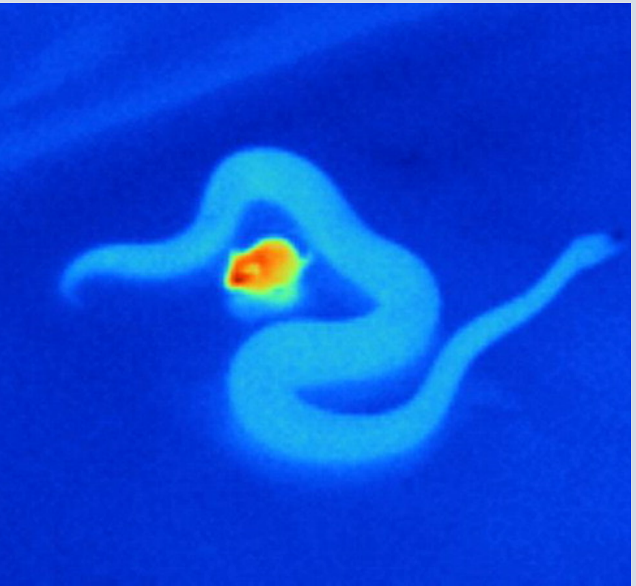


Thermometers within: Diverse mechanisms of thermosensation in animals

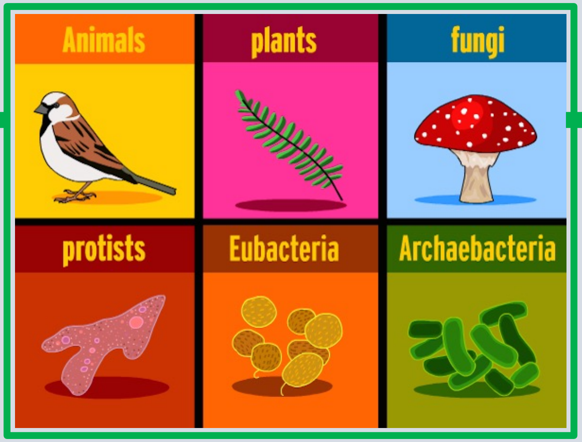
Willem Laursen

HHMI Interfaces Scholar Award Lecture

Brandeis QB Bootcamp

January 14, 2021

Life exists within a relatively narrow thermal range



Liquid Helium

-269.15 °C
(−452.2°F; 4 K)

Antarctica

−89.2°C
(−128.6°F; 184 K)

Death Valley

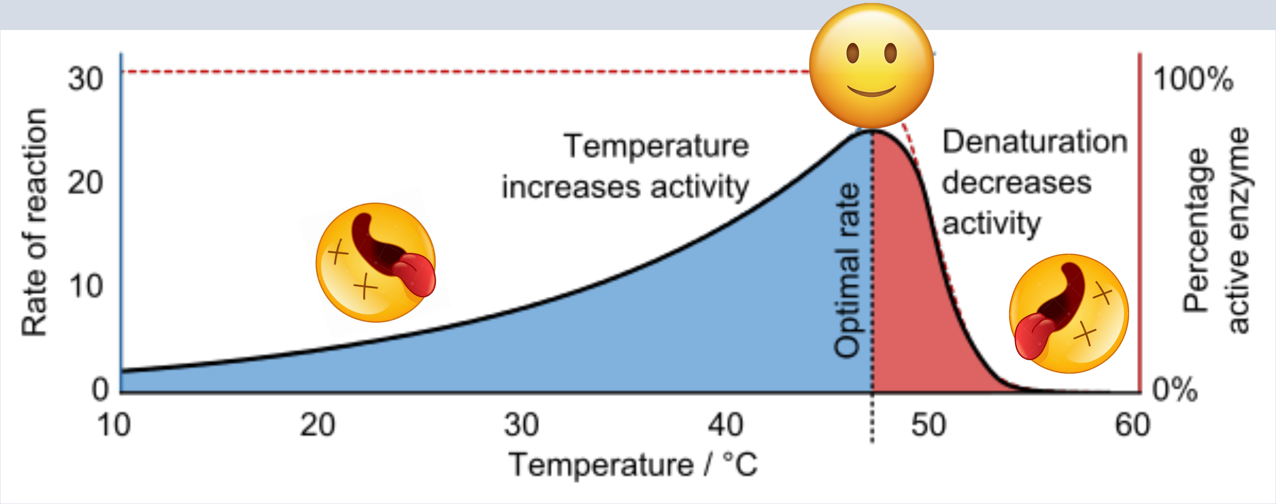
57.6°C
(134°F; 329 K)

Candle flame

~1000°C
(1832°F; 1273 K)

*not to scale

Temperature is ubiquitous and effects all biological processes



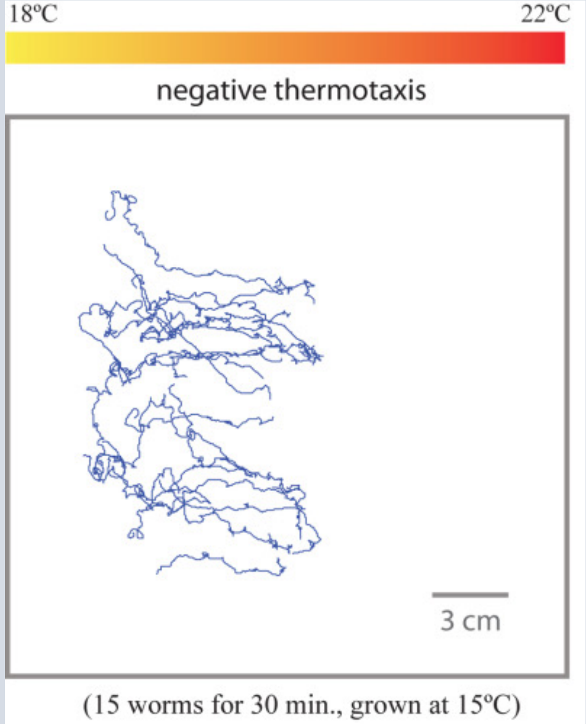
$$\boxed{k = A \bullet e^{-Ea/RT}}$$

k= rate constant
A= frequency factor
R=gas constant
E_a = activation energy
T=Temperature

Thermosensation: an ancient sensory modality

- Organisms have evolved to sense and respond to temperature in order to avoid damage and maintain homeostasis

Nematode (*C. elegans*)

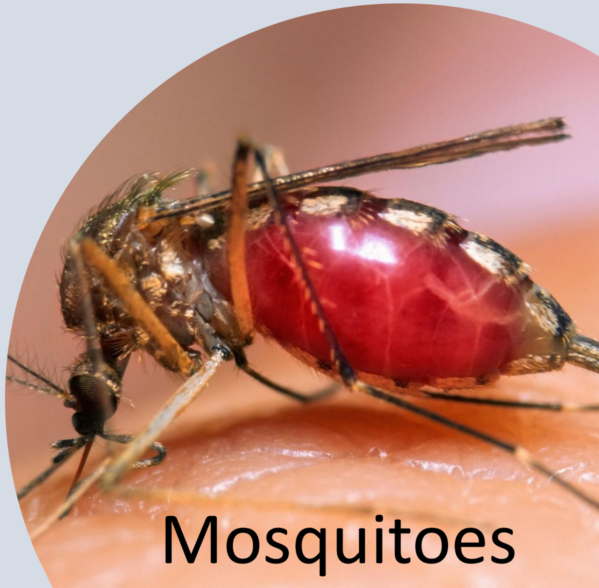


WormBook

Human (*Homo sapiens*)

Some animals have evolved highly sensitive thermodetection systems to drive specialized behaviors

<u>What are the mechanisms responsible for their enhanced thermosensitivity?</u>

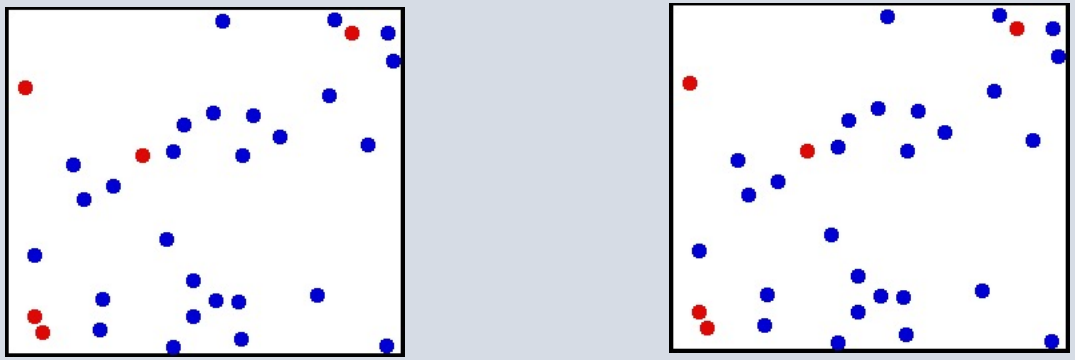


Outline

- What are temperature and heat?
- How is temperature information detected by nonspecialists?
- What mechanisms have evolved for enhanced sensitivity in thermosensory specialist species?
- What are the outstanding questions in thermosensation?

Temperature and heat

- Temperature= measure of average kinetic energy of molecules in system (intensive property)

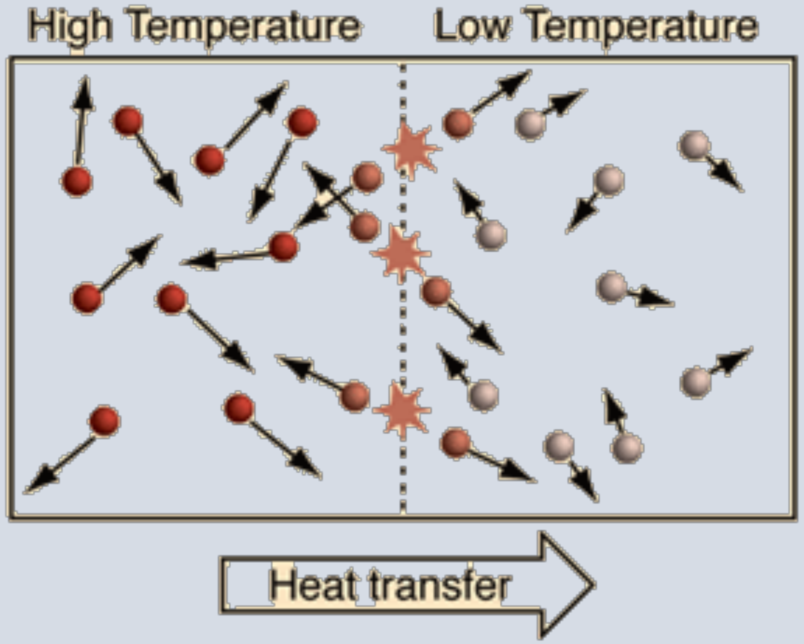


Low Temp. **High Temp.**

$$\boxed{K = 3/2 \bullet (R/N_a) \bullet T}$$

K= Avg Kinetic energy
R=gas constant
N_a = Avagadro's number
T=Temperature

- Heat= thermal energy transferred from higher temp. to lower temp. system



$$\boxed{q=m \bullet C \bullet \Delta T}$$

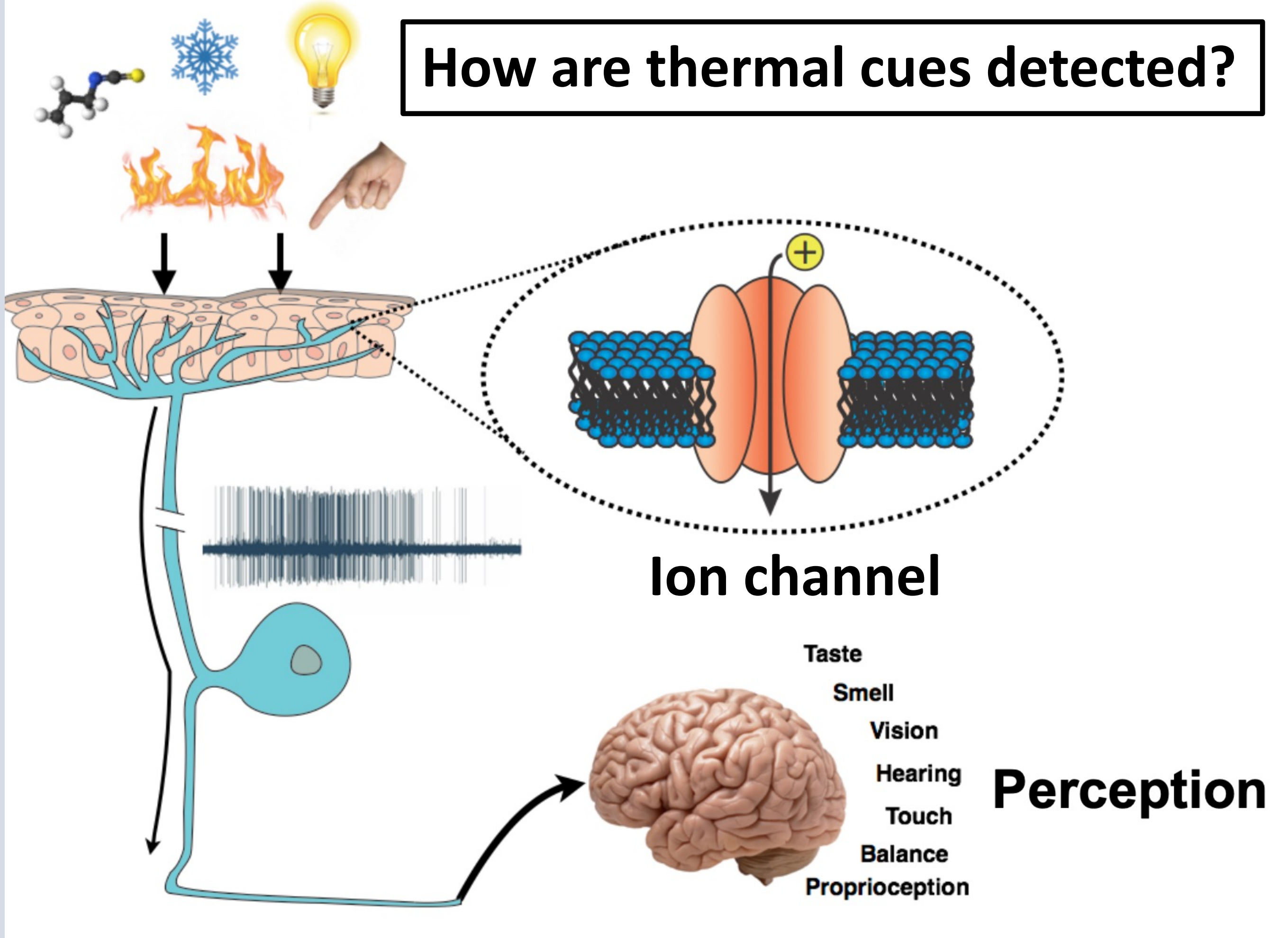
q=heat
m=mass of substance
C=specific heat capacity
ΔT=change in temp

Thermosensation presents unique problems

Temperature is everywhere and easily crosses biological barriers

All of biology is temperature-sensitive

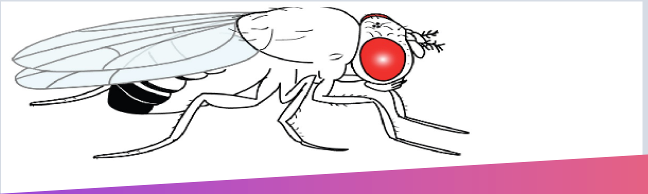
- Sensors should be sensitive “canaries in coal mine” to prevent damage
- Sensors must be able to detect signal from noise
- How can these be specifically detected?
  - Direct/indirect mechanisms



Part I.
New uses for old machinery: Mechanisms of thermosensation in Flies and Mosquitoes
(our work in the Garrity Lab at Brandeis)

Artwork by Crystal Zhu

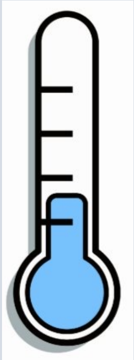
The “labeled line” model of *Drosophila* thermotaxis



cool

warm

< 25˚C



↓

Cool Receptors ?

(IR21a)

↓

Cold avoidance

+

>25˚C

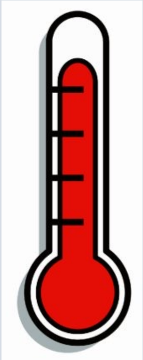
↓

Hot Receptors

(TRPA1, Gr28BD)

↓

Hot avoidance

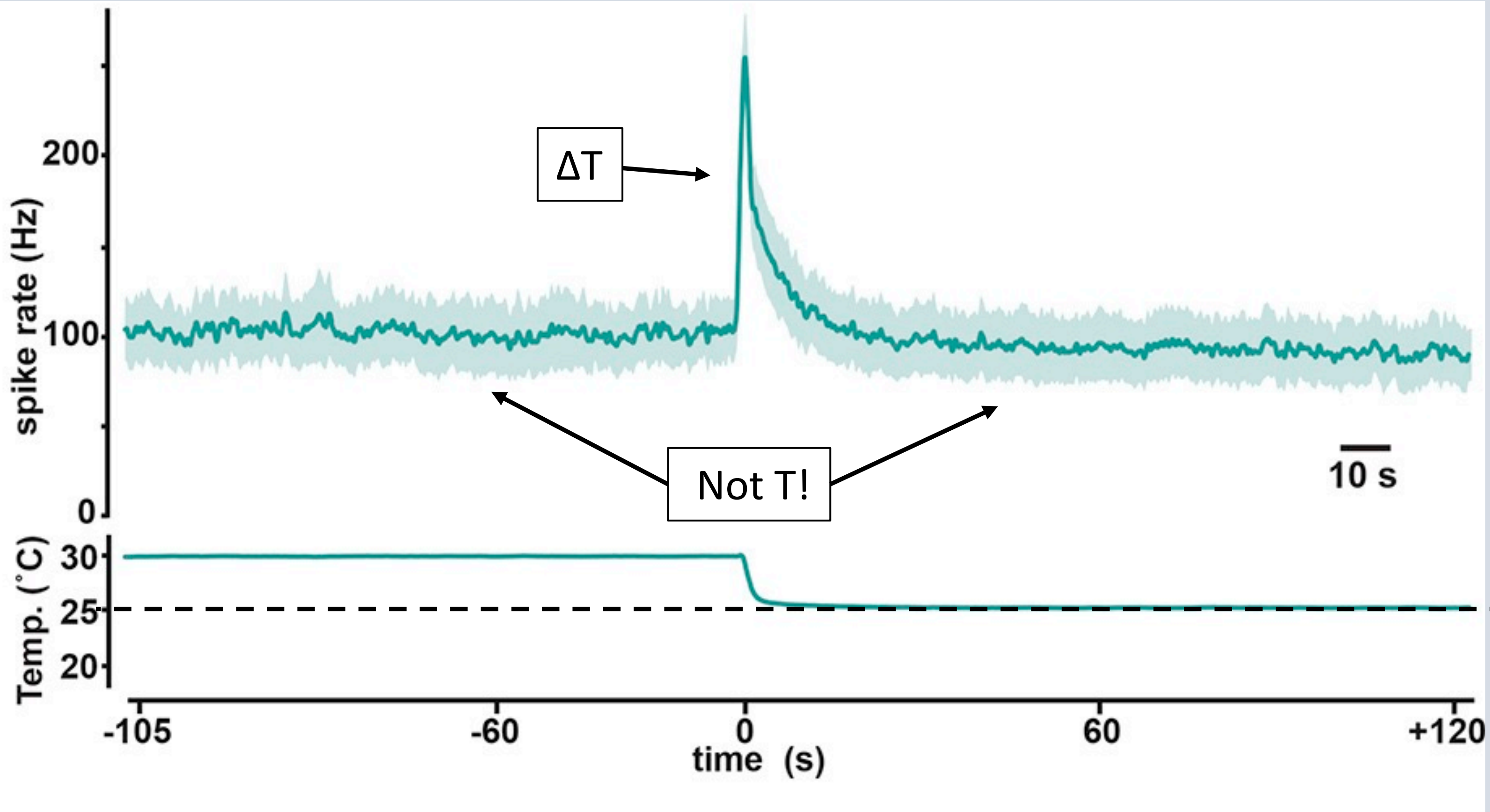


Preferred temp

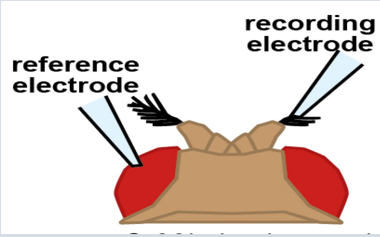
~25˚C

Ni et al. Nature (2013)
Gallio *et al.* Cell (2011)
Hamada et al. Nature (2008)
Barbagallo & Garrity (2015)

Drosophila cooling cells respond to temperature change, not absolute temperature!



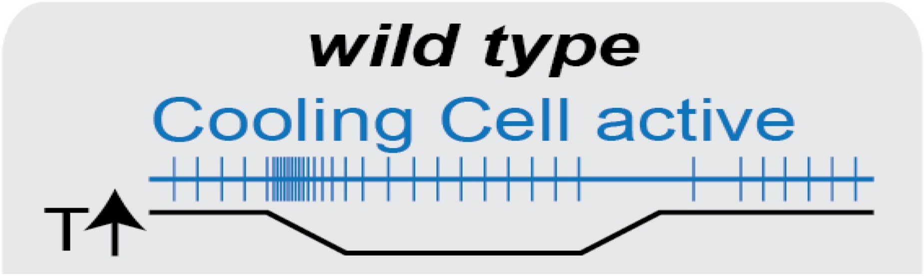
Preferred temp



- Behaves similarly above or below preferred temp
- Not a thermometer!

Budelli et al., Neuron (2019)

Drosophila cooling cells signal temperature change in both directions!

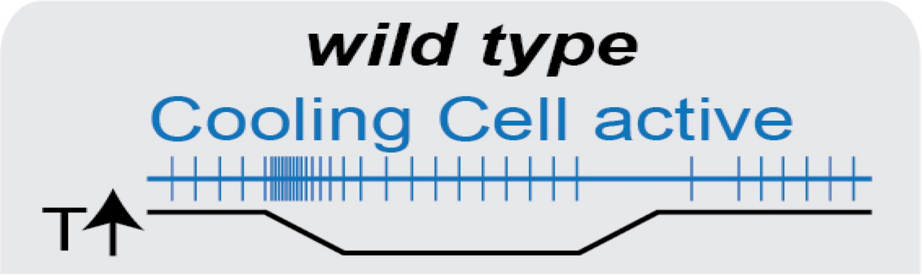


Activation cooling! **Inhibition by warming!**

Budelli et al.,
Neuron (2019)

Ionotropic receptor subunit Ir21a mediates cooling detection in Drosophila…

…But Ir21a drives BOTH cold and warm avoidance!

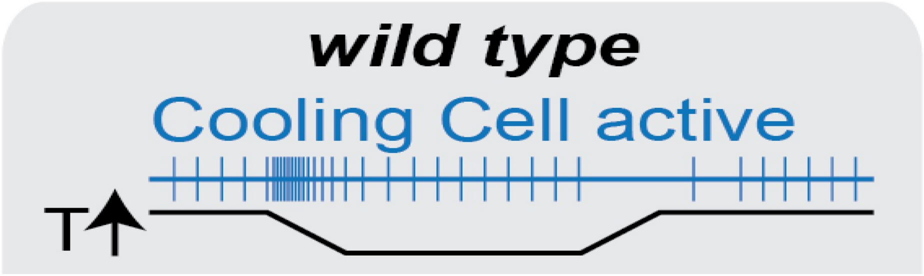


Activation cooling! **Inhibition by warming!**

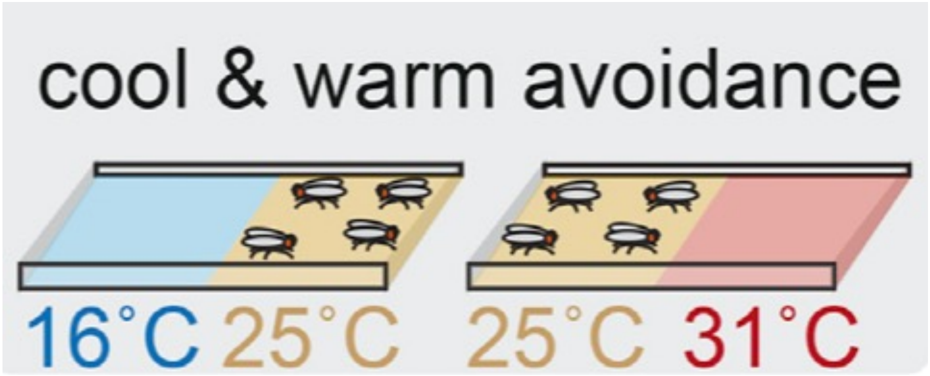
Changes in electrical impulse patter
about temperature changes in both

Budelli et al., Neuron (2019)

Ionotropic receptor subunit Ir21a drives BOTH cold and warm avoidance in Drosophila!

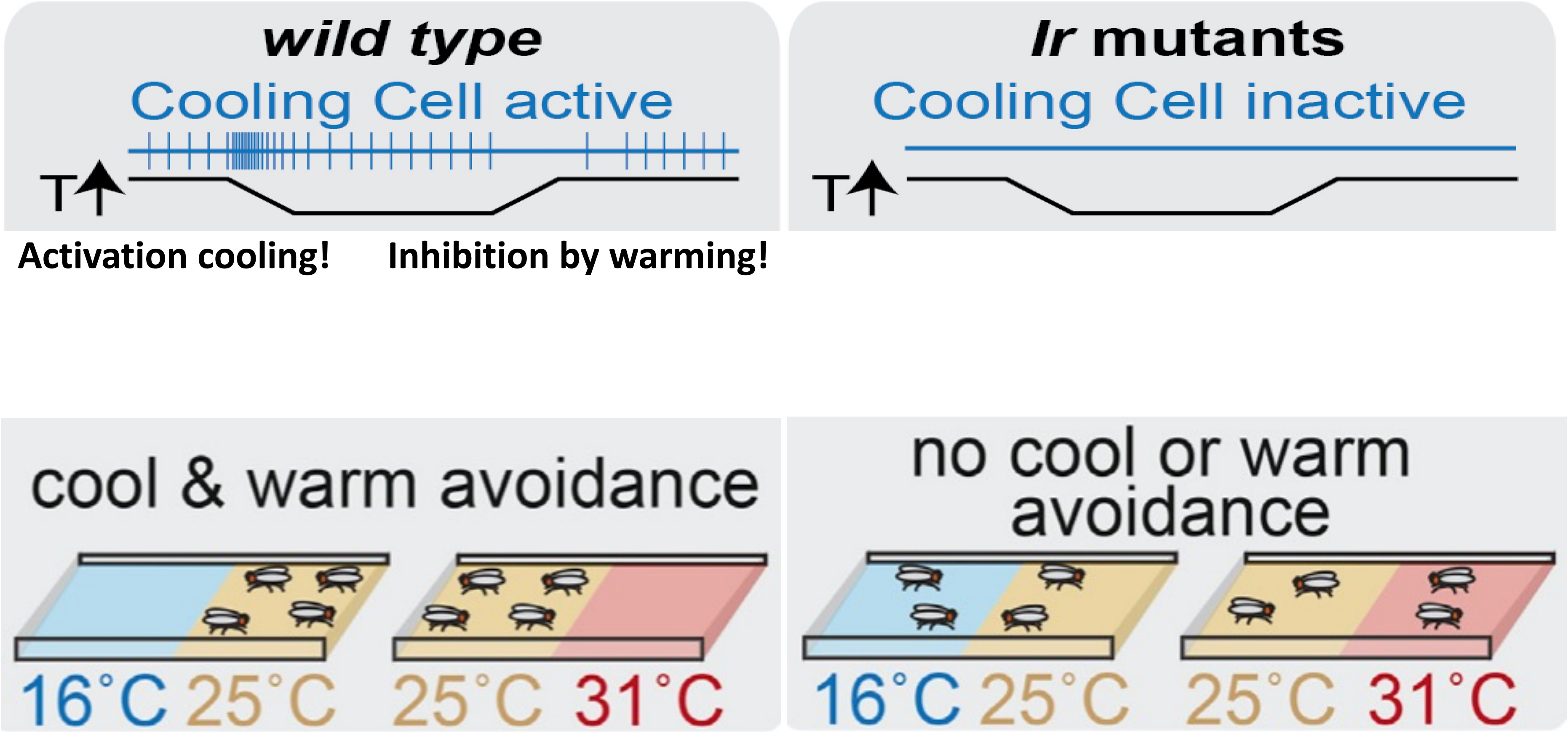


Activation cooling! **Inhibition by warming!**



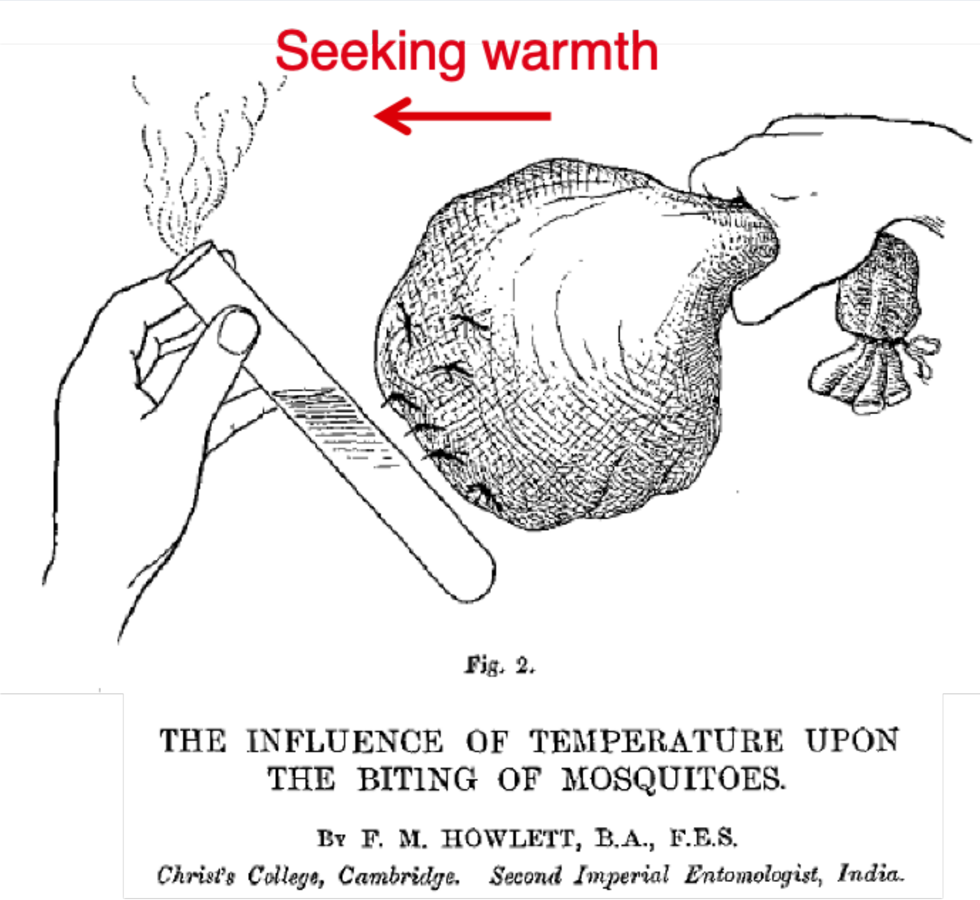
Budelli et al., Neuron (2019)

Ionotropic receptor subunit Ir21a drives BOTH cold and warm avoidance in Drosophila!

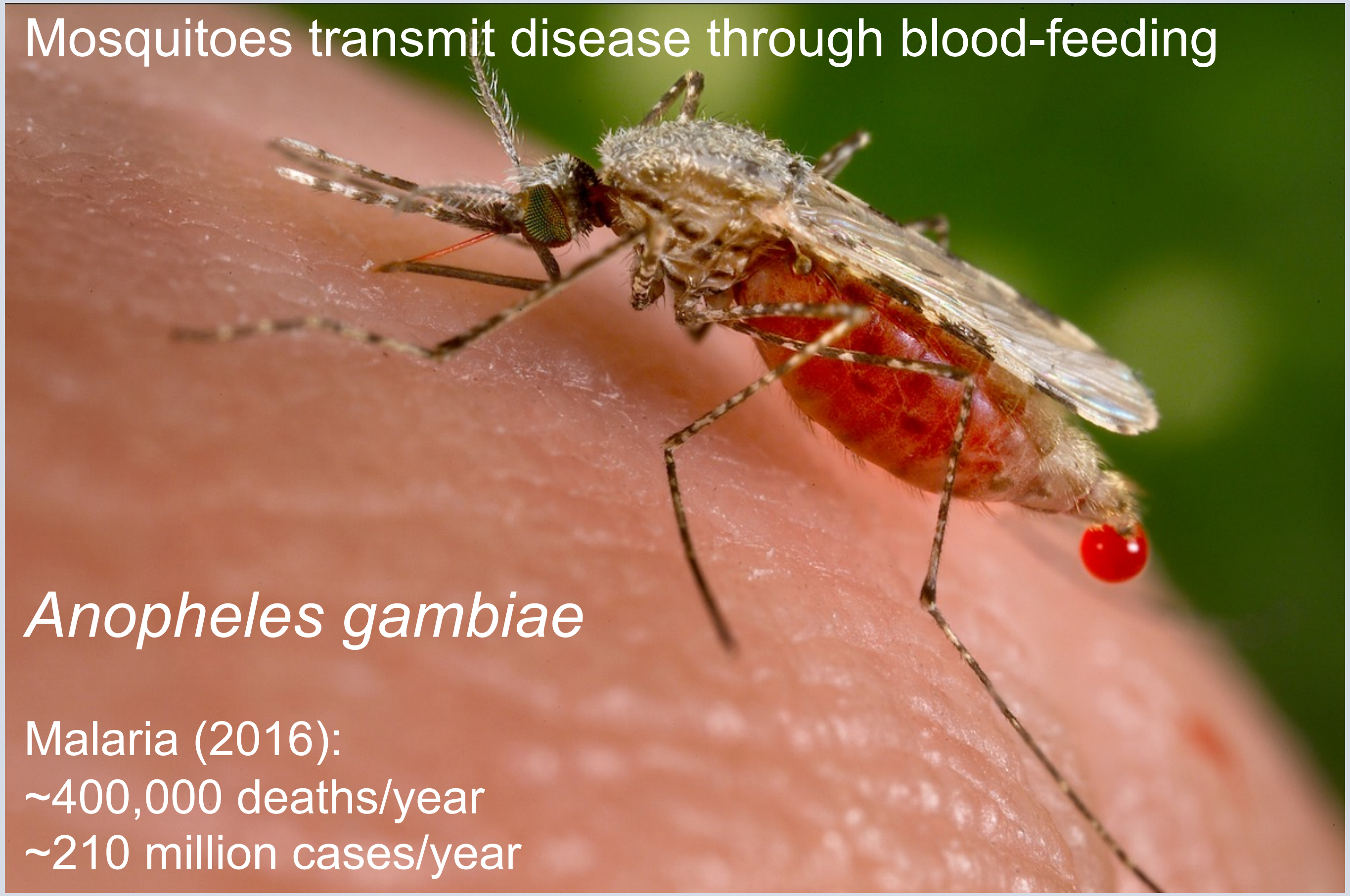


Budelli et al., Neuron (2019)

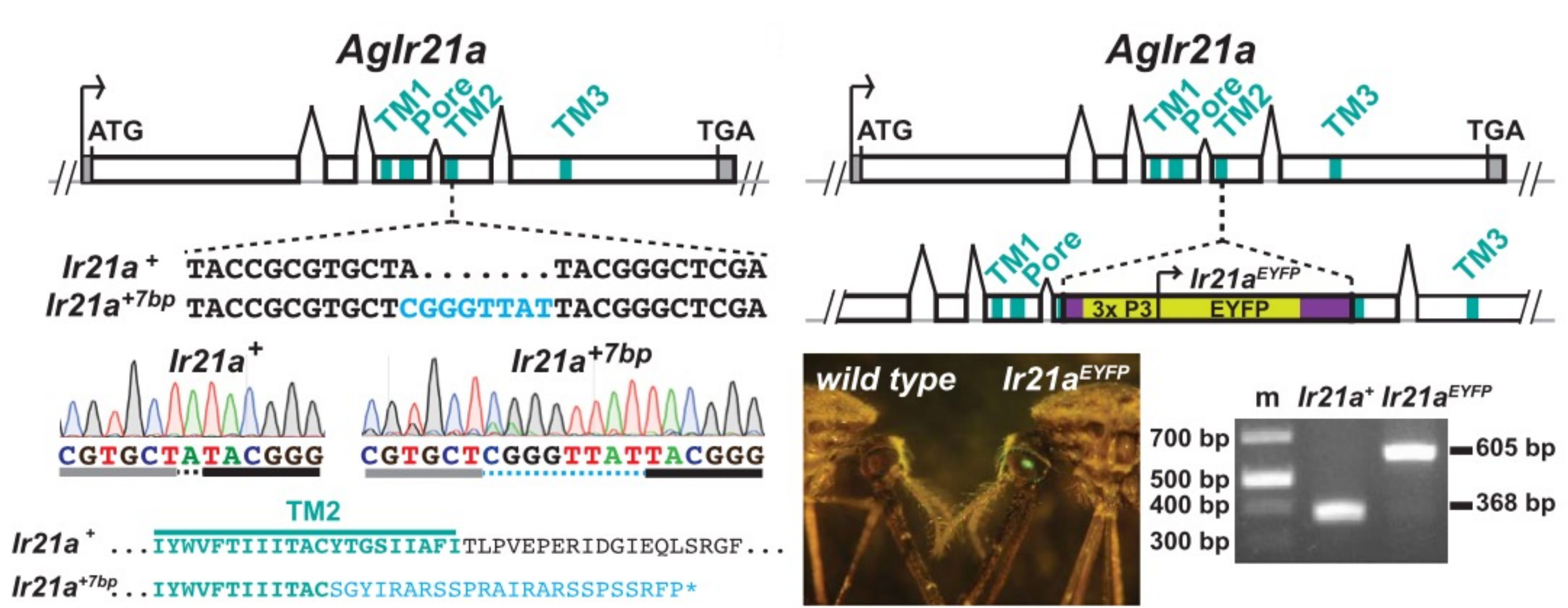
What drives heat-seeking in mosquitoes?



Howlett (1910) Parasitology, 3, 479-484.

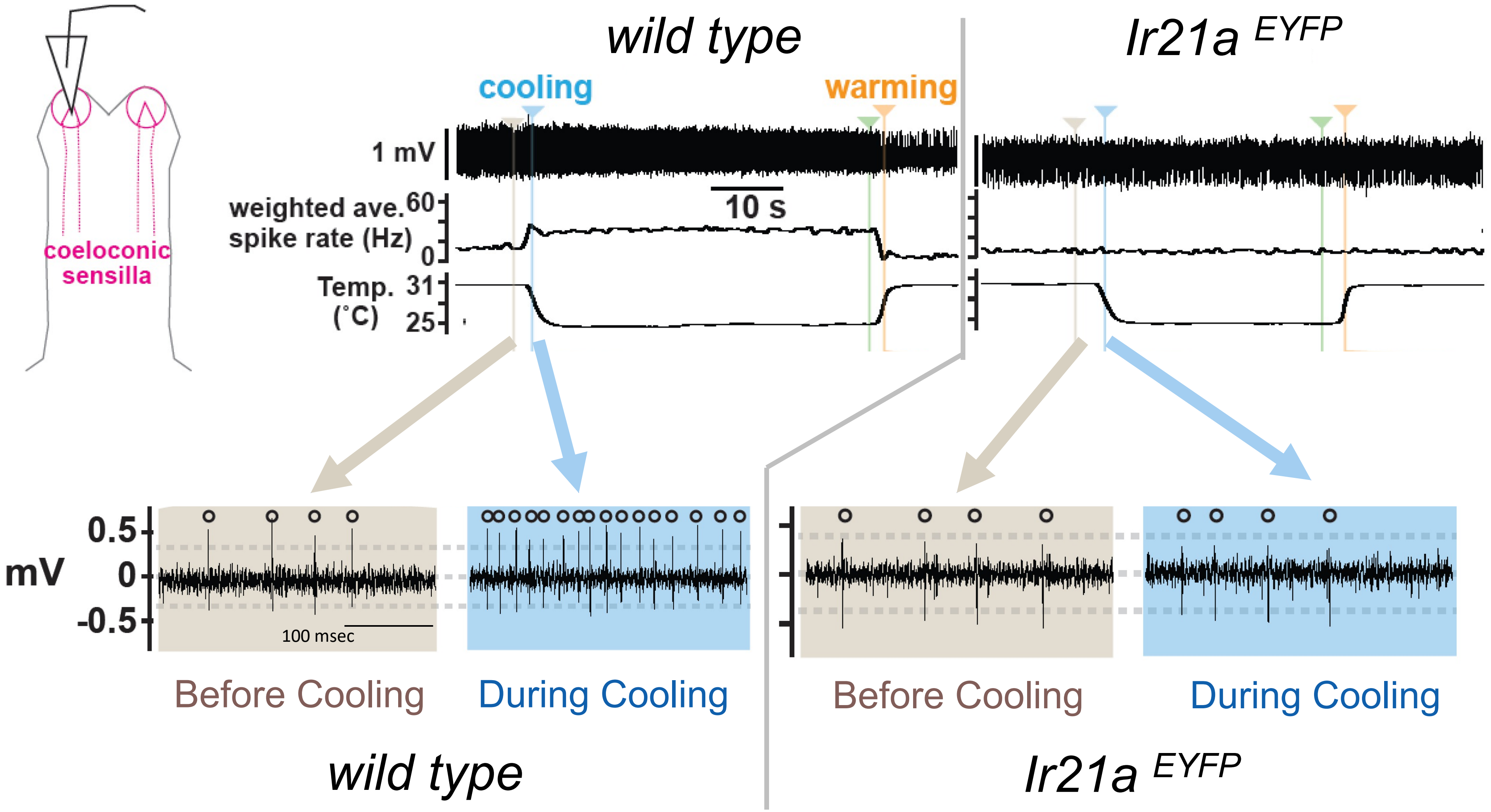


Genetic ablation of mosquito IR21a with CRISPR-Cas9



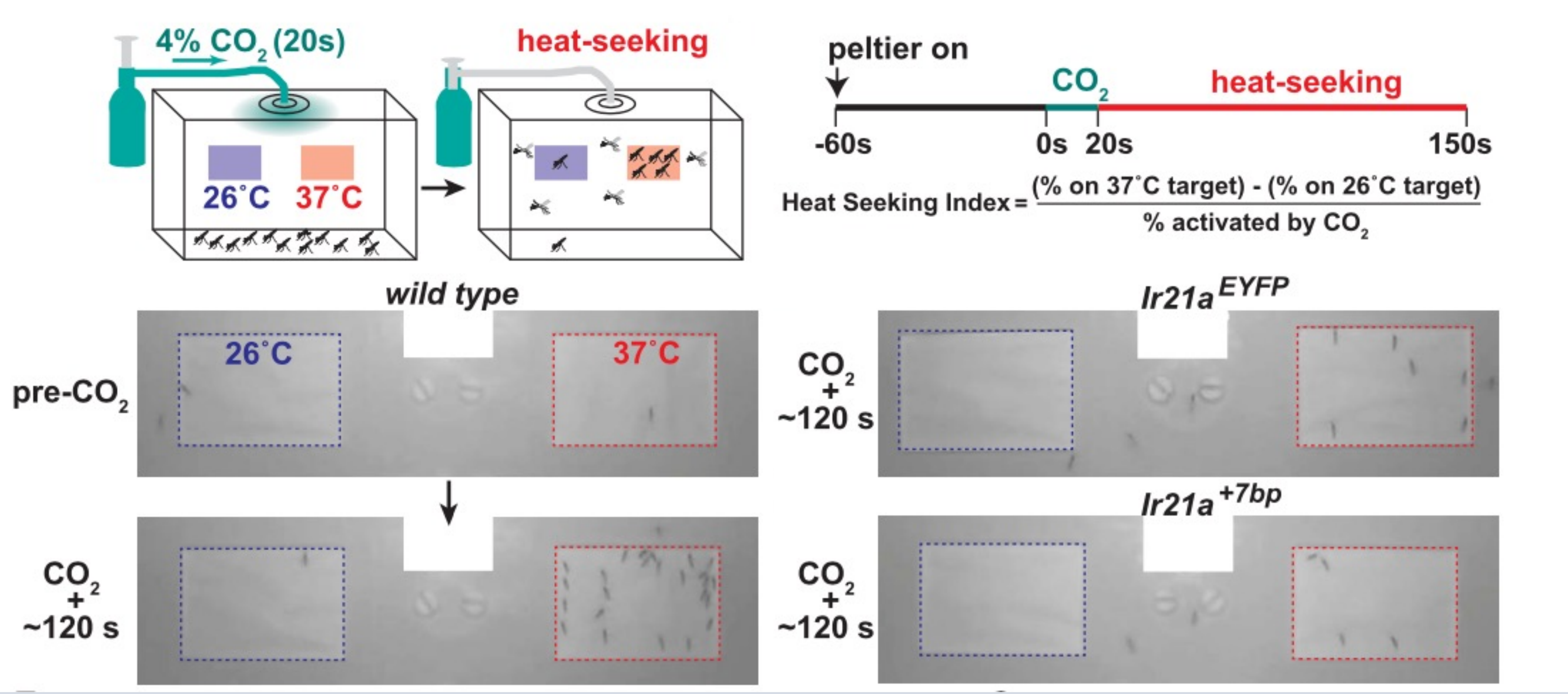
Greppi, Laursen et al, 2020

Mosquito *Ir21a* functions similarly to the Drosophila ortholog



Gonzalo Budelli
Chloe Greppi

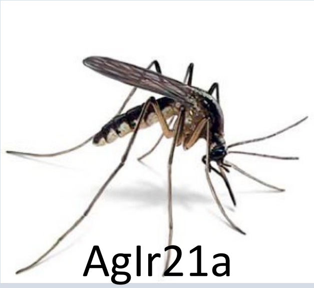
IR21a promotes mosquito heat-seeking



Greppi, Laursen et al., 2020

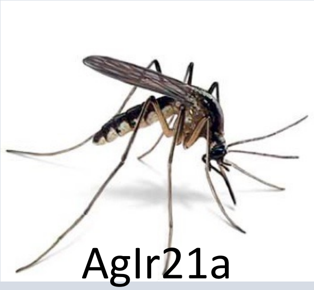
Same molecular function, opposite behaviors

- **Molecular function → conserved**
  - ***D. melanogaster*: Cooling Receptor**
  - ***An. gambiae*: Cooling Receptor**



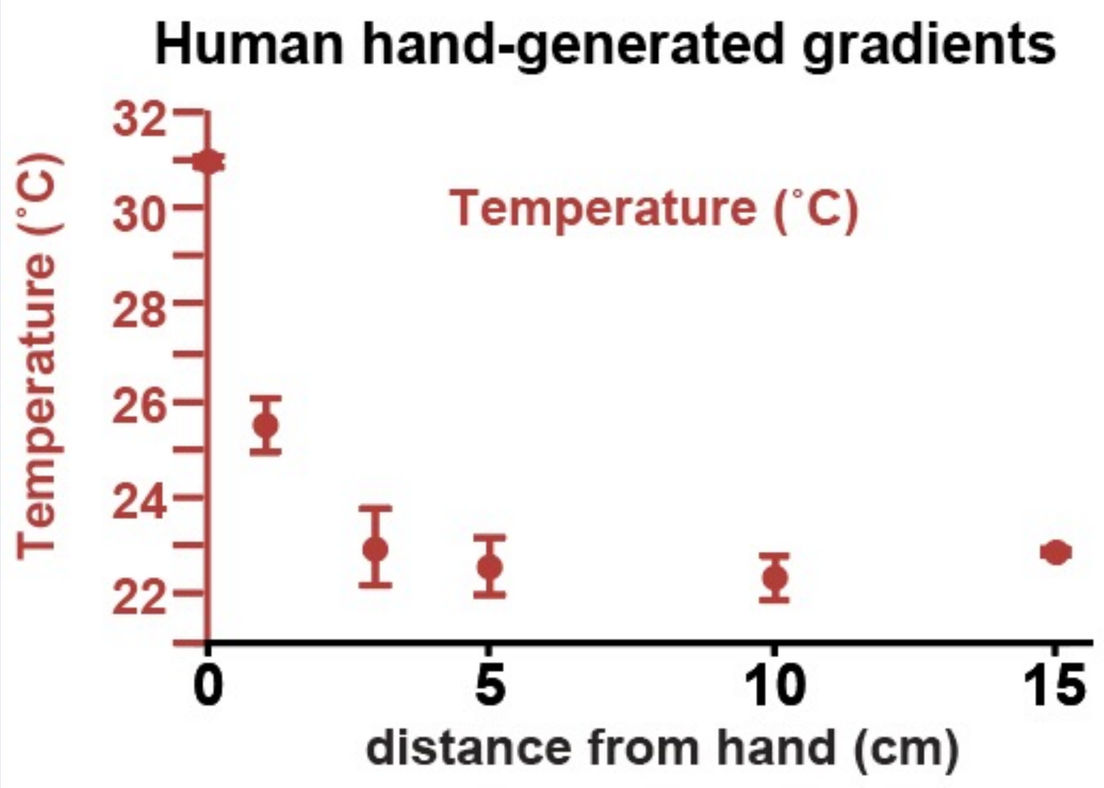
≈

- **Behavioral role → opposite**
  - ***D. melanogaster*: Warm avoidance**
  - ***An. gambiae*: Warm-seeking**



≠

Steep thermal gradients limit distance of temperature detection



Elaine Chang

Host seeking relies on multiple cues across different spatial scales

10-50 meters: CO_2

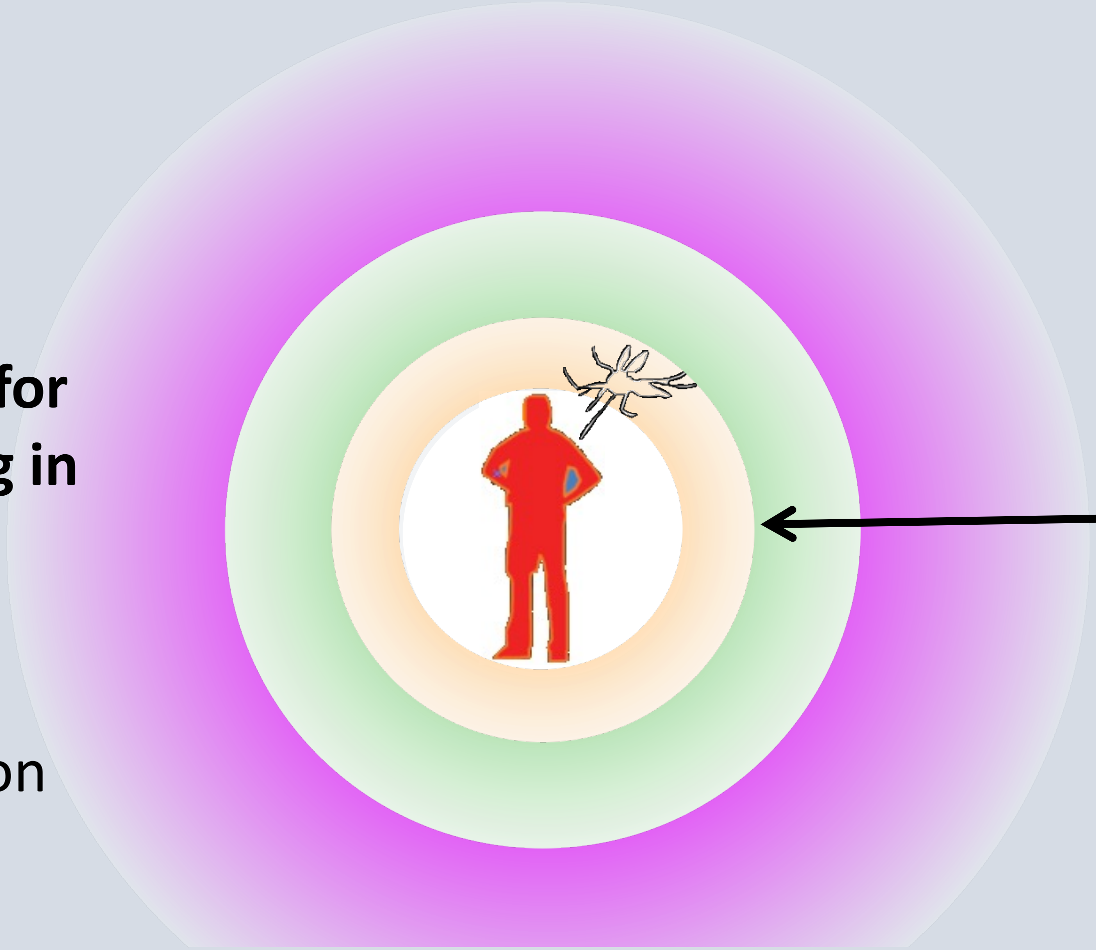
5-10 meters: odor
→vision

≤20 cm: heat, moisture

Short range detection ok for multisensory host seeking in mosquitoes:

-Heat influences landing decisions (gives information about proximity)

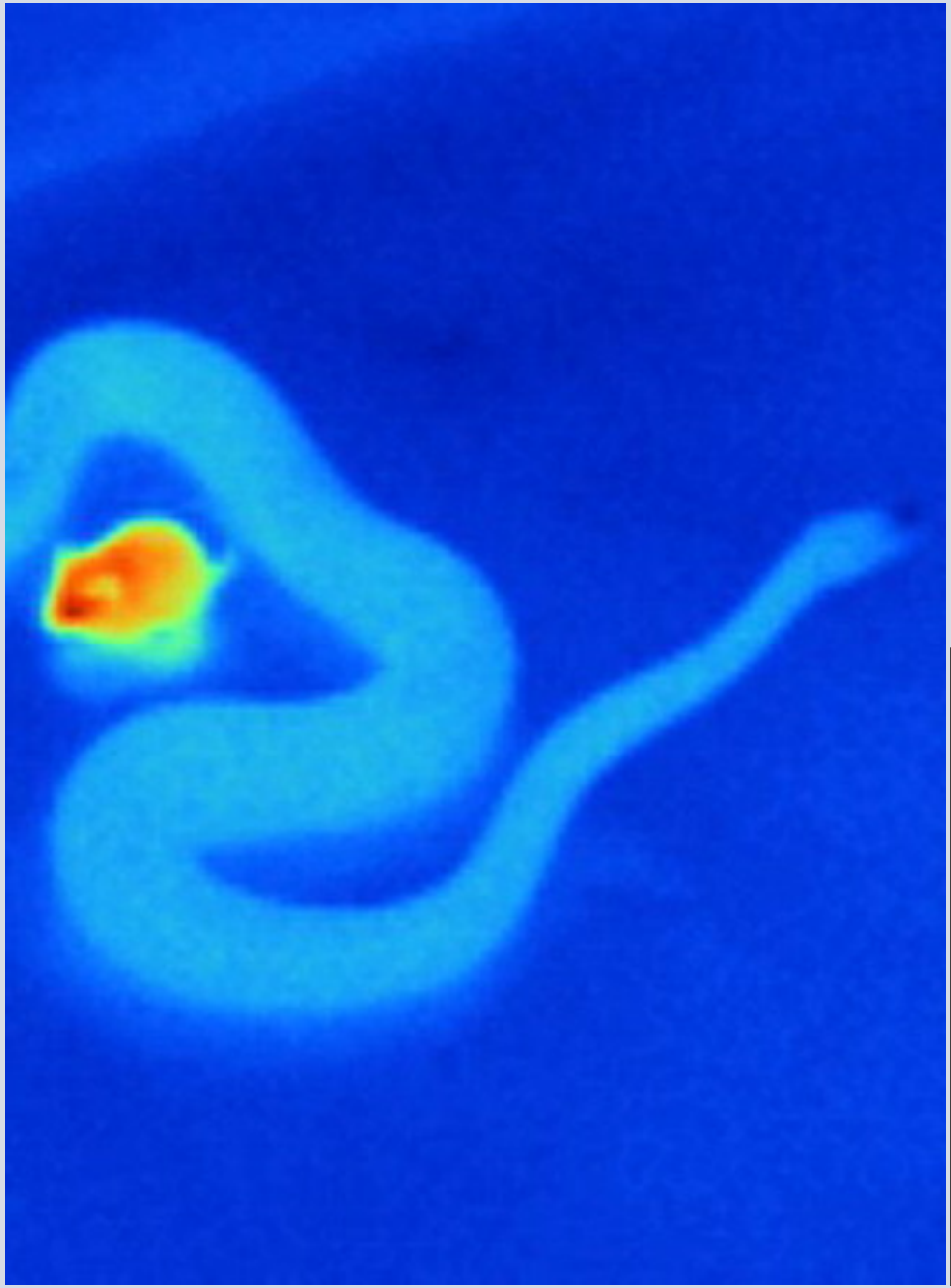
-Can be used locally to find vascularized regions of skin?



Heat is an important **close range** cue!

Animals with deficits in any one modality can still find hosts

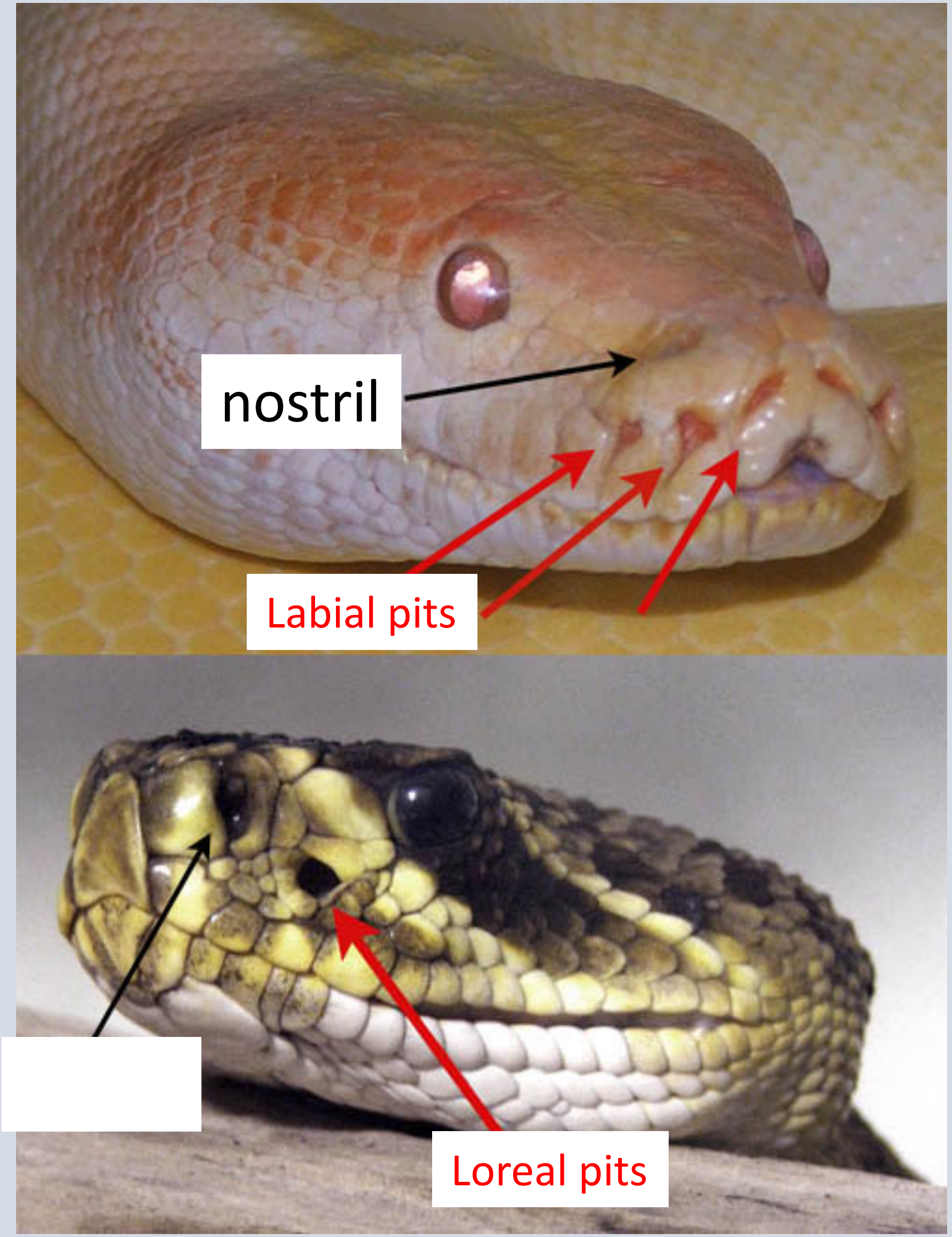
What if you want to detect temperature cues from a distance?



Part II.
Heat "vision" in snakes:
Increasing sensitivity and extending range of heat detection

Facial pits in pythons, boas, and crotaline vipers

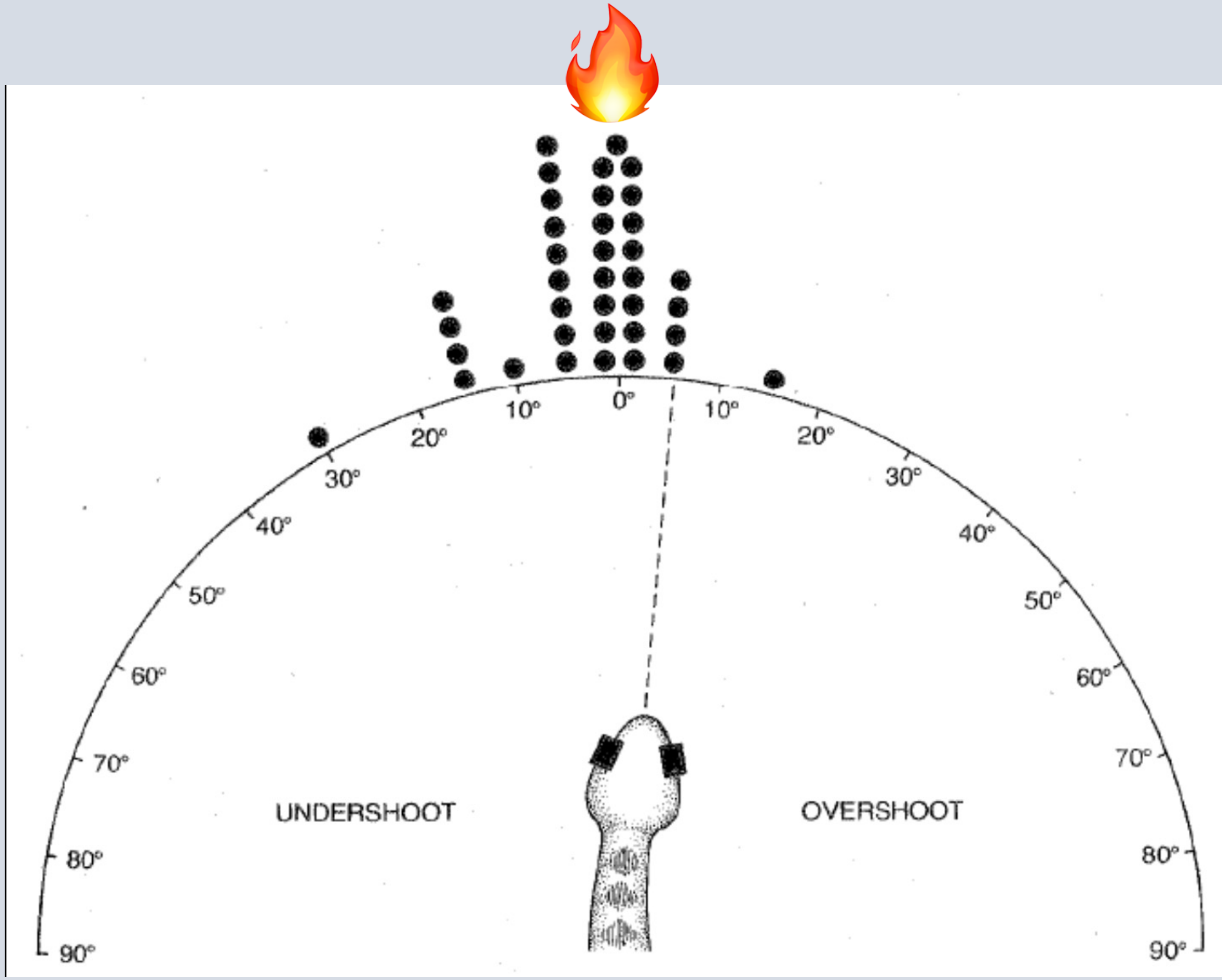
- Pit organs evolved once once in pit vipers and multiple times in boas and pythons
- Function long unknown--proposed to be ears, tactile sensors, tear sacs, chemical detectors, etc.
- Eventually discovered to house highly sensitive heat sensors for finding prey (1930s)



Don’t turn your back on blindfolded snakes

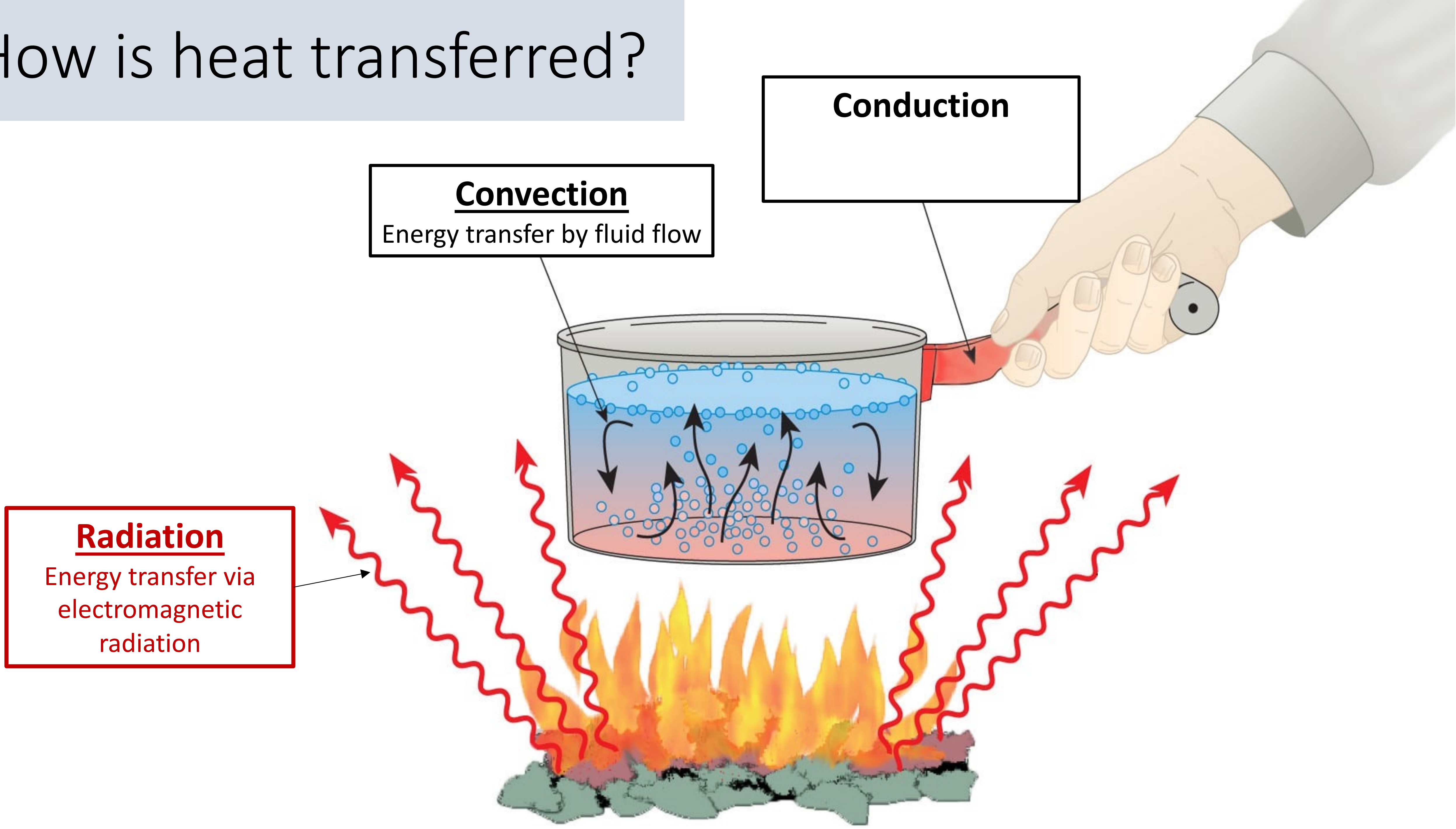
- Blindfolded snakes can accurately strike at warm moving objects at distances up to ~50cm, even when the temperature difference at snake pit is <0.2°C

- How can distant warm objects be detected even when thermal gradients are barely distinguishable?

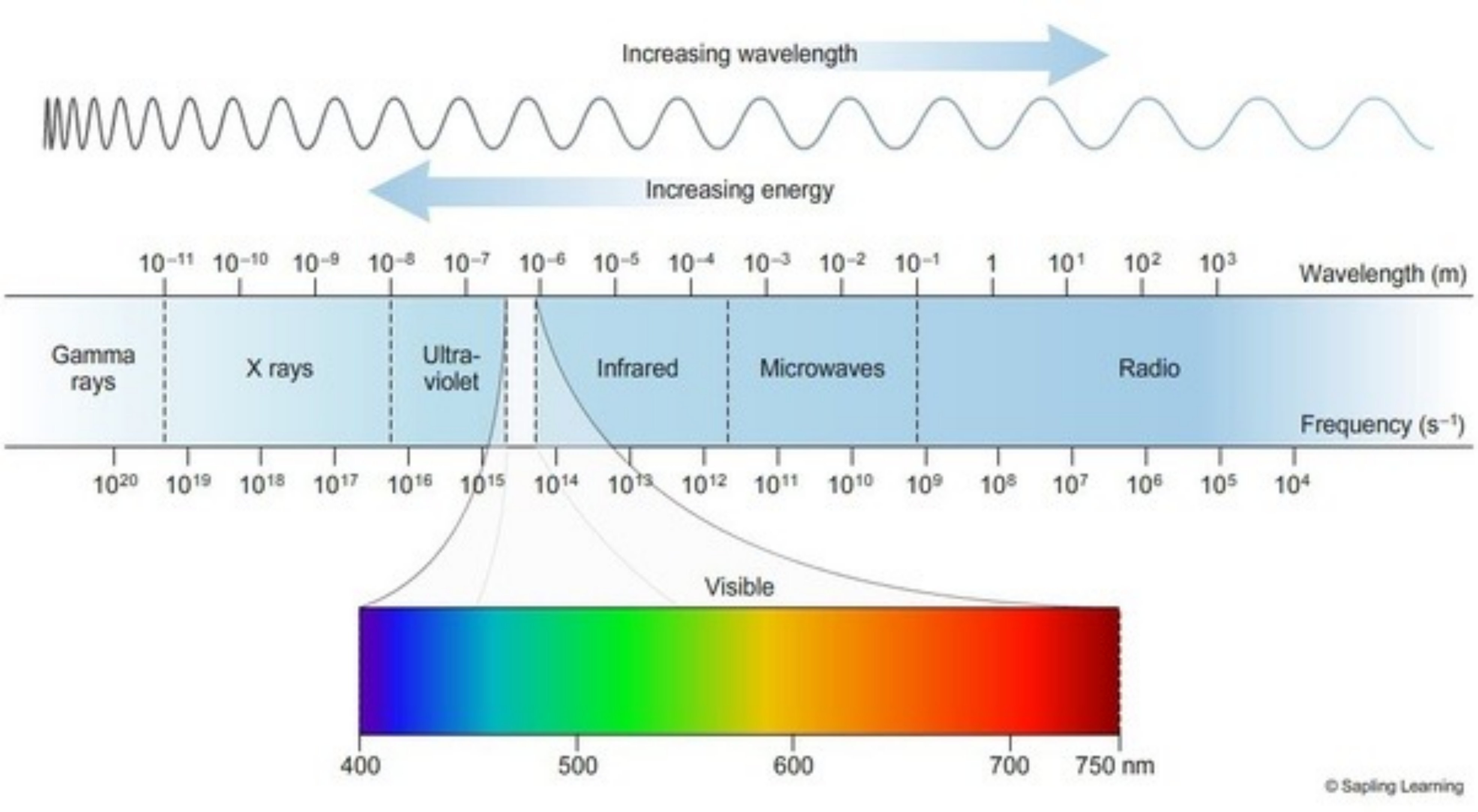


Newman and Hartline 1982

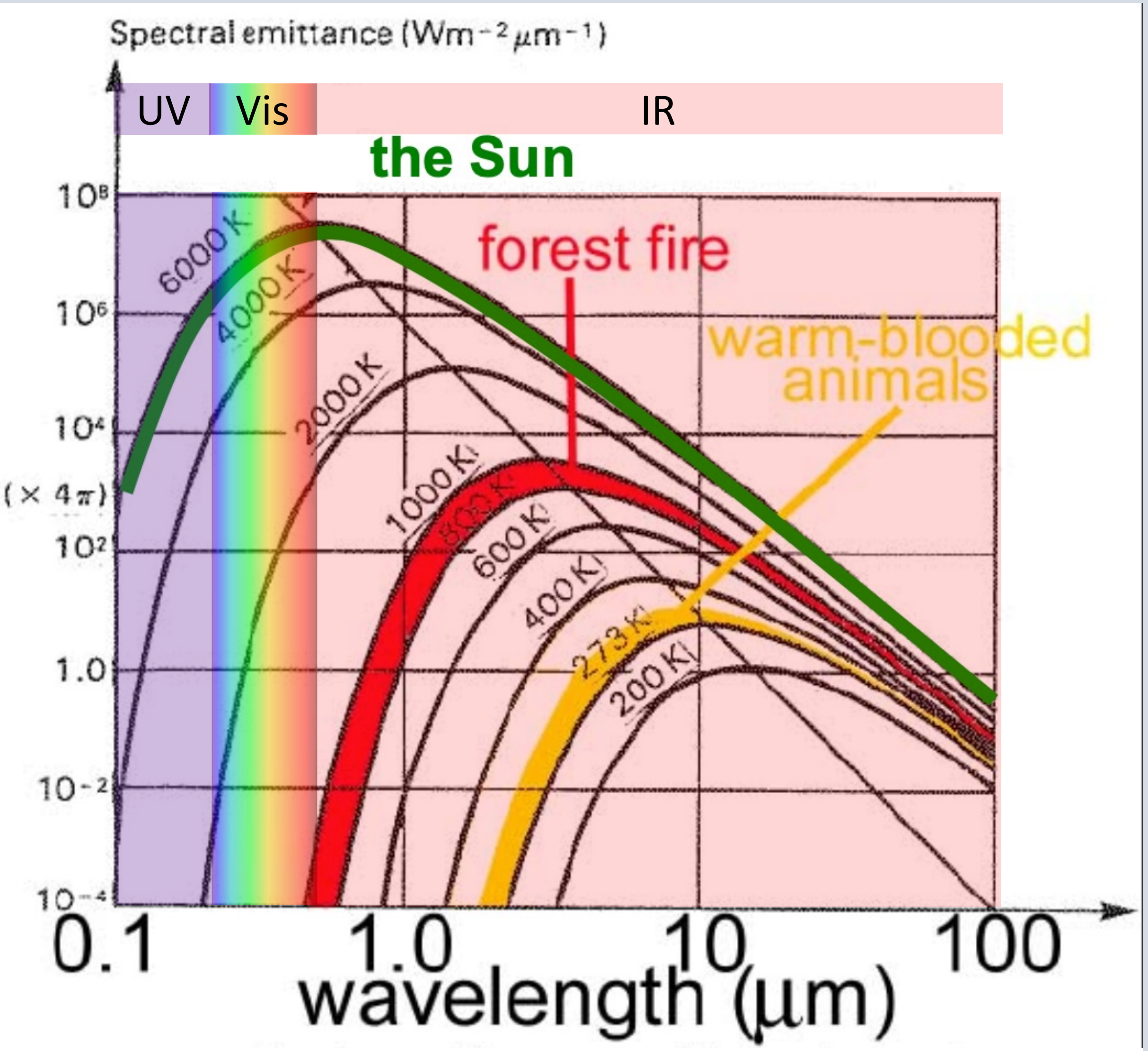
How is heat transferred?



The electromagnetic spectrum



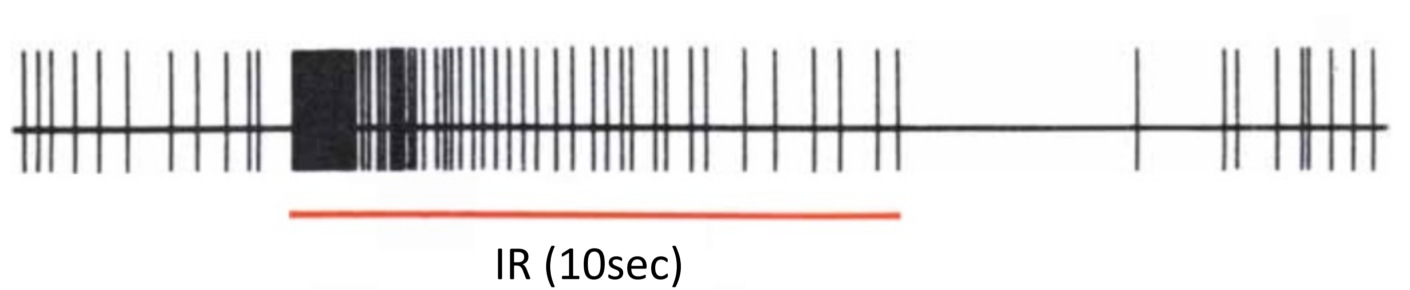
Objects emit blackbody radiation



Spectral emittance of black body

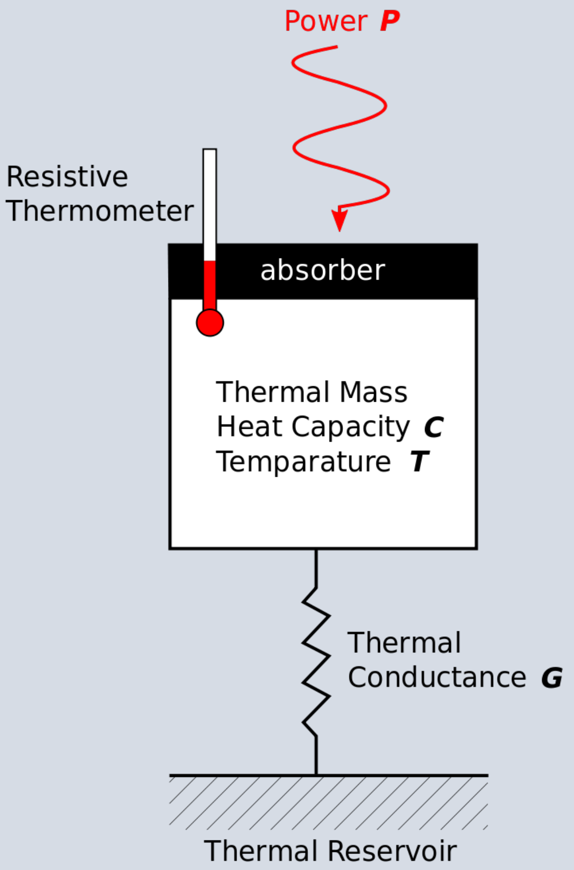
Snake pits are tuned to detect IR-radiation!

- Broad spectral response (400-10,600 nm), quickly adapting
- Using filters to block visible light has little effect on response, blocking IR wavelengths prevents stimulation
- Visible light is detected via photosensitive pigments tuned to different wavelengths, but none have been found with such broad sensitivity or sensitivity in infrared range (would likely be too noisy)
- How is IR radiation detected?



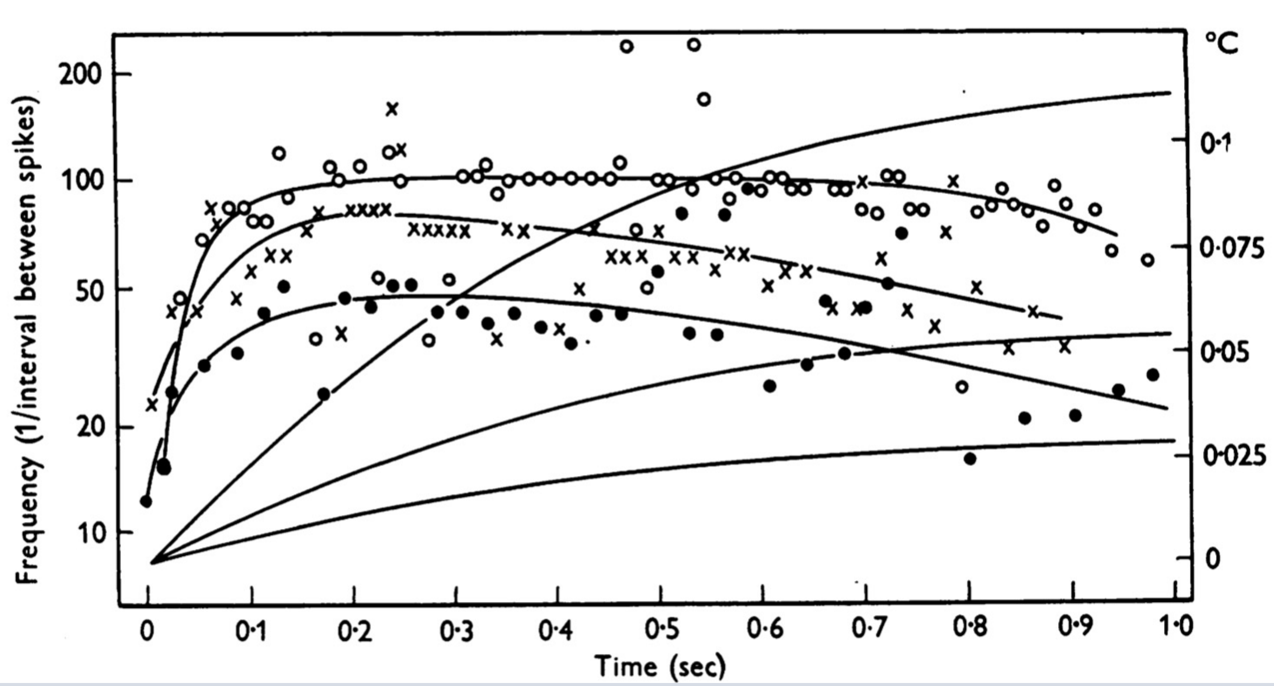
Newman & Hartline, 1982
Moiseenkova et al, 2002

Snake pits function as bolometers*



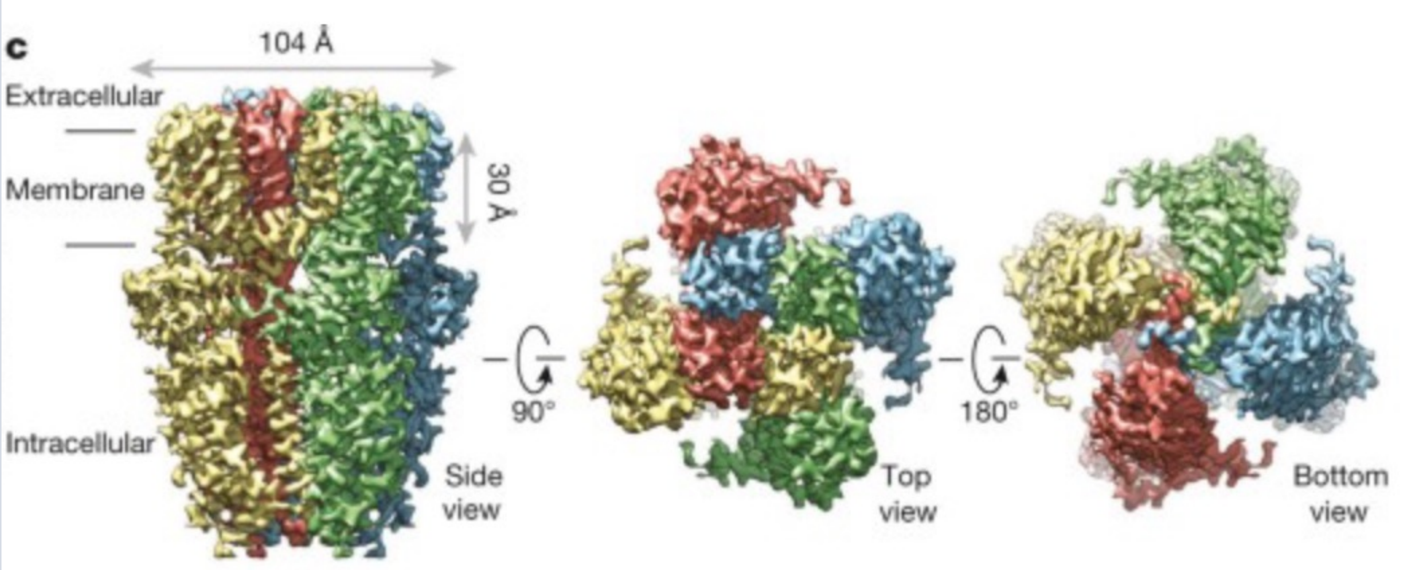
*Bolometer= device that measures electromagnetic radiation through heating an absorbing material

Flowing warm water activates pit neurons with ΔT threshold of 0.003℃/0.06s!



Bullock & Diecke, 1956

Ion channels in pit neurons respond to temperature

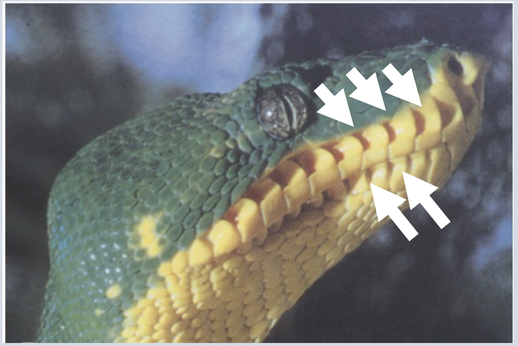


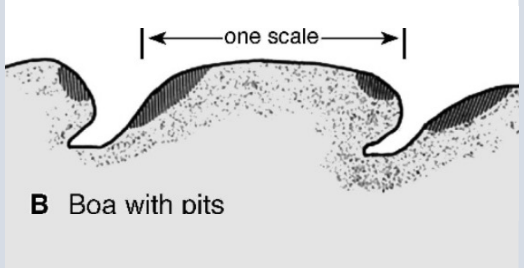
- Thermosensitive ion channel TRPA1 expressed in pit neurons (respond to warm temp)
- Transduces thermal stimuli to electrical signal
- Also present in non-IR sensitive species, so what gives?

Paulsen et al, 2015

Pit anatomy enhances heat detection

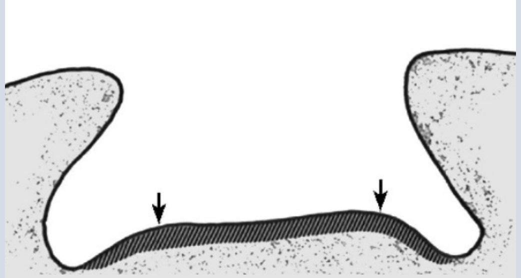
Boa





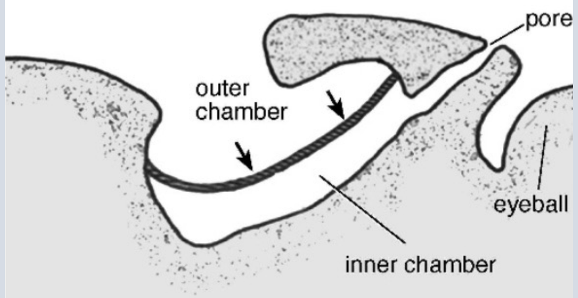
Scales

Python



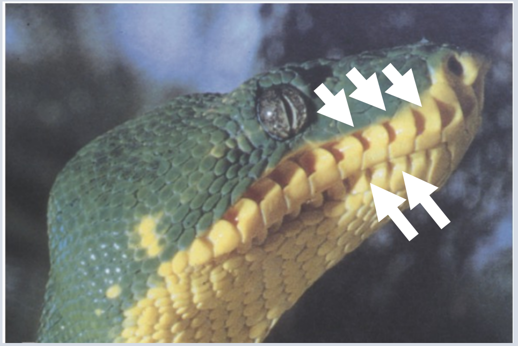
Shallow pits

Pit viper



Elaborate pits

Structure correlates with sensitivity

Boa	**Python**	**Pit viper**
		
Scales (least sensitive)	Shallow pits	Elaborate pits (most sensitive)

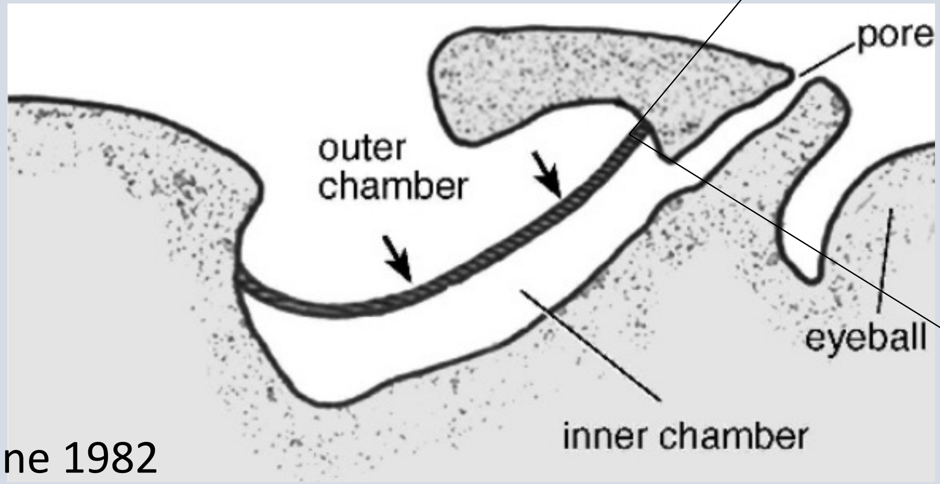
Detection Range

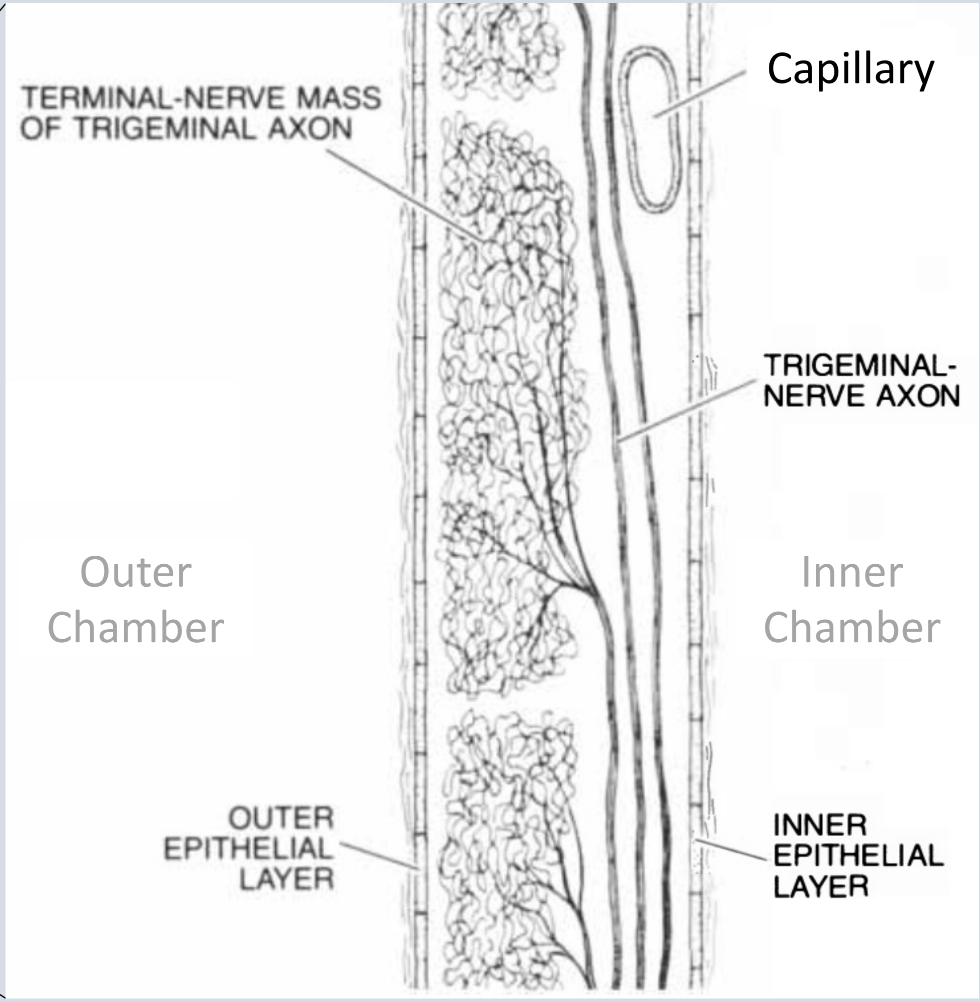
Rat (25°C ambient)	**28 cm**	**49 cm**	**115 cm**
Rat (15°C ambient)	**48 cm**	**82 cm**	**194 cm**
Mouse (15°C ambient)	**20 cm**	**34 cm**	**81 cm**

Viper pits are adapted for sensitivity

~7000 thermoreceptor neurons innervate vascularized ~15um thick pit membrane

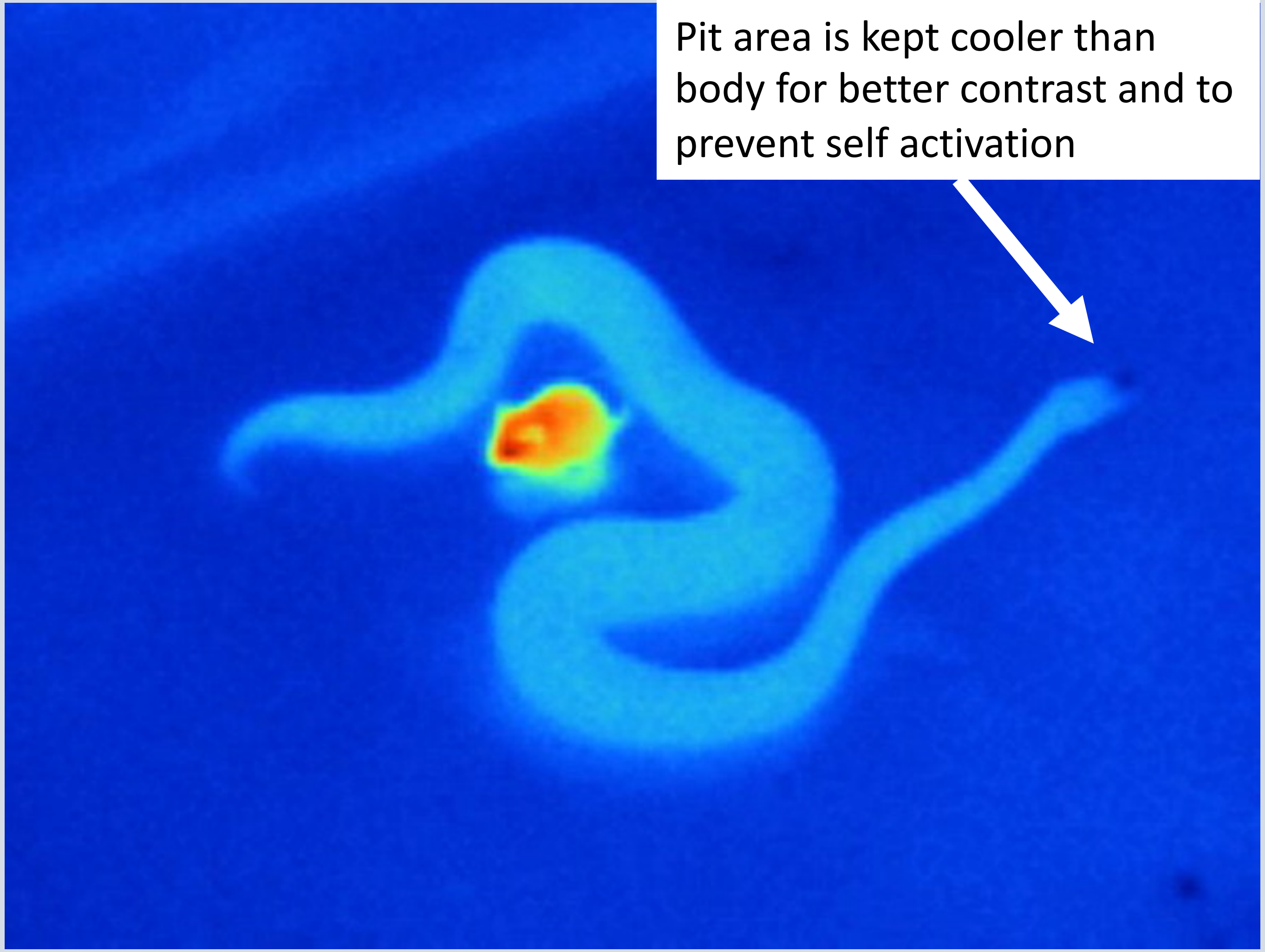
- Thin tissue and proximity to surface→ takes 20x less energy to warm than deeper thermoreceptors in mammals
- Vasculature serves as heat sink for better time resolution





Goris, 2011
Newman & Hartline 1982

How to avoid self-activation of heat detectors?



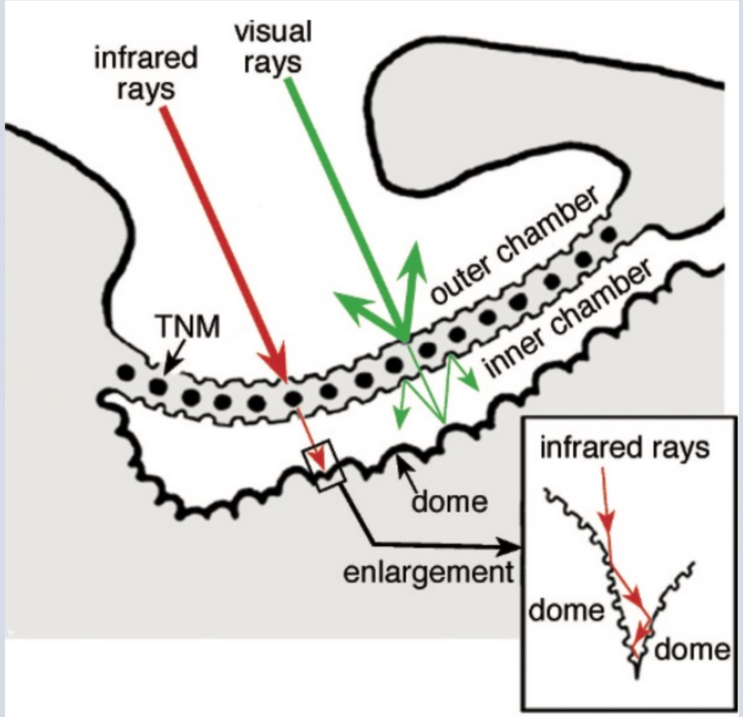
Same is true for heat-sensing vampire bats!

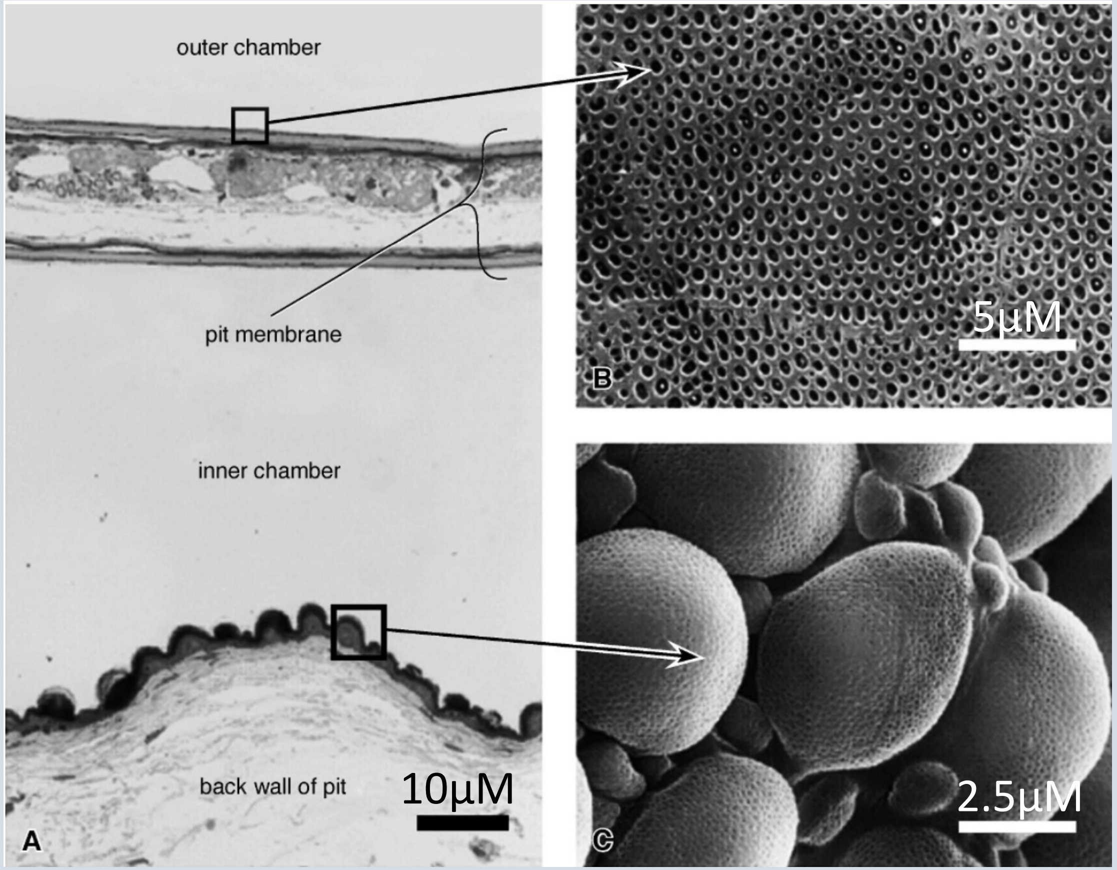
Fig. 2. Distribution of surface temperature on the face of *Desmodus rotundus* (as reference see Fig. 1a). Drawn from thermographic photographs. *Double-hatched:* 29 ± 0.6 °C; *hatched:* 33 ± 0.6 °C; *punctuated:* 37 ± 0.6 °C

Kurten & Schmidt, 1982

Pit surface is selective for IR

- Pit membrane contains optical grating to reflect visible light; absorb IR
- Domes on back wall act as light trap to prevent backscatter

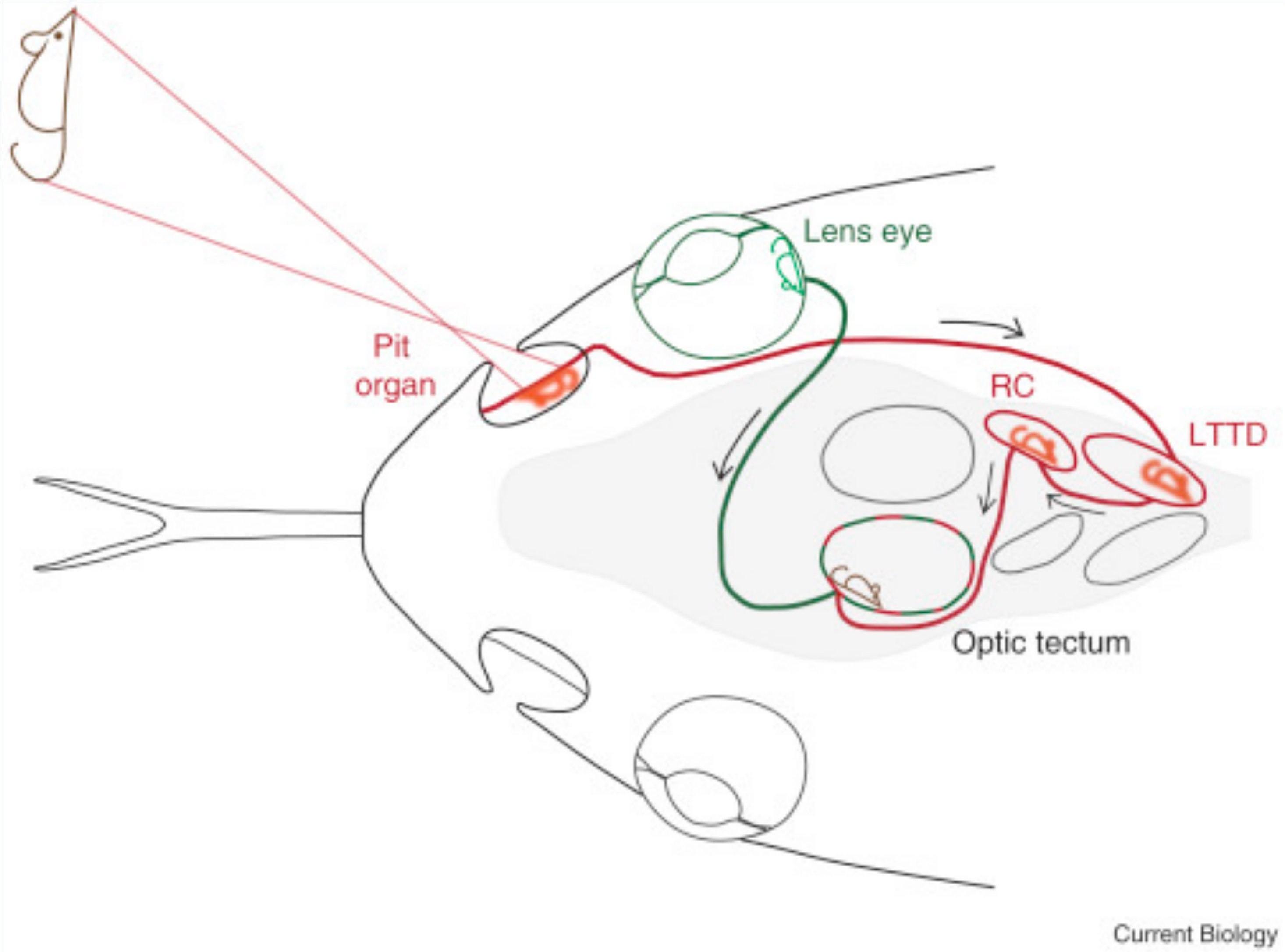




Goris, 2011

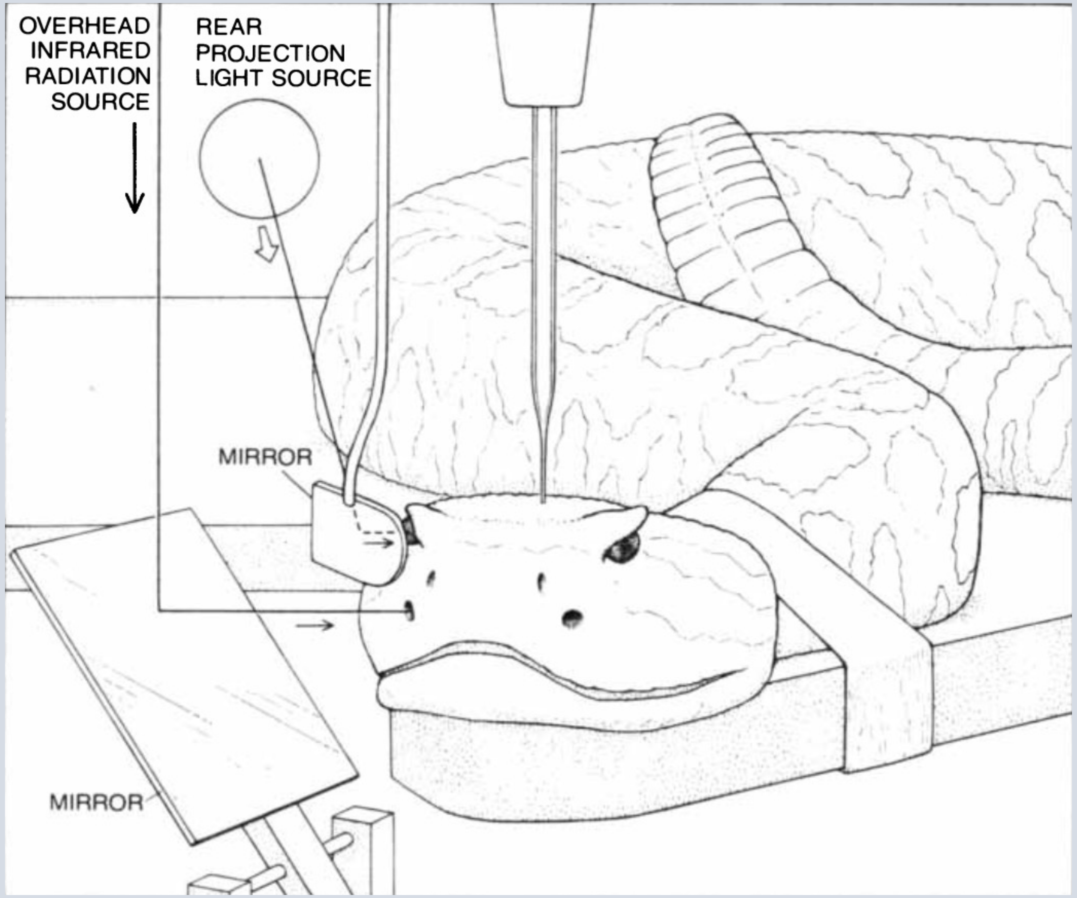
Pit organ functions as a pinhole camera

- Many similarities with visual system
- Pit opening (1-5mm) functions as aperture
- IR radiation emitted from object is projected onto pit membrane to generate an inverted image
- Information is eventually integrated with visual inputs in optic tectum!

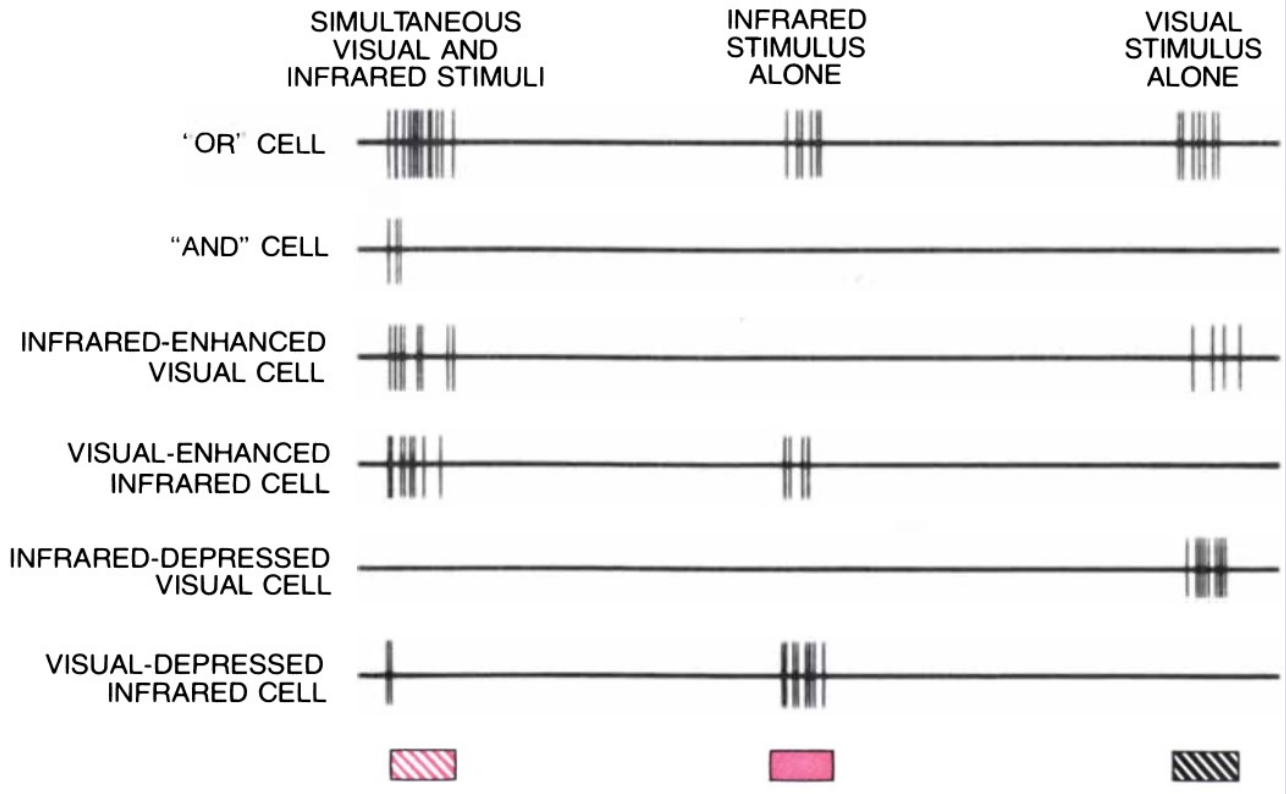


Kelber, 2019

“Seeing” in IR



IR and visual signals are integrated in tectum of the brain



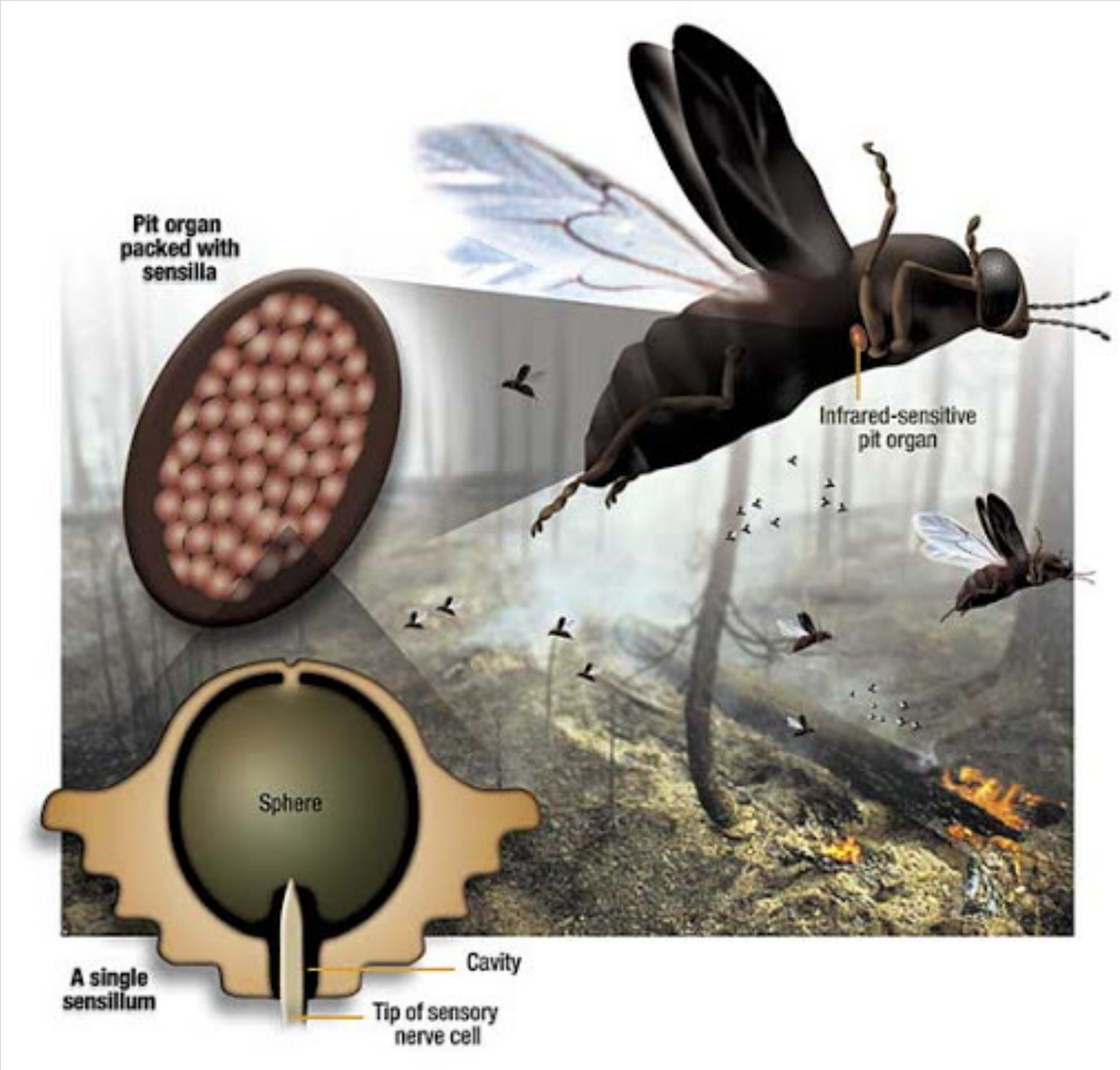
Visual and IR signals integrated in optic tectum to begin to generate internal representation

Newman & Hartline 1982

Part III. Going the distance: Novel thermosensory mechanisms greatly extends detection range in fire beetles

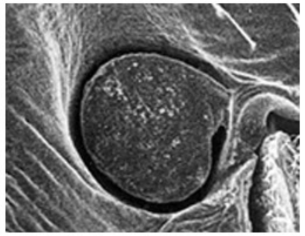
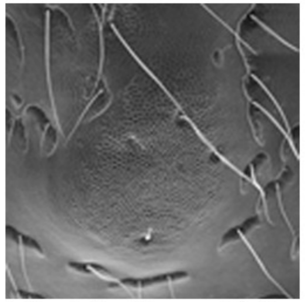
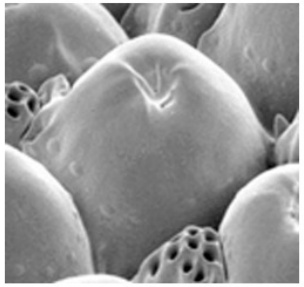
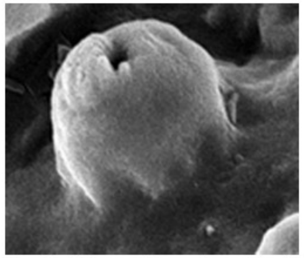
Heat detection in fire beetles

- Fire beetles and other pyrophilus (“fire-loving”) insects seek out forest fires to lay eggs in freshly burnt wood
- Often some of the earliest arrivals to fires
- Observed to travel from >80km away!?
- Extreme sensitivity comes at a cost: they are known to get confused and congregate at refineries, smelting plants, oil fires and football stadiums filled with smoking fans



IR detection in multiple pyrophilus insects

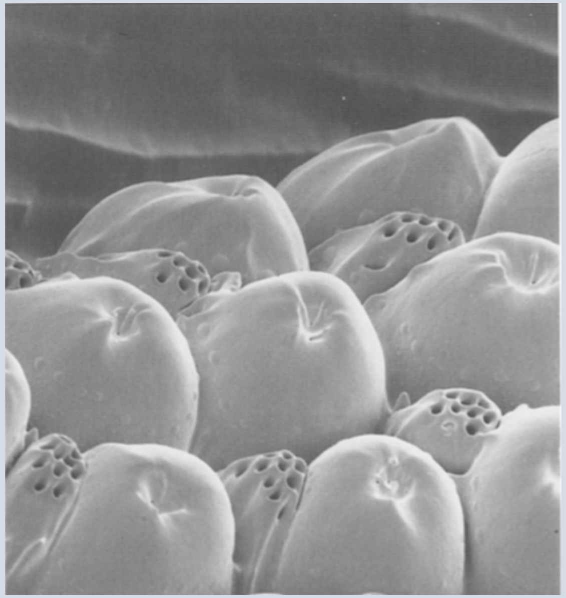
Table 1 Infrared receptors in pyrophilous insects

	"Little ash beetle" Acanthocnemus nigricans *(Only species in the genus)*	*"Australian fire beetle"* Merimna atrata *(Only species in the genus)*	*"Black fire beetle"* Melanophila spec. *(11 species)*	*"Pyrophilous flat bugs"* Aradus spec. *4 IR sensitive species in the genus* Aradus *(200 species)*
Taxonomy Ventral habitus IR ogans/receptors indicated in yellow	Beetle (family: Acanthocnemidae) 	Jewel beetles (family: Buprestidae) 		Flat bugs (family: Aradidae) 
Legs omitted L: body length	L: 4 mm	L: 20 mm	L: 10 mm	L: 4 mm
Position of IR receptors	Prothorax	Abdomen	Metathorax	Pro-/mesothorax
Picture of IR organ or sensillum	 Left IR organ (sensory disc with about 90 sensilla)	 Left anterior IR organ (shallow cuticular depression)	 Single IR sensillum (about 70 dome-shaped sensilla in a sensory pit)	 Single IR sensillum (sensilla interspersed between hair mechanoreceptors)

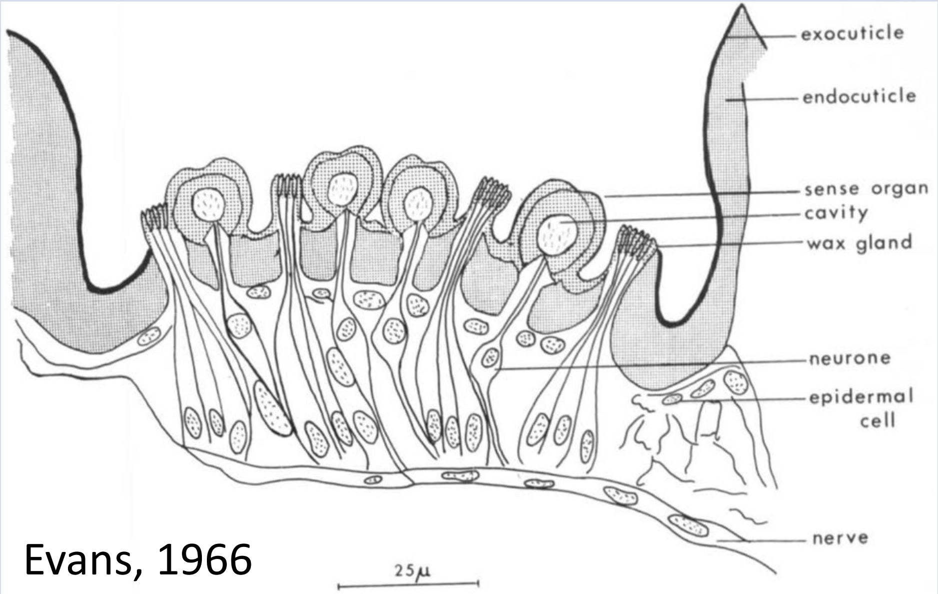
Schmitz & Schmitz, 2017

IR detection organ of *Melanophila*

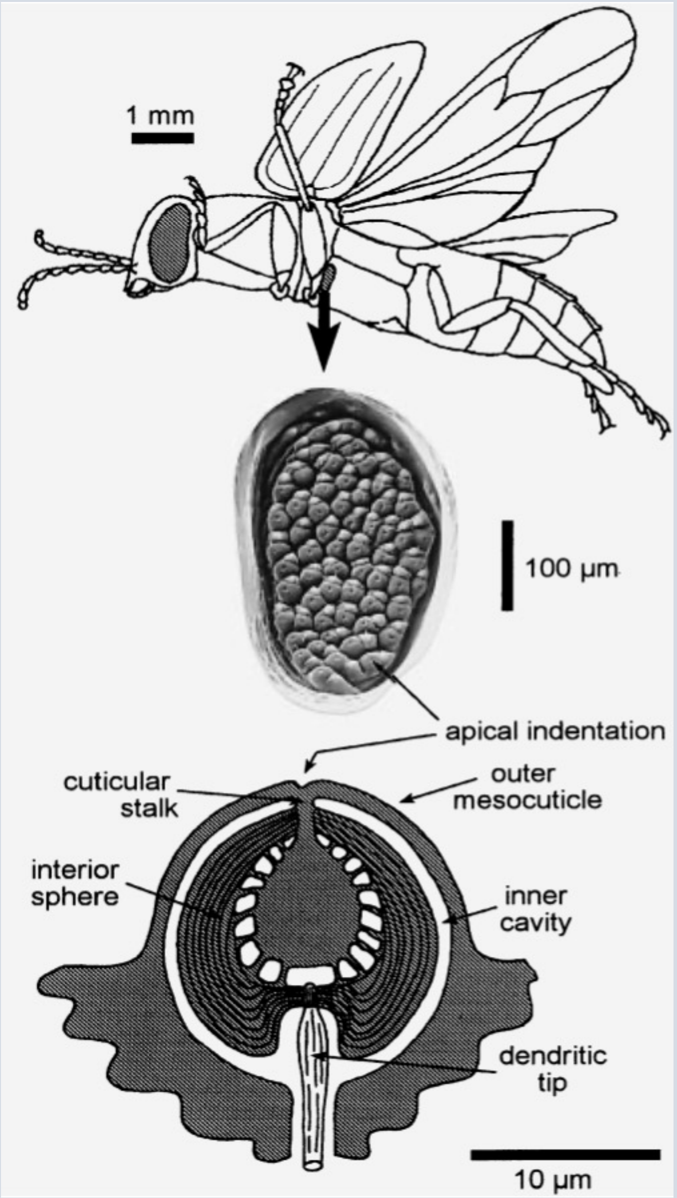
- 100um deep pit filled with ~100 domes and associated multiporous wax glands
- Function of wax poorly understood, but strands fill the pit
- Pore contains a fluidic core surrounded by lamellated zone of exocuticle
- Beetles fly with legs extended to give access to radiation



Vondran et al., 1995



Evans, 1966

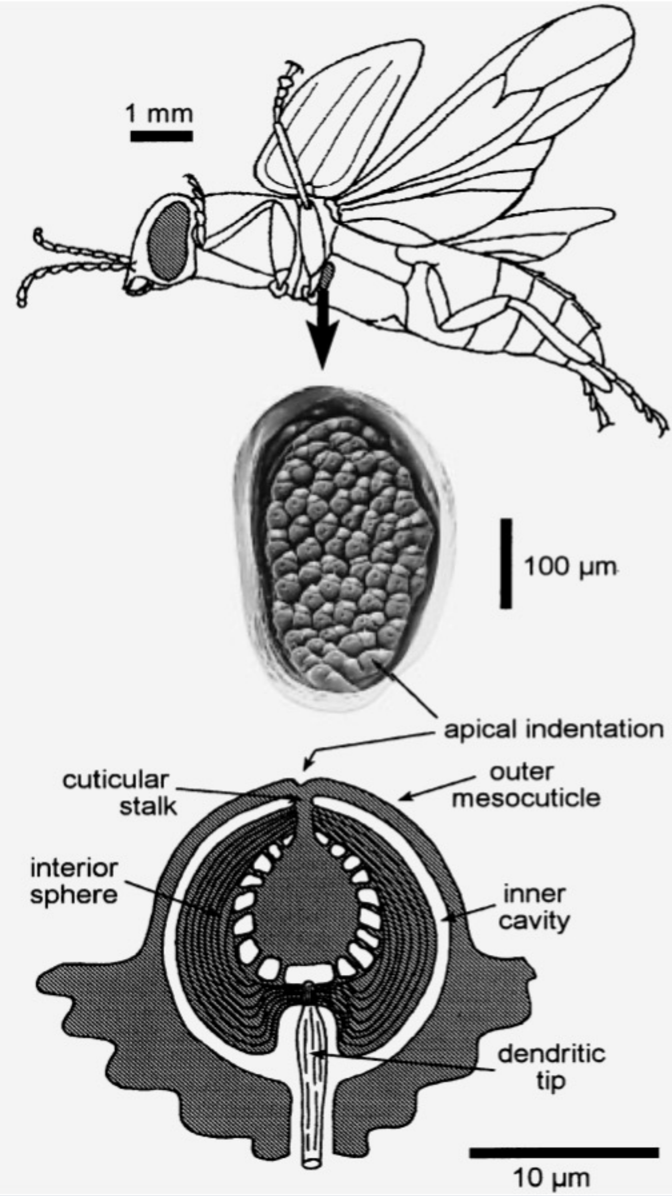


Schmitz & Bleckmann, 1998

Photomechanical mechanism of IR detection

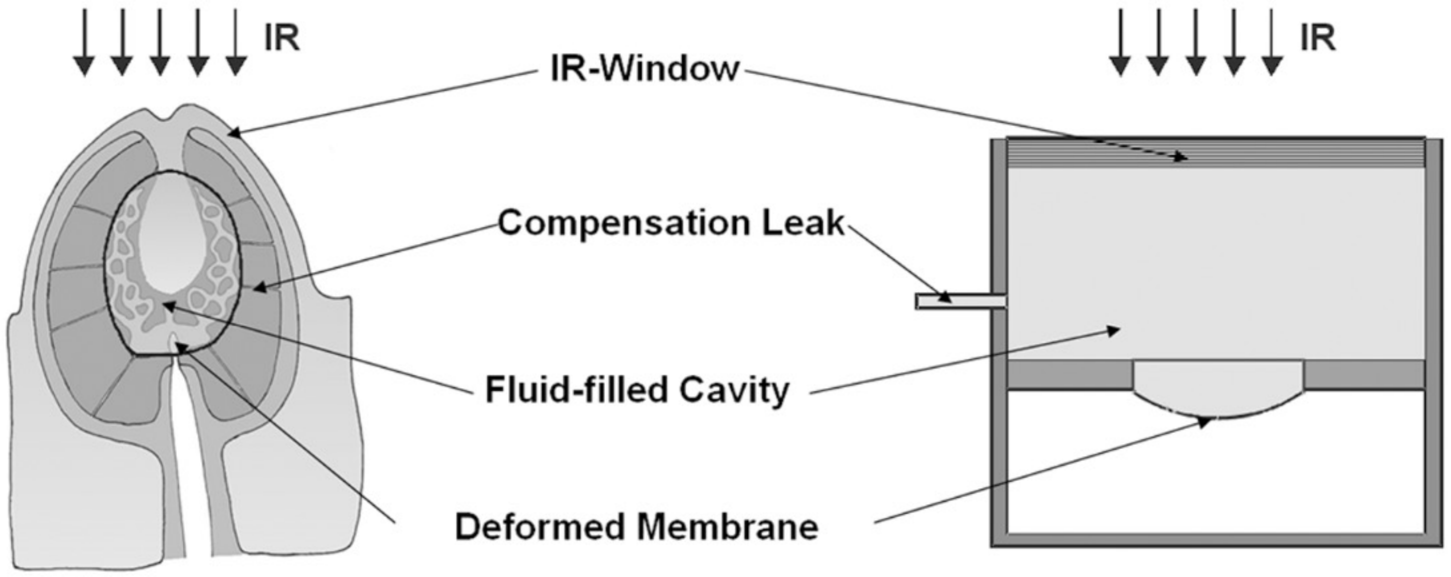
- Respond to $\Delta T < 0.01K$ with threshold energy of 60-500uW/cm^2
- Movement of recording electrode also stimulates cells
- Domes composed of chitin with stretch resonance at ~3um

Rapidly absorb IR→ ↑T → increases spherical volume→ activates mechanosensitive neuron innervating base



Schmitz & Bleckmann, 1998

Fire beetle IR-detectors as Golay cells



Beetle receptor

Golay Cell

- Golay cells→ opto-acoustic IR detectors
- IR radiation is absorbed by material in a fluid filled chamber
- Fluid expands with heating, causing deflection of a membrane that can be sensed via changes in light deflection

What is the fire detection range?

<

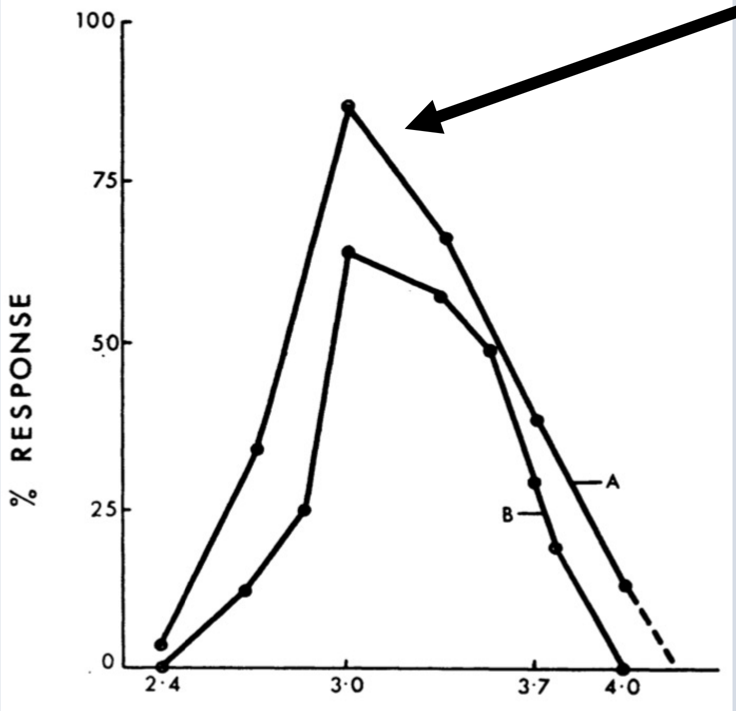
Respond to ΔT <0.01K
Threshold 60-500uW/cm^2

Respond to ΔT 0.003K
Threshold 10-100uW/cm^2

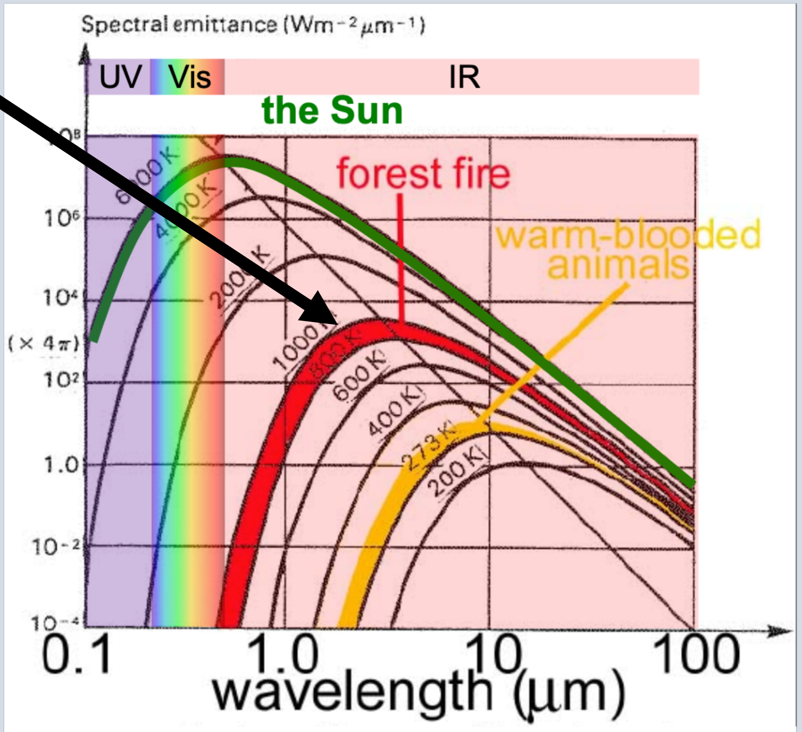
Less sensitive, but longer detection range?

How far could fires be detected?

Peak sensitivity of beetle matches output from burning wood!



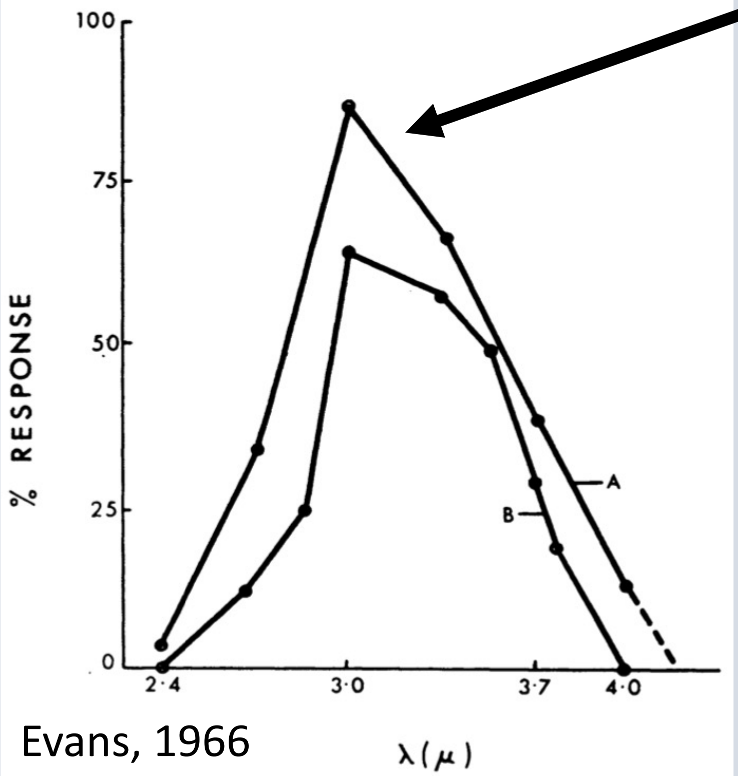
Evans, 1966



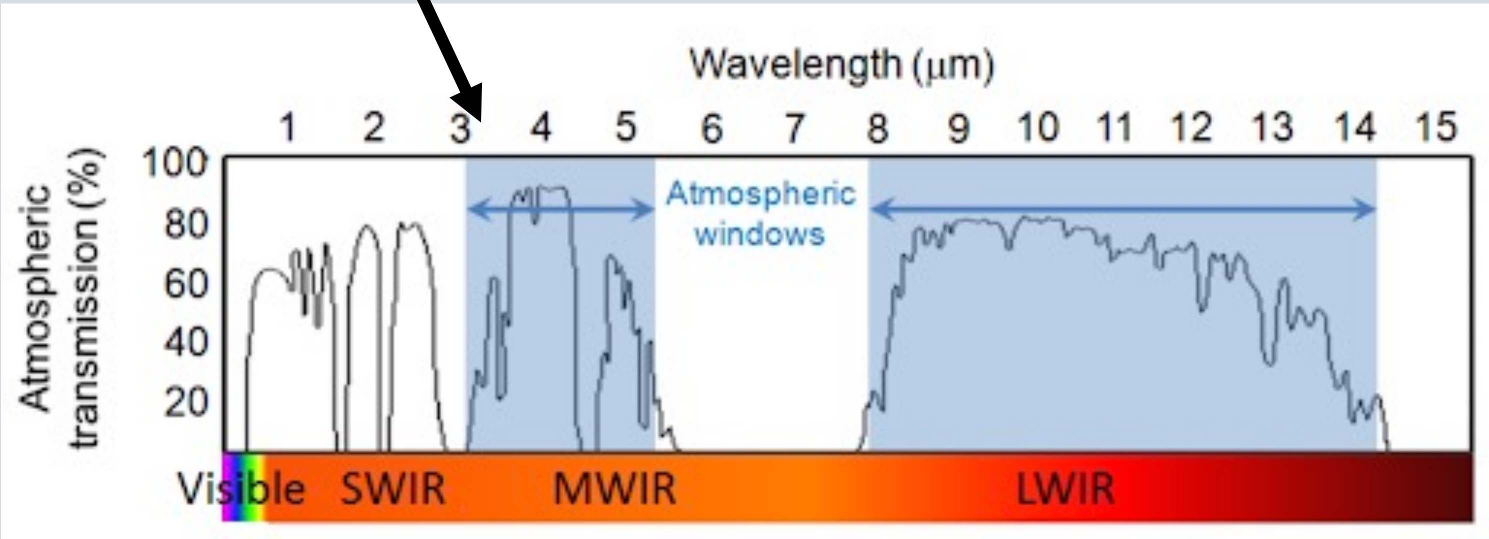
Spectral emittance of black body

How far could fires be detected?

Also corresponds to atmospheric
window for IR transmission!

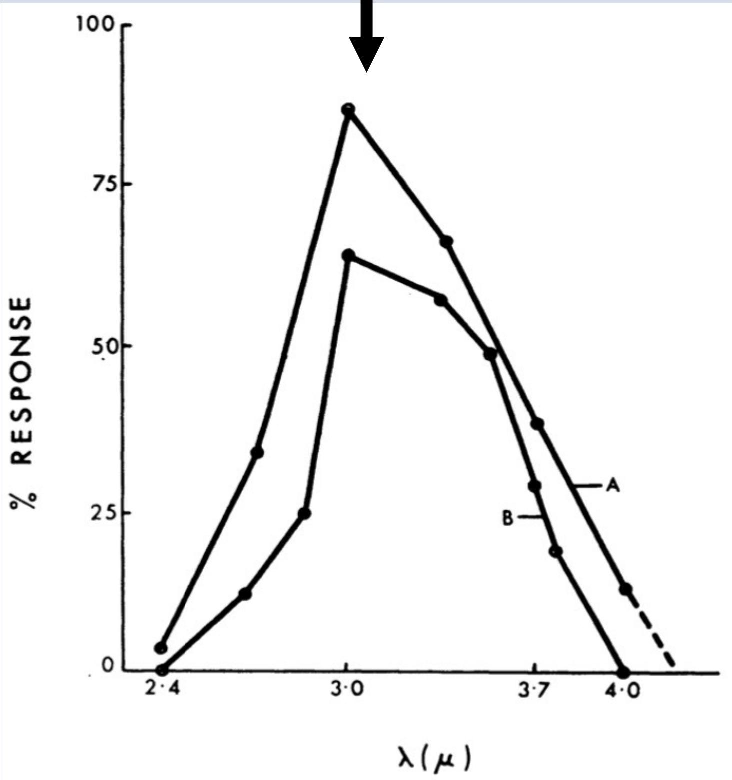


Evans, 1966

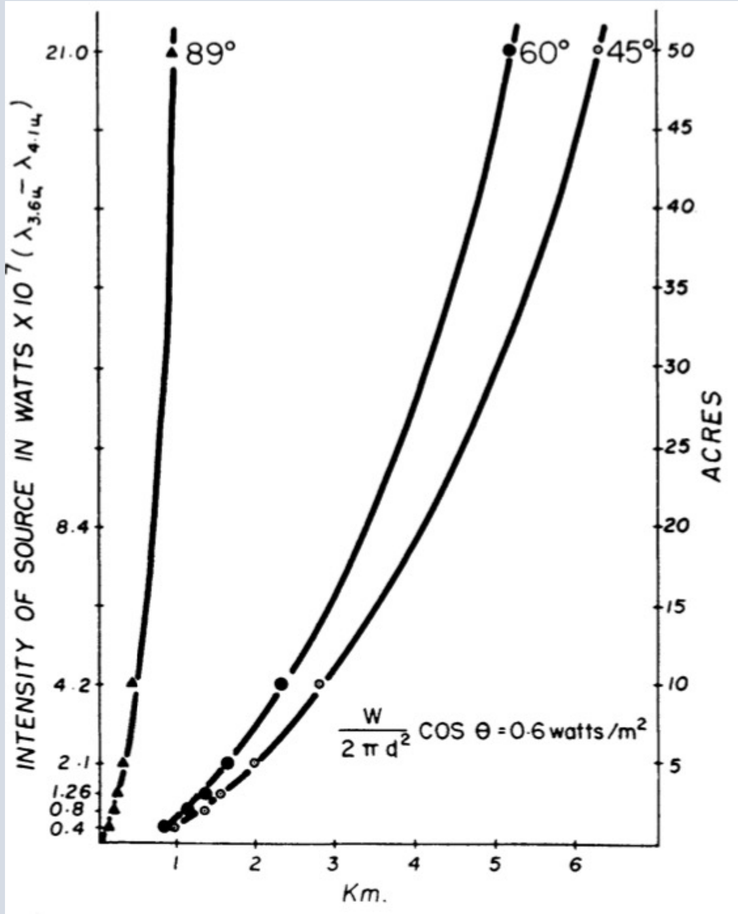


How far could fires be detected?

Peak sensitivity of beetle matches output from burning wood!



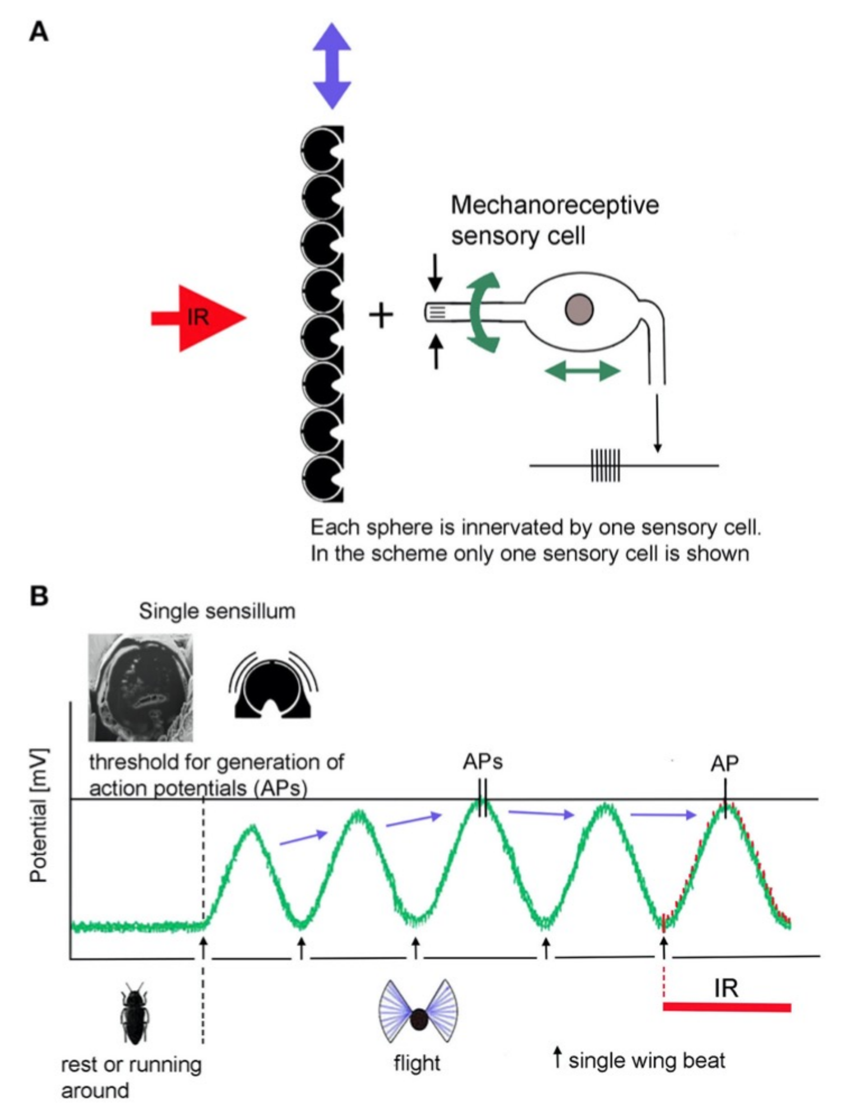
50 acre fire could be detected from kms away, especially from elevated position!



Evans, 1966

Active amplification to increase sensitivity?

- Muscular energy from flight coupled to IR-detectors →lowers threshold for activation
- Comparing responses between sides could uncover additional signals from noise



Schneider et al. 2015

Thermosensation: more than just thermometers

- Life has evolved diverse mechanisms for detecting thermal cues
- Thermometers, derivative sensors, bolometers, Golay cells, others??
- Specialized behaviors can be driven by conserved molecular transducers are paired with new circuits and/or anatomical structures
- Animals exhibit a range of sensitivities and detection ranges to suit particular life histories

km	Fire Beetles:	ΔT ~0.01°C
	Pit vipers:	ΔT ~0.003°C
ft	Pythons:	ΔT ~0.03°C
	Vampire Bats:	ΔT ~0.03°C
	Flies/mosquitoes:	ΔT ≤0.005°C
cm	Humans:	ΔT <0.06°C

IR sensitive

Outstanding questions in thermosensation

- What molecular transducers underlie thermosensation?
- What is the biophysical basis for ion channel thermosensitivity?
- How does anatomy influence thermosensation?
- What is the relative contribution of direct versus indirect mechanisms?
- How is thermosensory information integrated with other sensory modalities?

Understanding temperature detection mechanisms will require a combo of materials science, structural biology, molecular simulations, biophysics, biochemistry, zoology, behavioral genetics, neuroscience and everyone else!

Garrity lab

Paul Garrity

Elaine Chang

Rachel Gerber

Gonzalo Budelli

Chloe Greppi

Rebecca Albuquerque

Abby Daniels

Ruocong Tang

Christina Mazzio

Tatevik Sarkissian

Rachel Busby

Crystal Zhu

QB program

Jeff Gelles, Jane Kondev

Laura St. Clair

Charles A. King Foundation

hhmi

Brandeis University