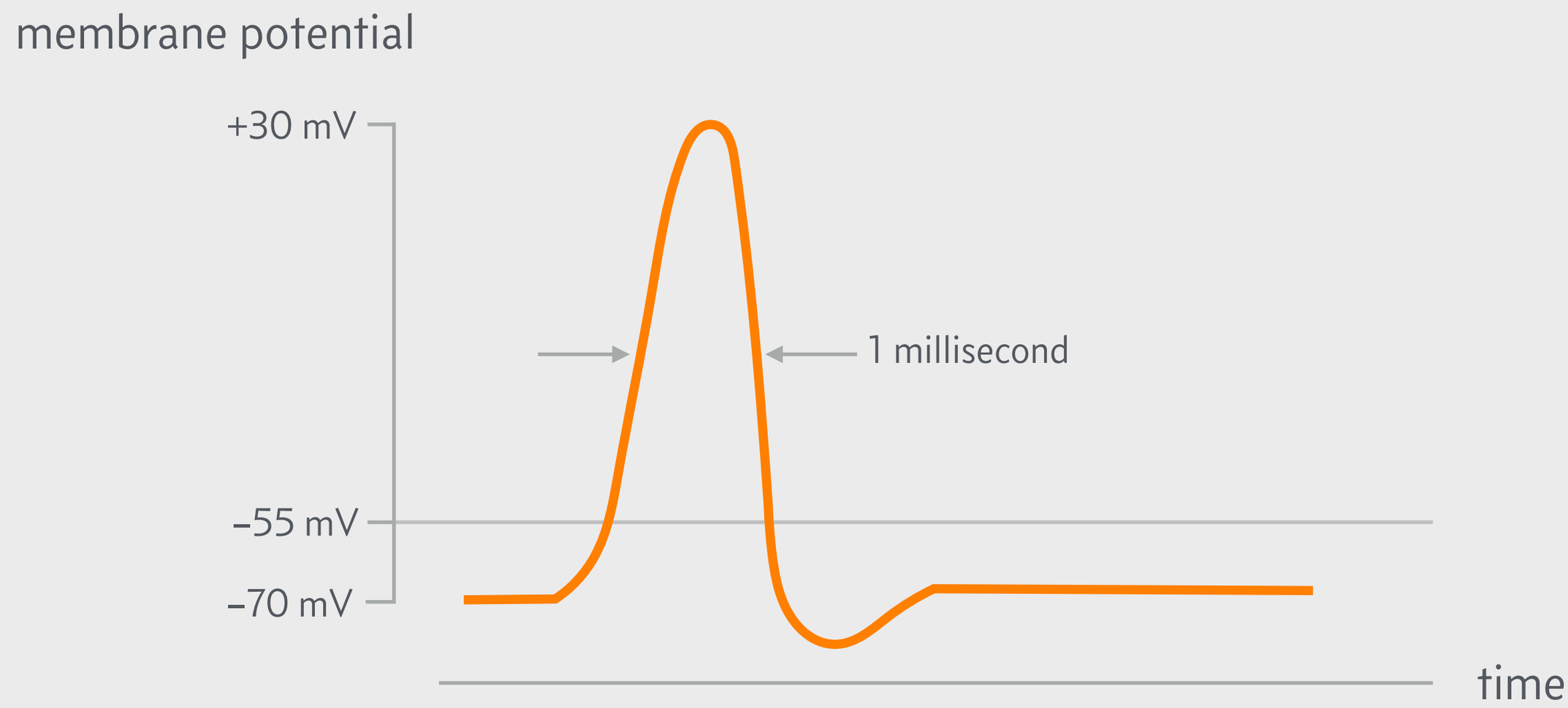
Channelrhodopsin is an optically-activated ion channel



Channelrhodopsin is an optically-activated ion channel



Induced charge difference mimics an action potential



Optogenetics: put opsins in specific neurons

Karl Deisseroth

Photo by Ioulex, *New Yorker*, 2015

Optogenetics is used to control the thirst sensation

Oka, et al., *Nature*, 2015

How does proximity of the Channelrhodopsin to motor neurons affect response?

C. elegans is an ideal organism for optogenetics

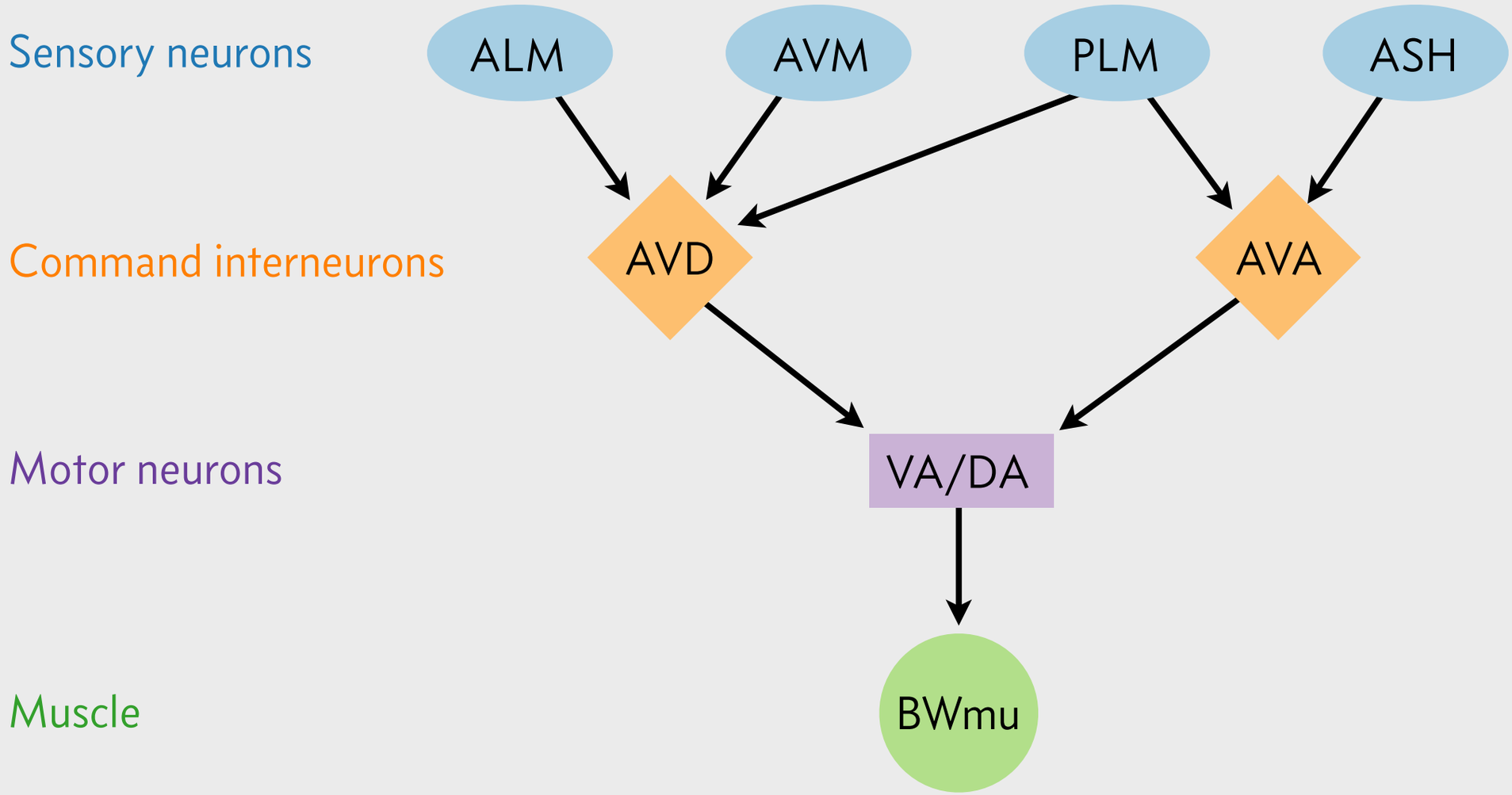
Complete set of genetic tools

Simple nervous system

Have limited light sensing

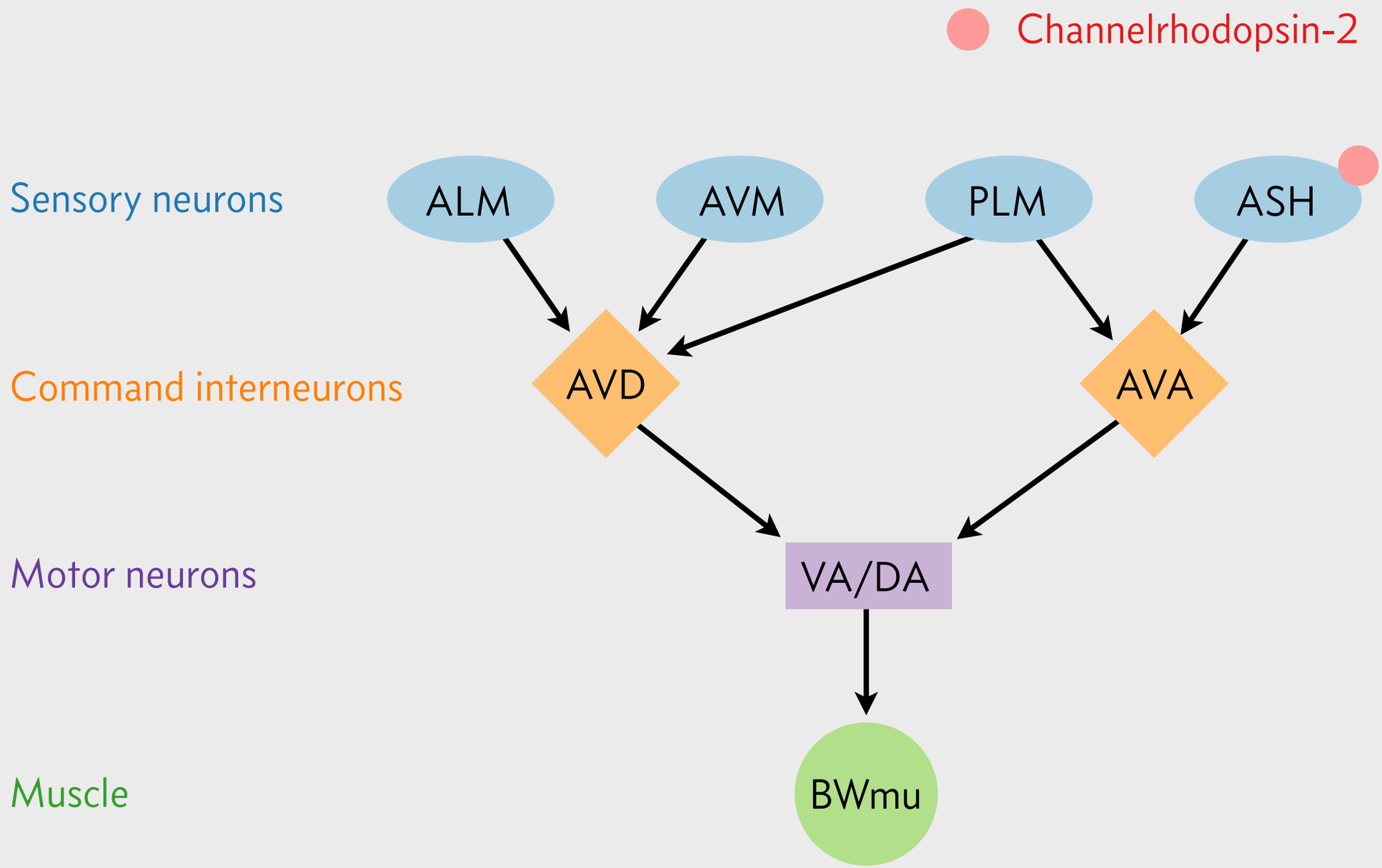
Transparent!

The *C. elegans* reversal circuit is well-mapped and simple



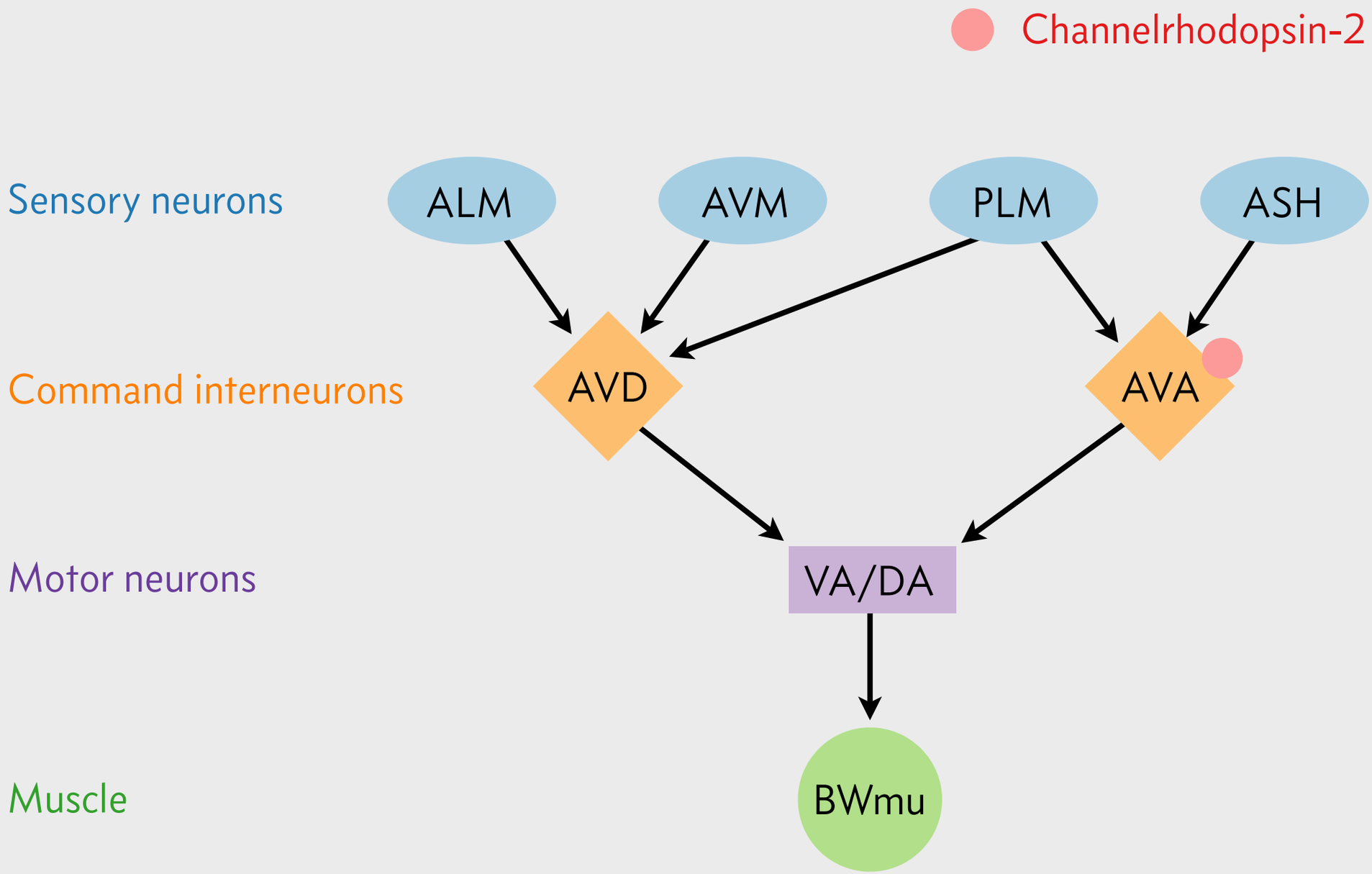
Adapted from WormAtlas

Channelrhodopsin can be expressed in specific neurons



Adapted from WormAtlas

Channelrhodopsin can be expressed in specific neurons



Adapted from WormAtlas

The experiment costs less than $300

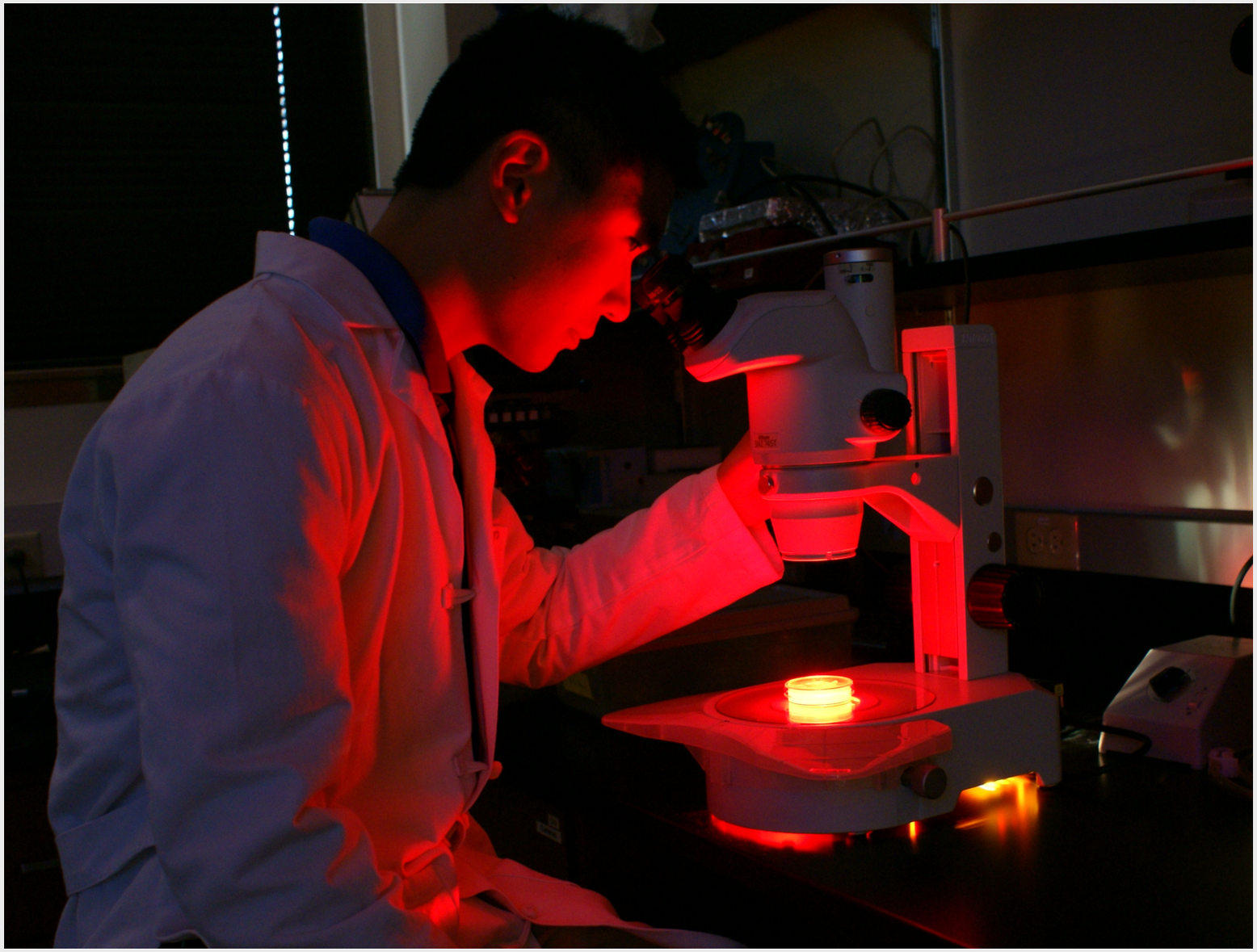
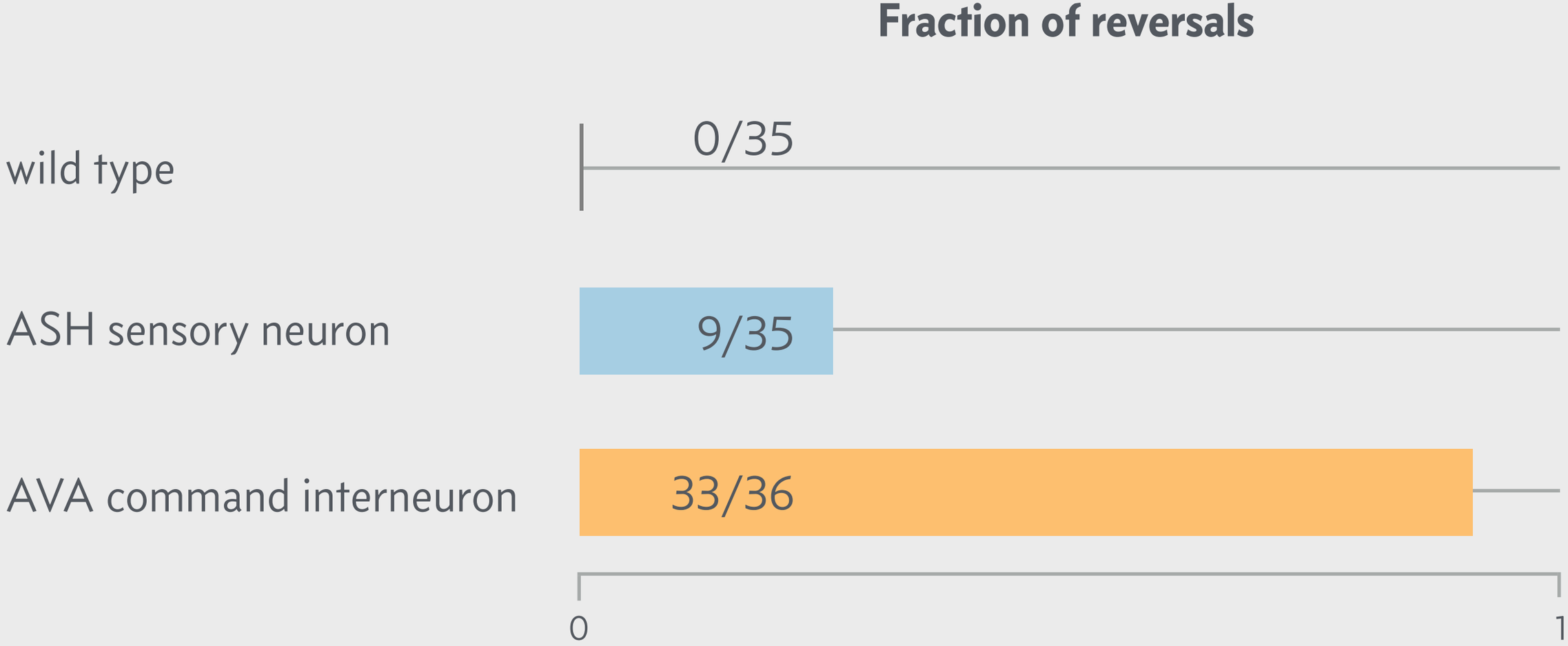


Photo: Griffin Chure

The command interneuron shows the strongest response



We use Bayes's theorem to quantify reversal probability

$$P(A \mid B) = \frac{P(B \mid A)\, P(A)}{P(B)}$$

$A = p_{\text{rev}} =$ probability of reversal
$B = n, r =$ r reversals in n trials

We use Bayes's theorem to quantify reversal probability

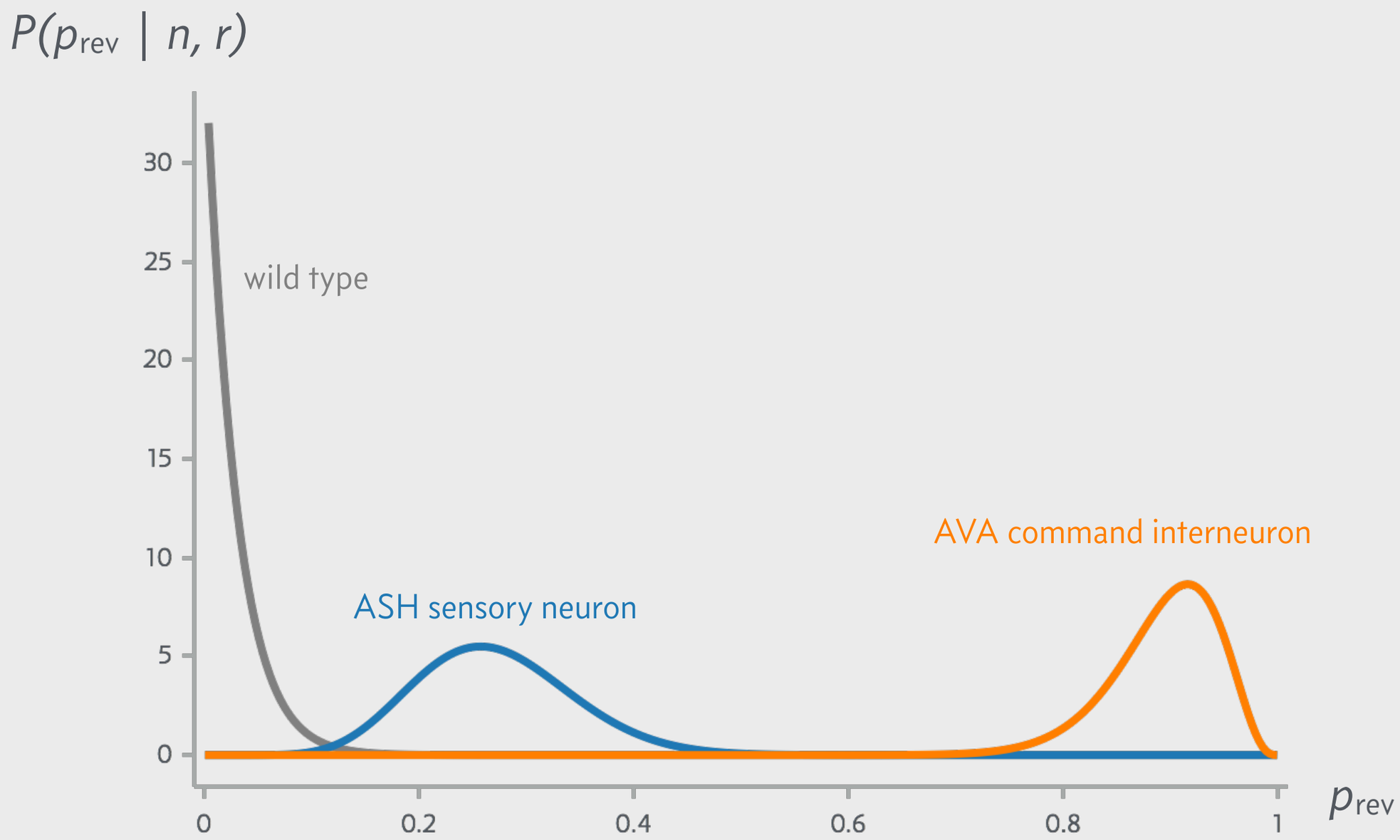
$$P(p_{\text{rev}} \mid n, r) = \frac{P(n, r \mid p_{\text{rev}})\, P(p_{\text{rev}})}{P(n, r)}$$

$$= \frac{\text{Binomial}(r \mid n, p_{\text{rev}}) \times \text{Uniform}(0, 1)}{\text{Uniform}(0, n{+}1)}$$

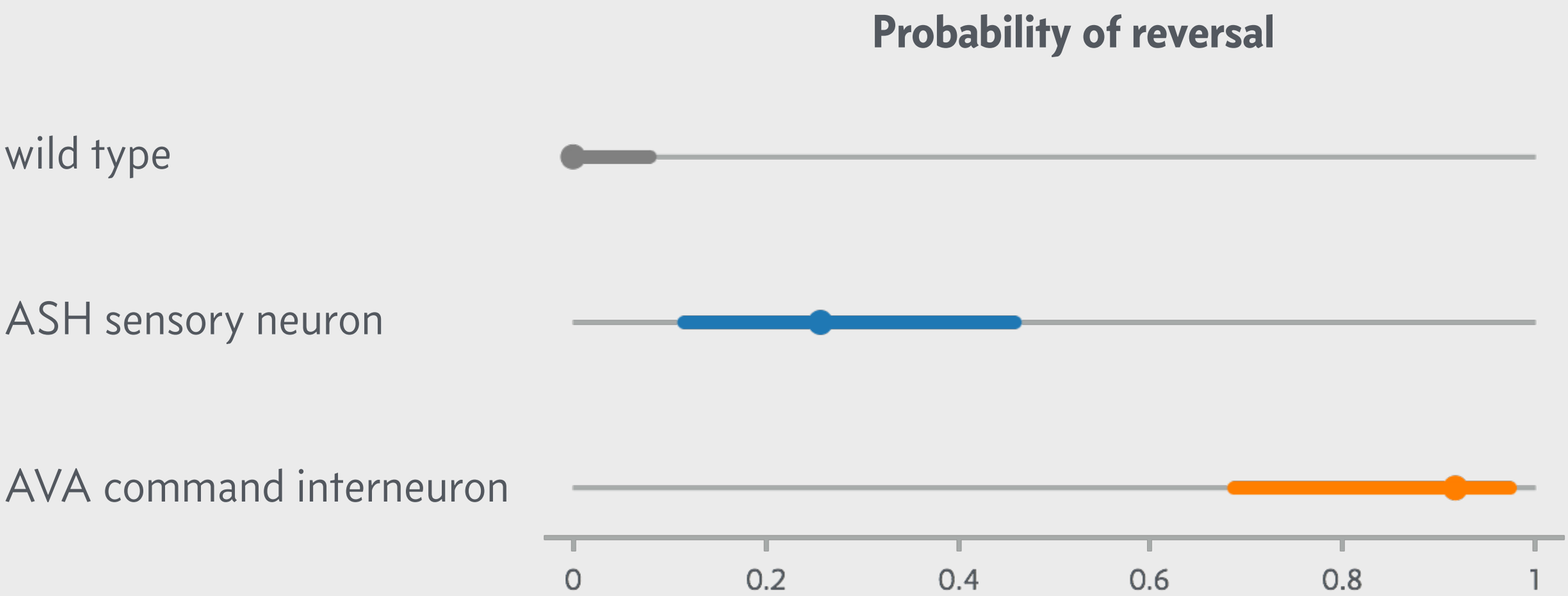
p_{rev} = probability of reversal

n, r = r reversals in n trials

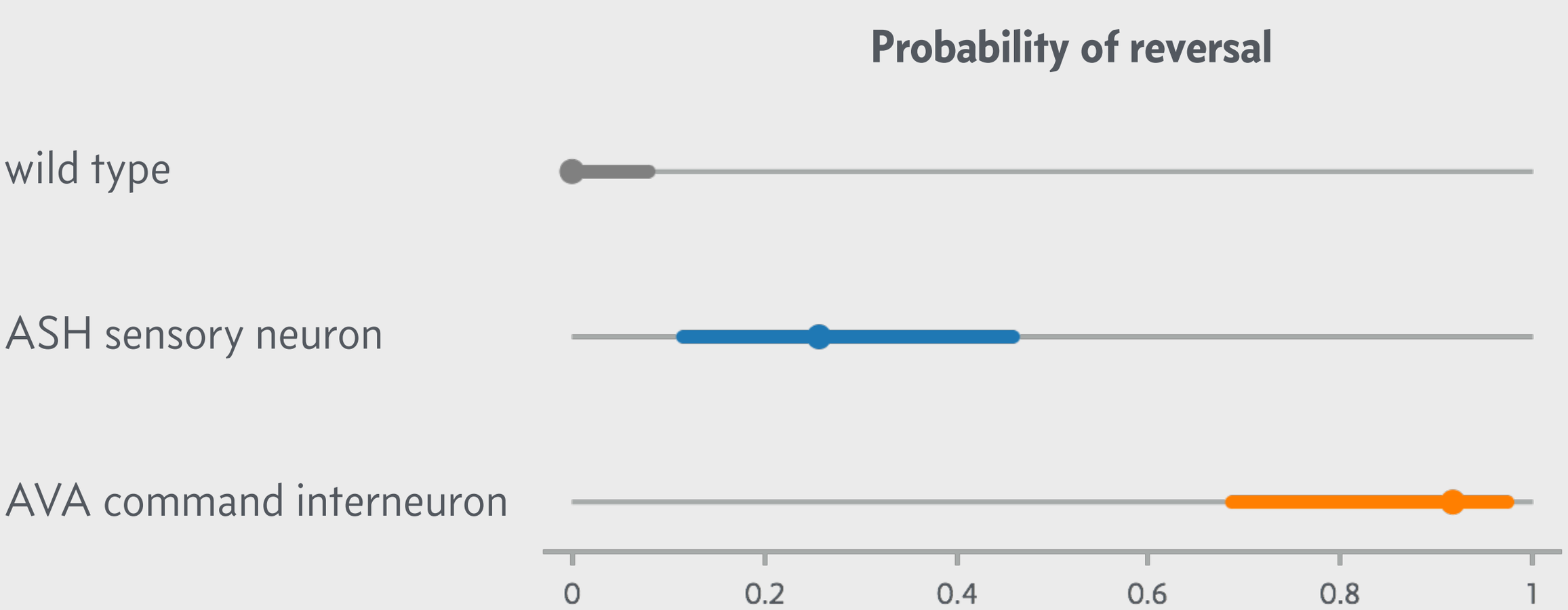
A Bayesian analysis give a complete description of reversal probability



95% confidence intervals reveal quantitative difference in reversal probability

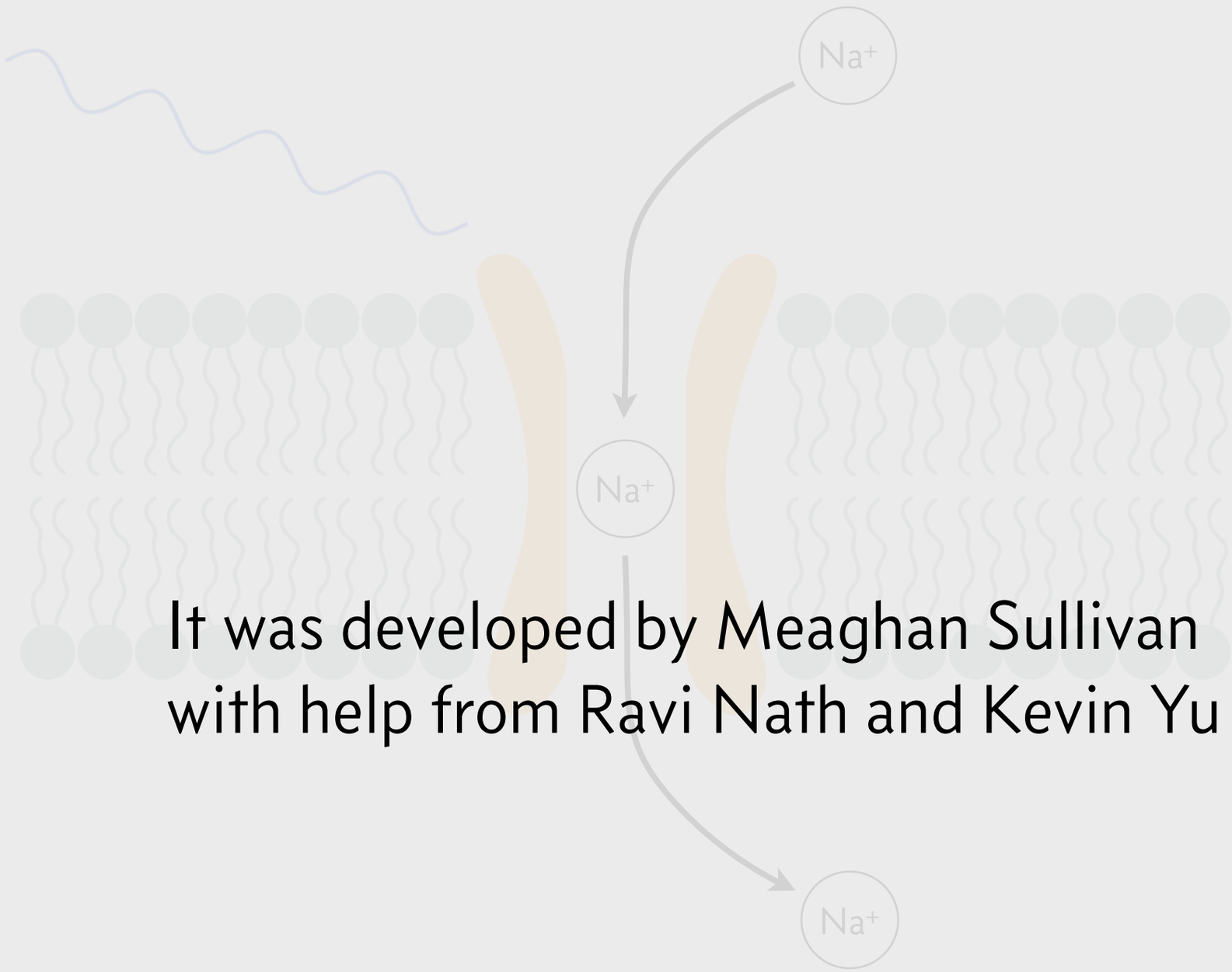


How does proximity of the Channelrhodopsin to motor neurons affect response?



Stimulation of the command interneuron is more than twice as likely to invoke a response.

This experiment was conducted by the students of Bi 1x 2015



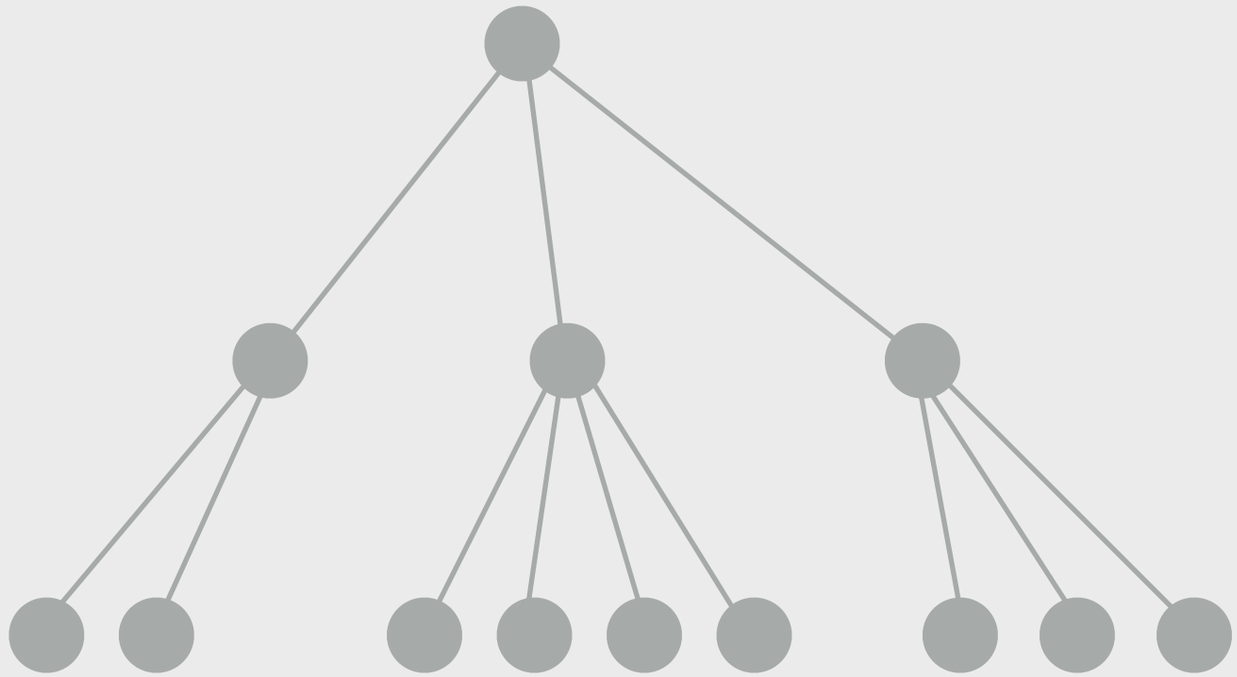
It was developed by Meaghan Sullivan with help from Ravi Nath and Kevin Yu

The talk content has a top-down hierarchical structure

Main message

Main points

Subpoints



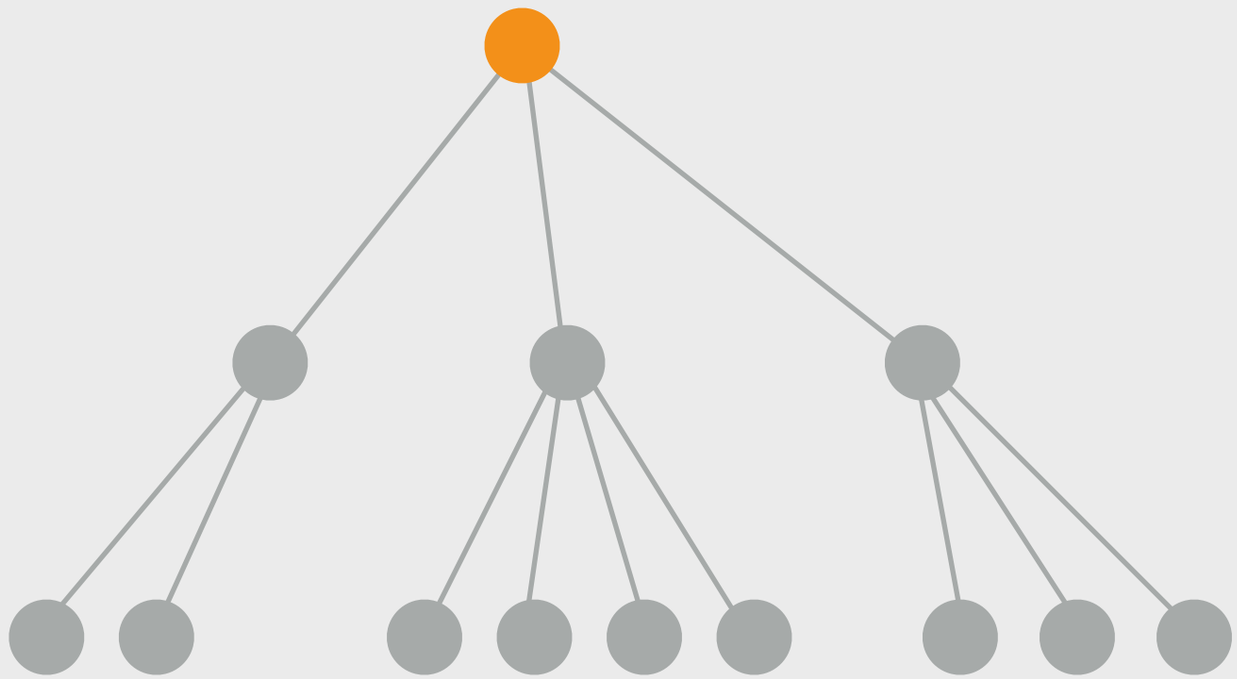
The talk content has a top-down hierarchical structure

A meaningful *C. elegans* optogenetics experiment was done cheaply in a freshman lab

Main message

Main points

Subpoints

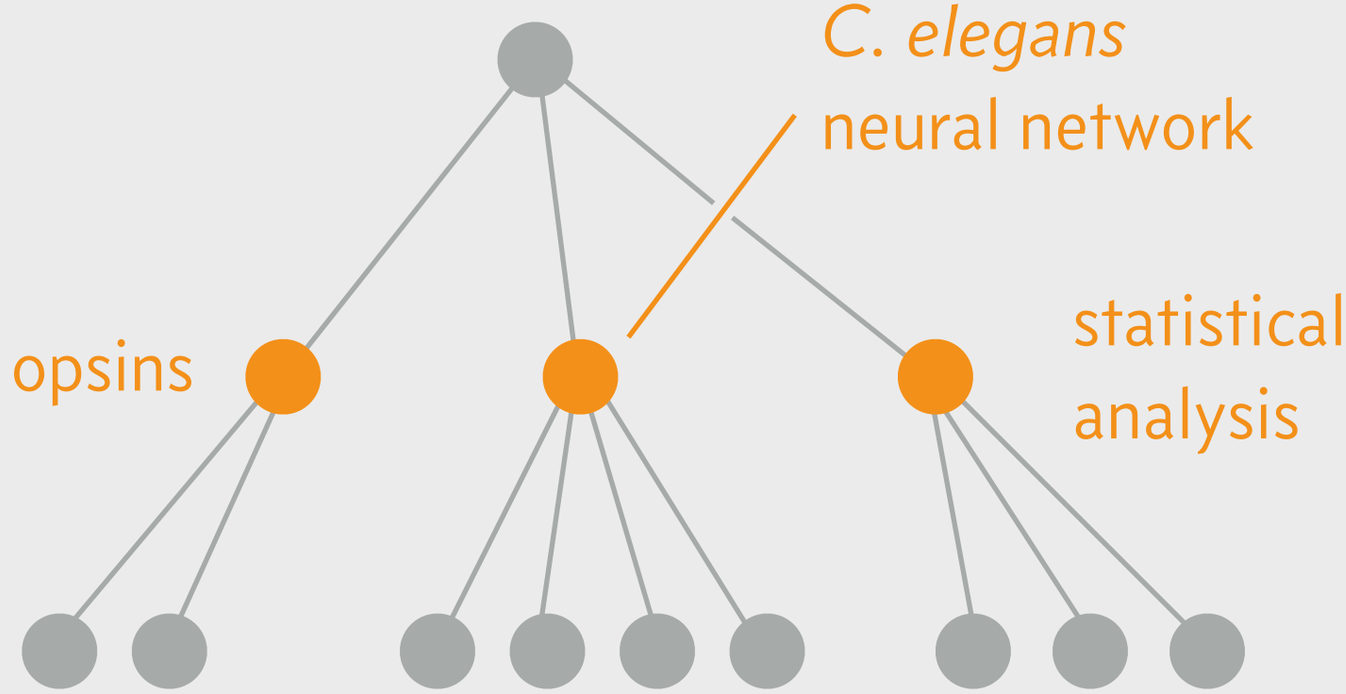


The talk content has a top-down hierarchical structure

Main message

Main points

Subpoints

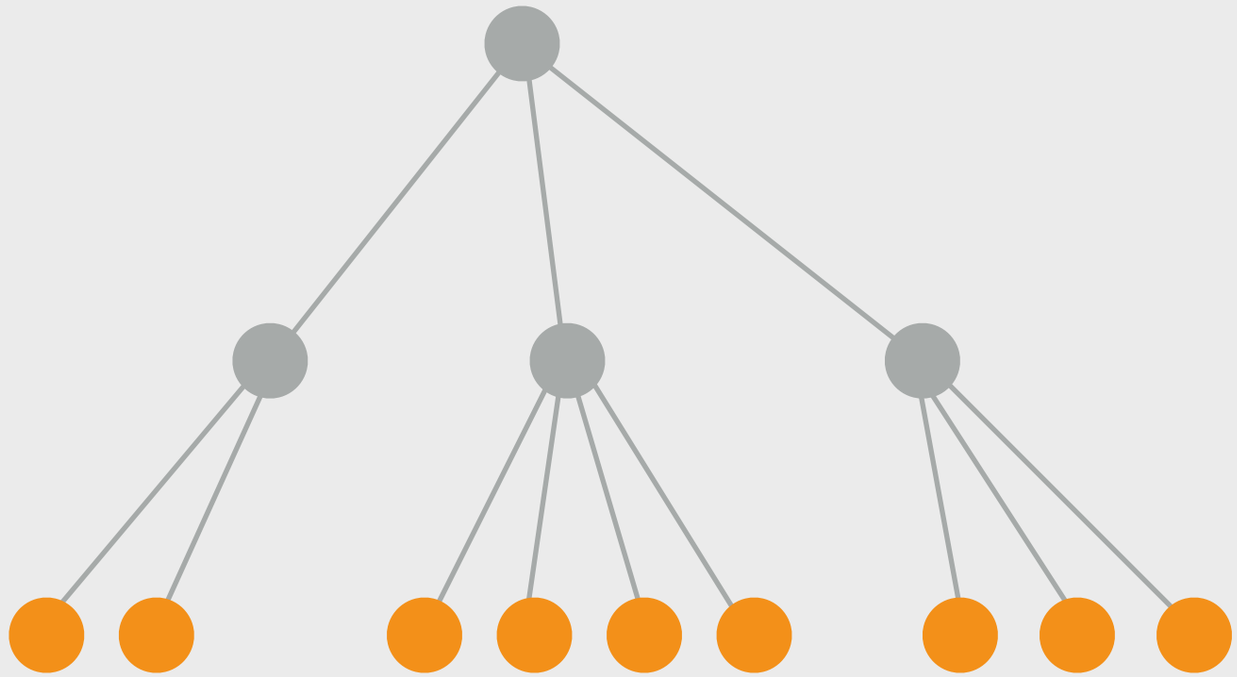


You should have one slide for each subpoint

Main message

Main points

Subpoints



The talk structure is linear

Introduction

- Attention getter
- Need
- Task
- Main message
- Preview

Body

- Main point 1
- Main point 2
- Main point 3

Closing

- Review
- Conclusion
- Close

The talk structure is linear

Introduction

Attention getter

Need

Task

Main message

Preview

Body

Main point 1

• • •

Main point 2

• • •

Main point 3

• • •

Closing

Review

Conclusion

Close

The Manchurian Candidate, United Artists, 1962

Effective experimental design requires exquisite control.

In the past decade, optogenetics has enabled unprecedented control of neuronal systems.

In an effort to train our students in this powerful experimental technique, my TAs and I developed a module using optogenetics in C. elegans and implemented it in my freshman lab course at Caltech.

Do not waste words, especially at the beginning

Avoid niceties

Do not read anything from your title slide

Get attention, then focus

Tip: memorize the first few sentences

Introduction

Attention getter

Need

Task

Main message

Preview

Body

Main point 1

• • •

Main point 2

• • •

Main point 3

• • •

Closing

Review

Conclusion

Close

Need

In an effort to train our students in powerful experimental and statistical techniques,

Task

my TAs and I developed a module using optogenetics in *C. elegans*

Main message

and implemented it in my freshman lab course, Bi 1x.

Introduction

Attention getter

Need

Task

Main message

Preview

Body

Main point 1

• • •

Main point 2

• • •

Main point 3

• • •

Closing

Review

Conclusion

Close

How optogenetics works

Our central research question on neural networks

Statistical analysis

Introduction

Attention getter

Need

Task

Main message

Preview

Body

Main point 1

• • •

Main point 2

• • •

Main point 3

• • •

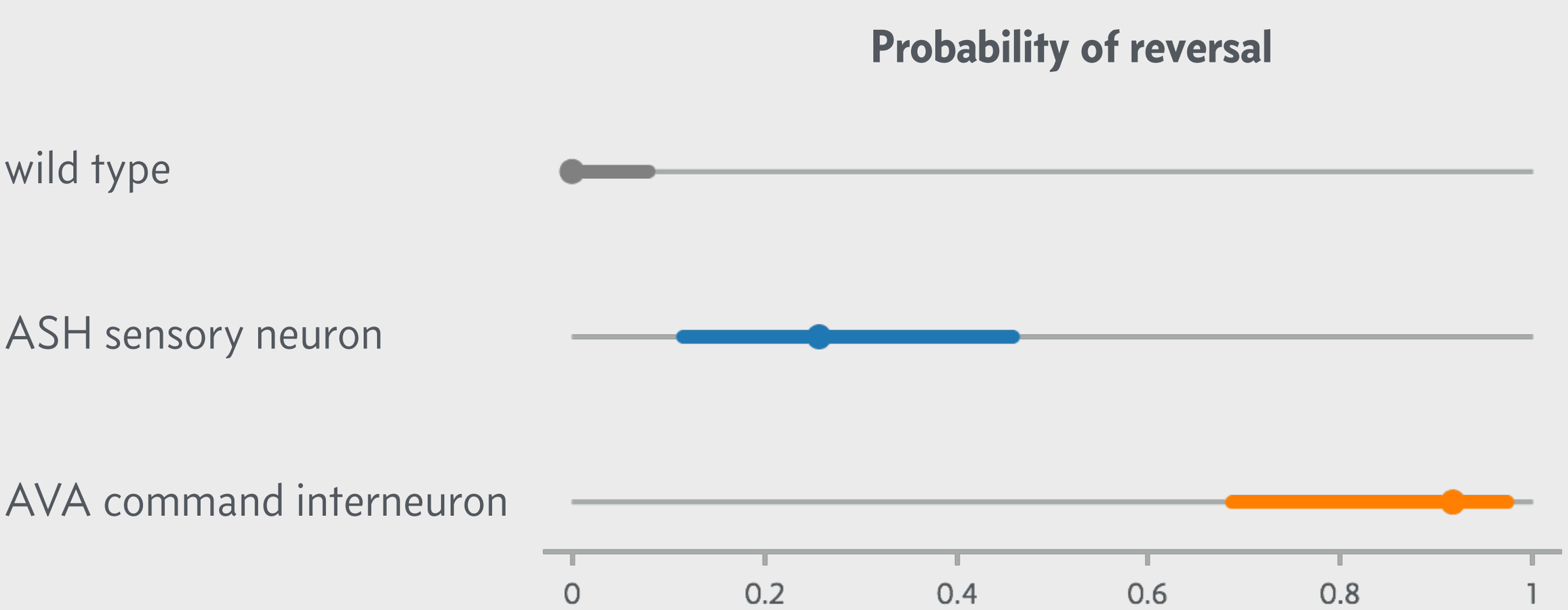
Closing

Review

Conclusion

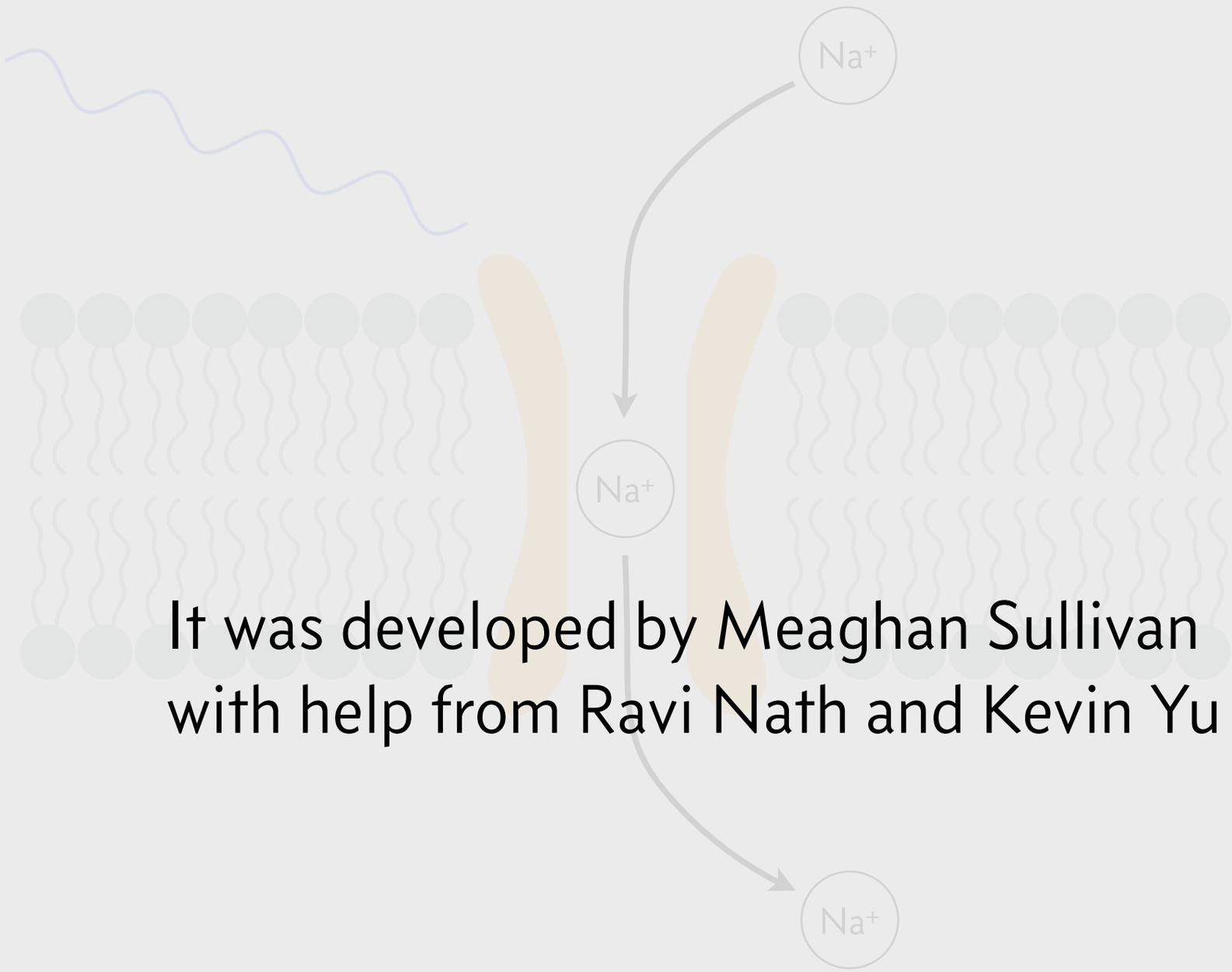
Close

How does proximity of the Channelrhodopsin to motor neurons affect response?



Stimulation of the command interneuron is more than twice as likely to invoke a response.

This experiment was conducted by the students of Bi 1x 2015



It was developed by Meaghan Sullivan with help from Ravi Nath and Kevin Yu

Answer questions directly and succinctly

Let person finish asking her question

Repeat long questions more concisely

Directly answer question with concise evidence, then move on

Constructively admit when you do not have a good answer

Always have your audience in mind

Speak about your work to the audience
not about yourself or your lab

Finish on time
or early; they'll thank you

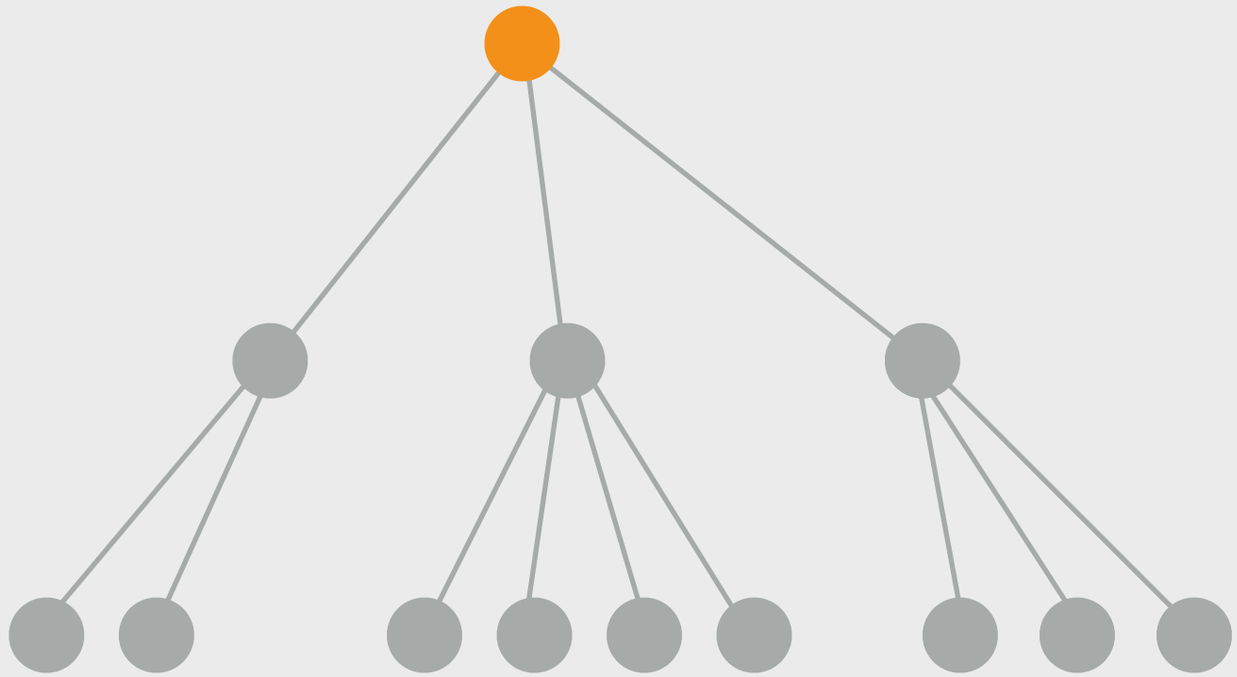
Develop audience-specific content
general audiences versus colleagues

Have one main message in your talk

Main message

Main points

Subpoints



Good delivery can make or break a talk

Stand firmly and do not move

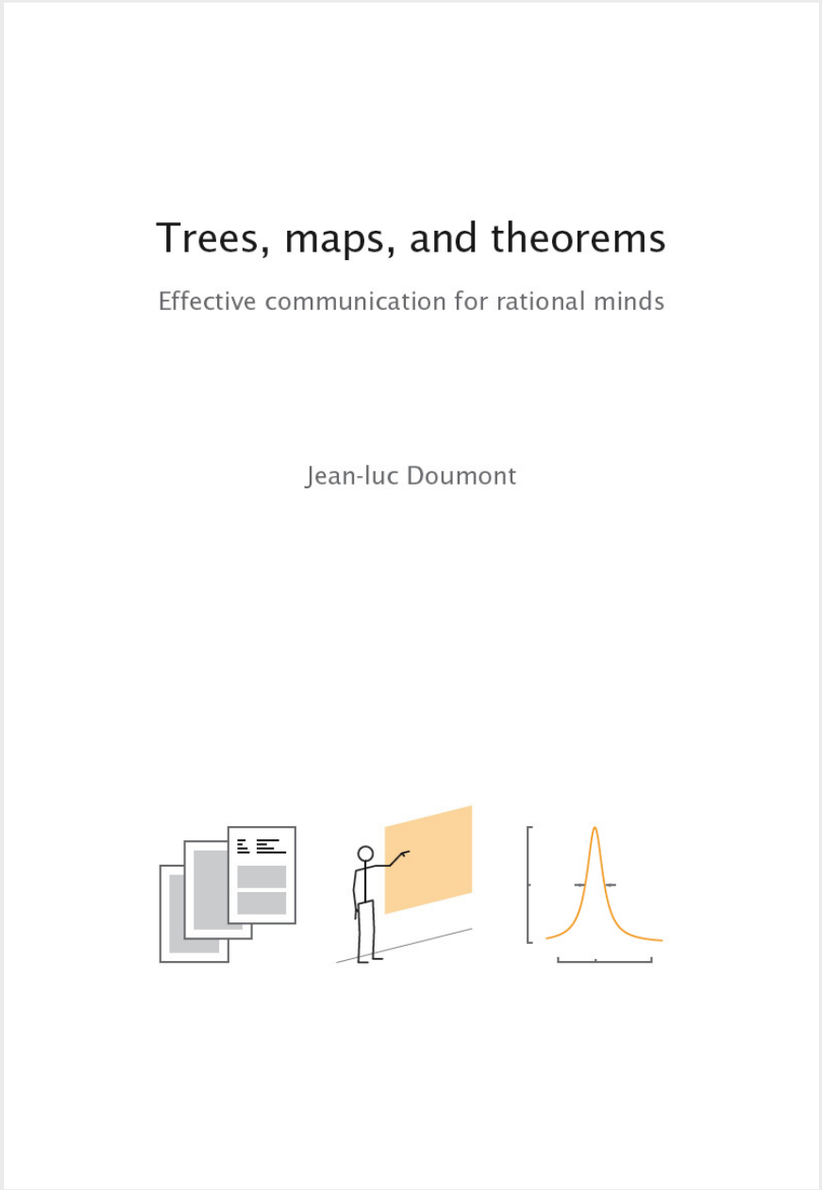
Vary your tone and cadence for effect

Do not fiddle or make noise

Look your audience straight in the eyes

Do not use laser pointers.

Jean-luc Doumont's work is an unparalleled resource



It usually takes me more than three weeks
to prepare a good impromptu speech.

—Mark Twain