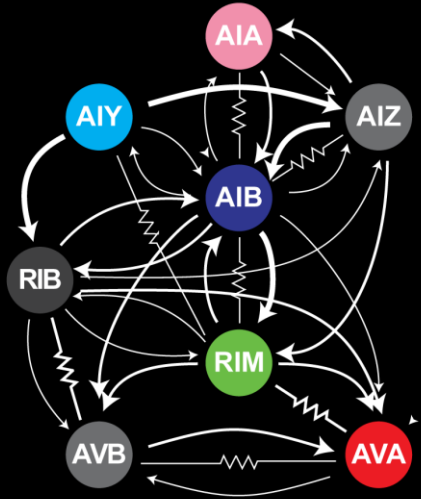


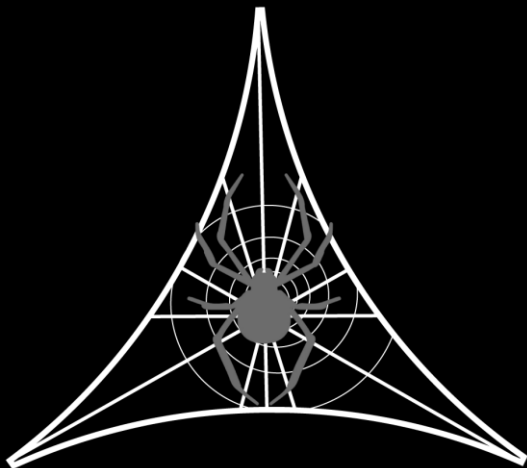
Foraging and the roles of neuromodulators



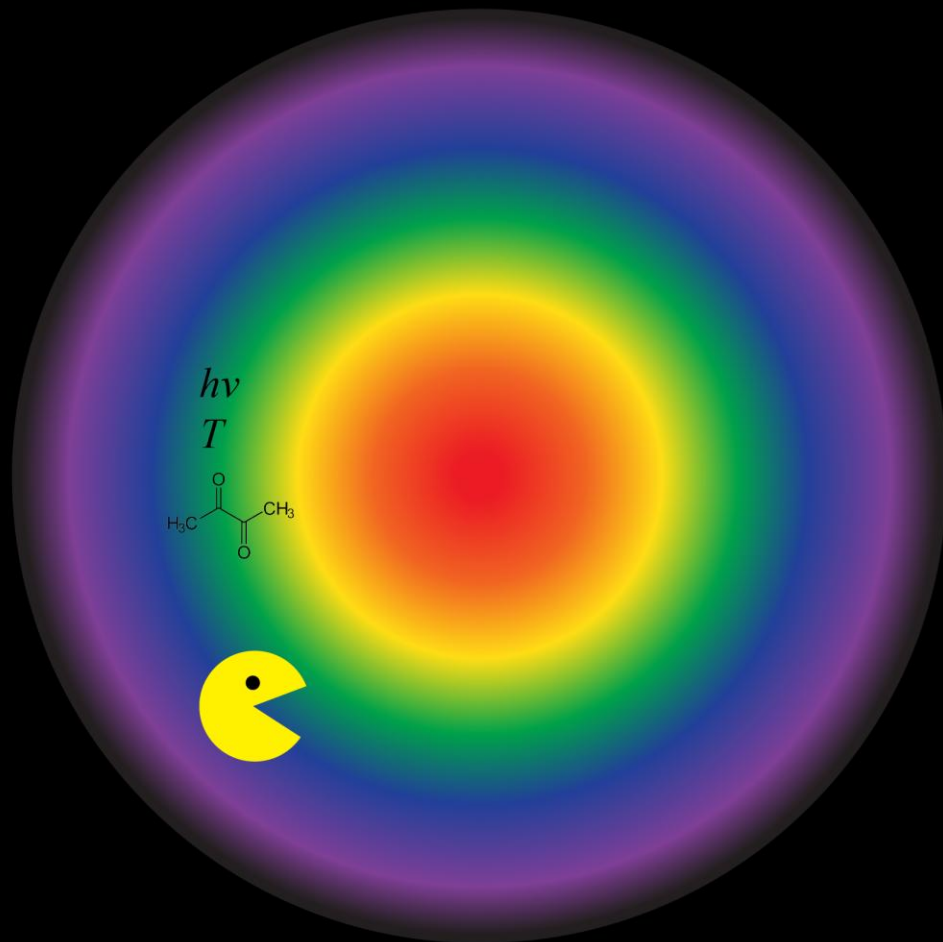
Andrew Gordus

KITP SNAV18

08.16.2018



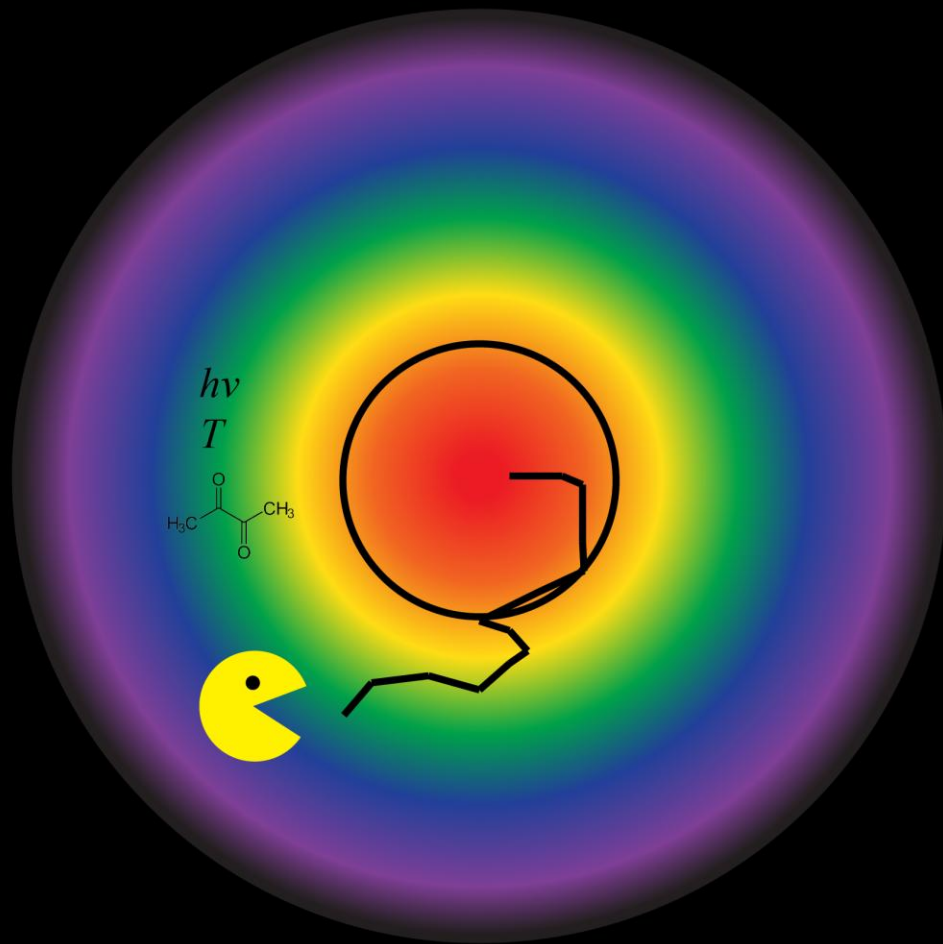
JOHNS HOPKINS
UNIVERSITY

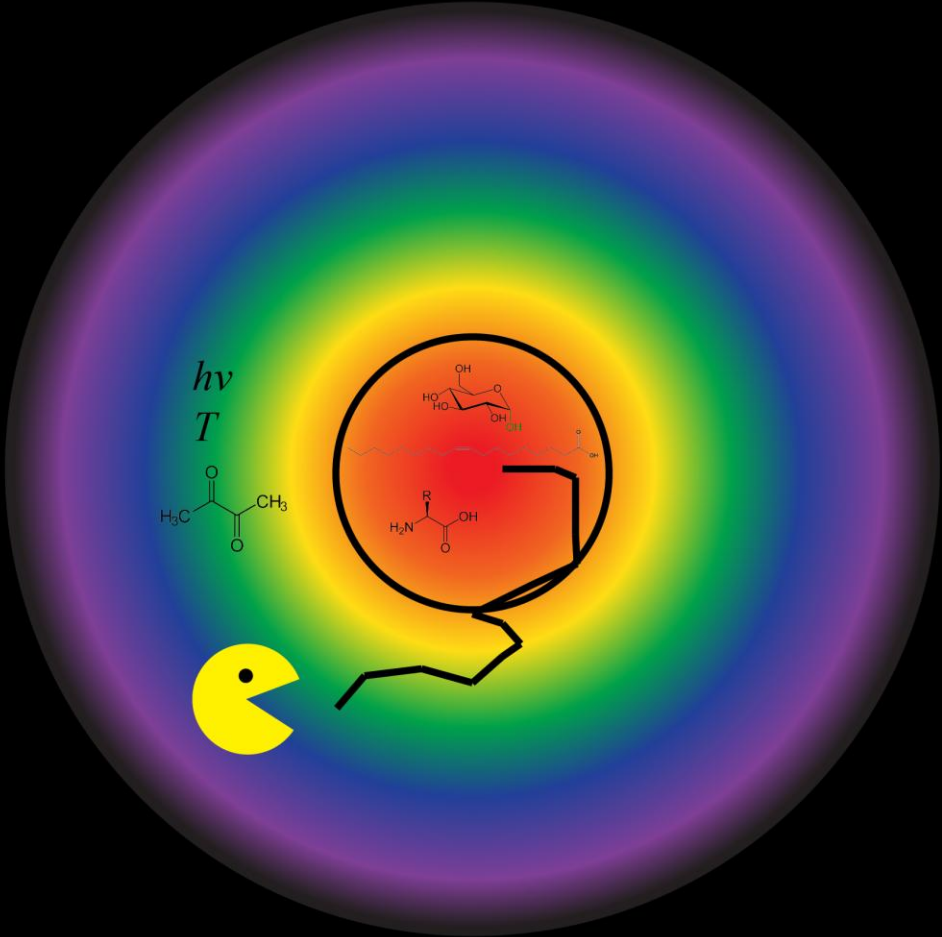


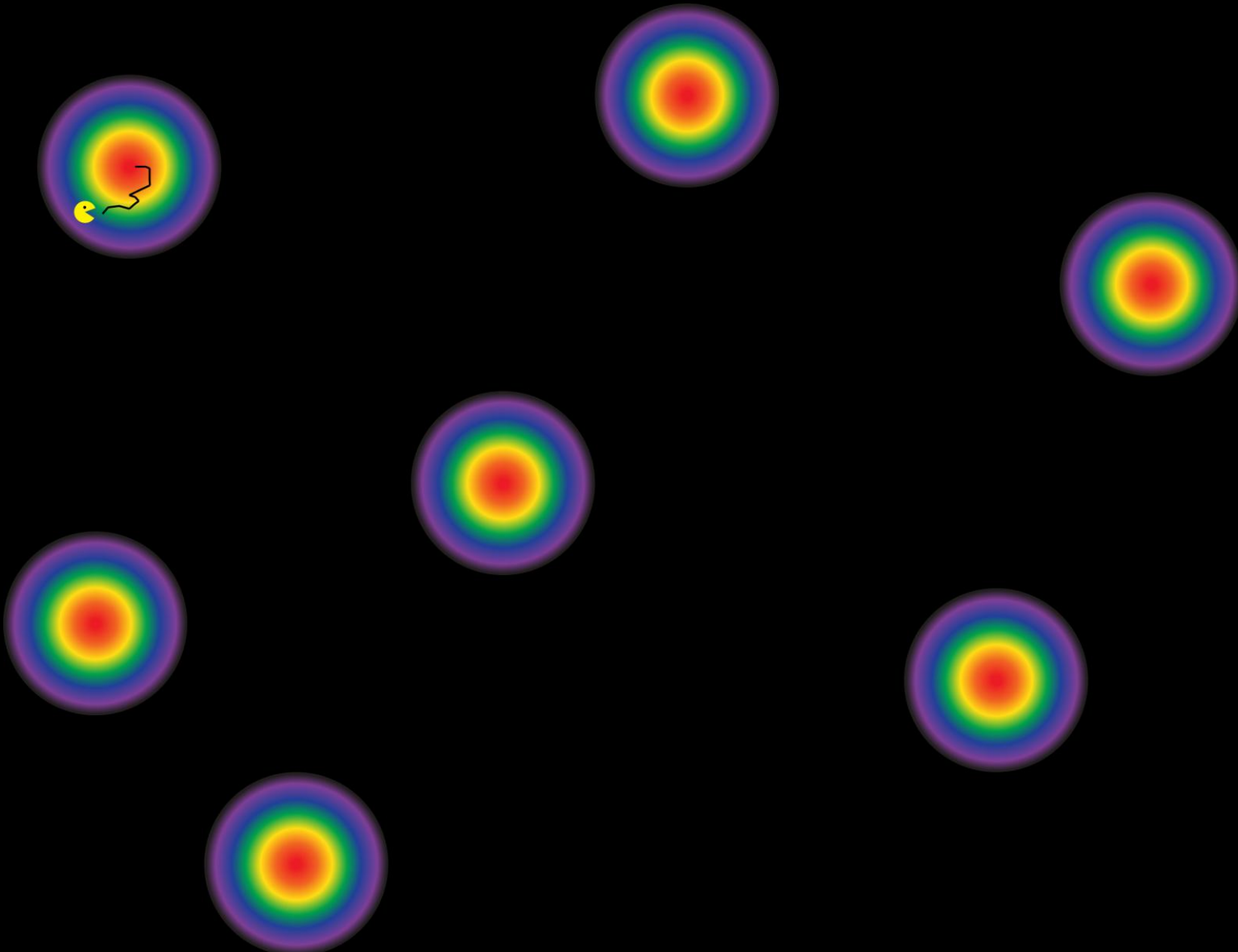
$h\nu$

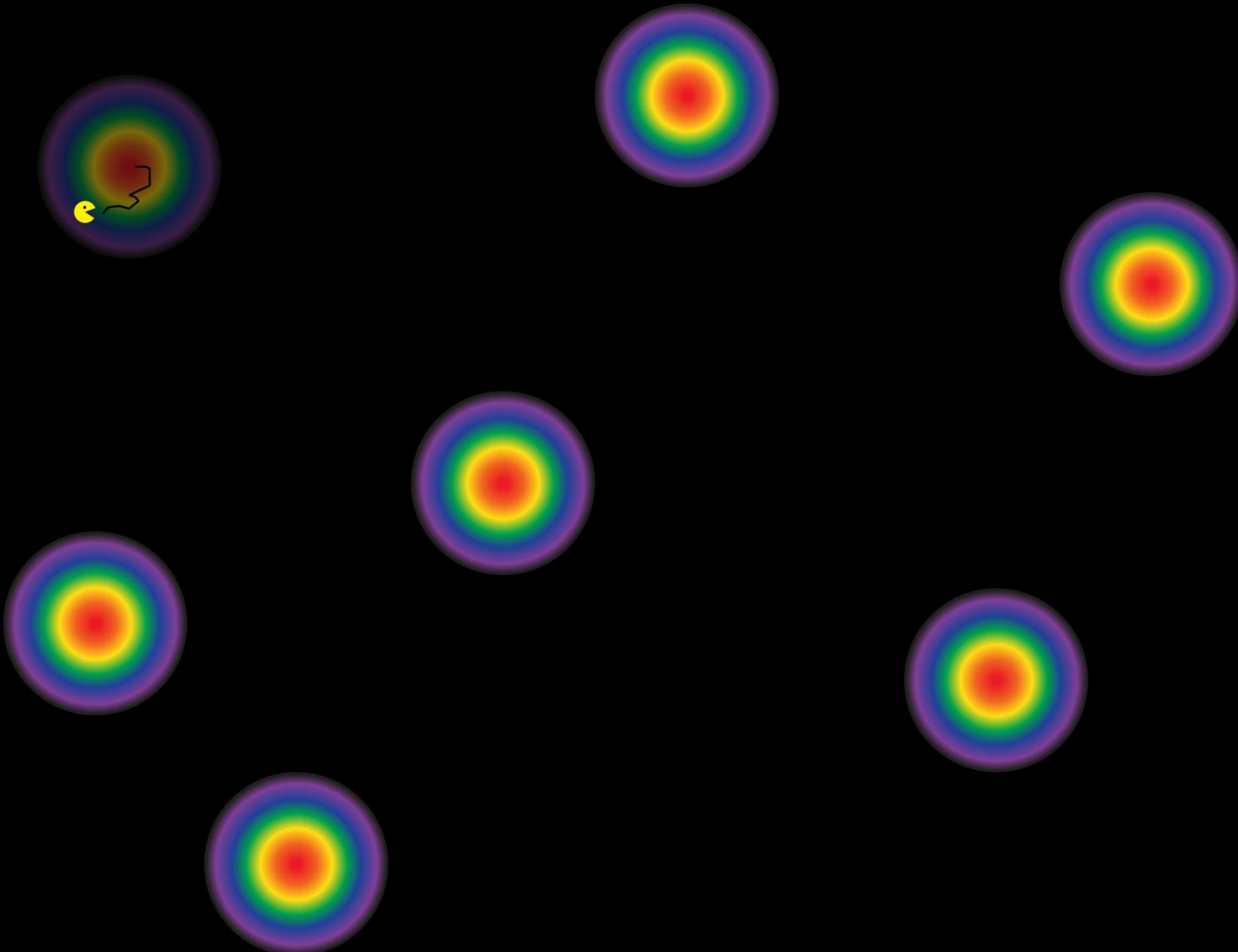
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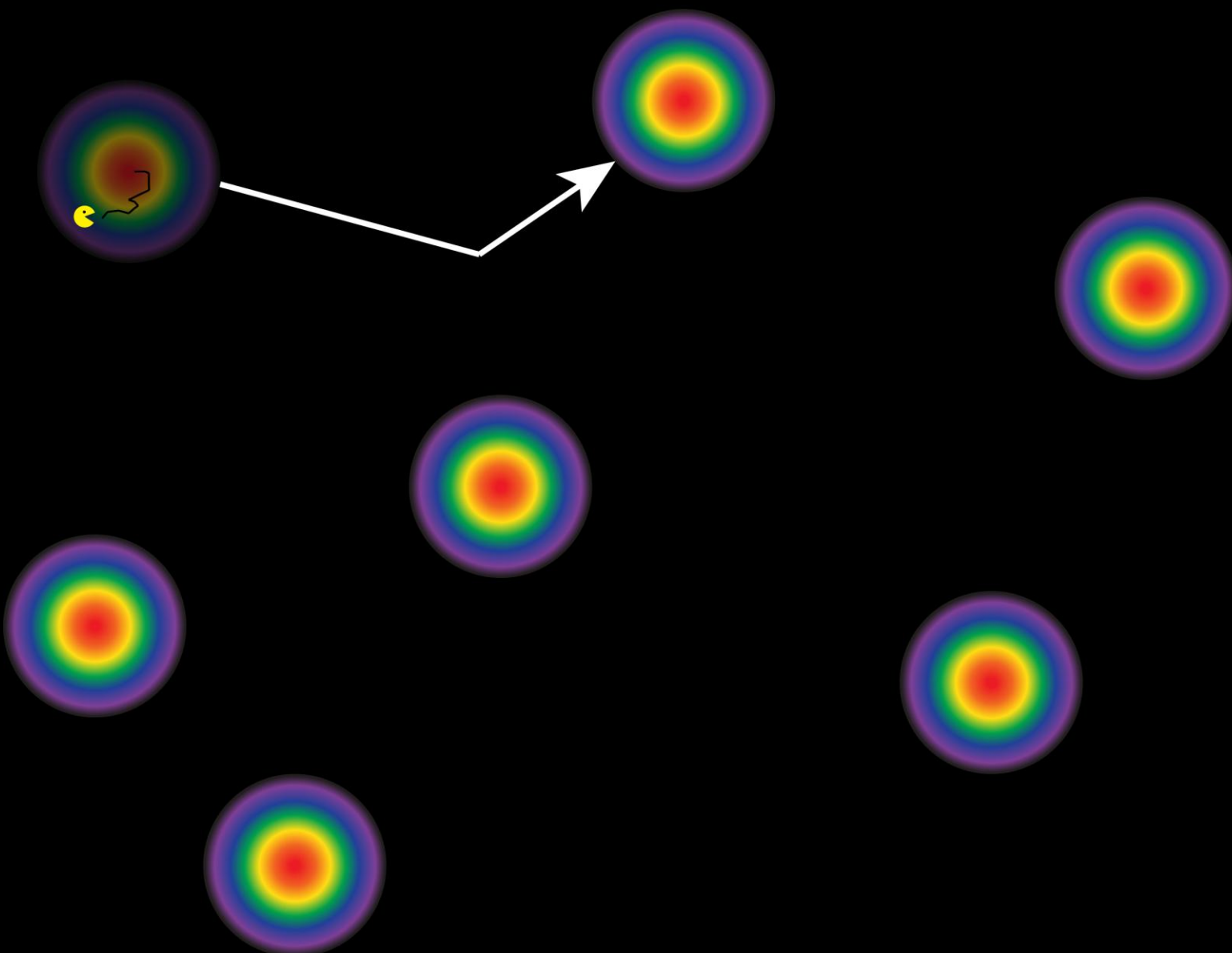


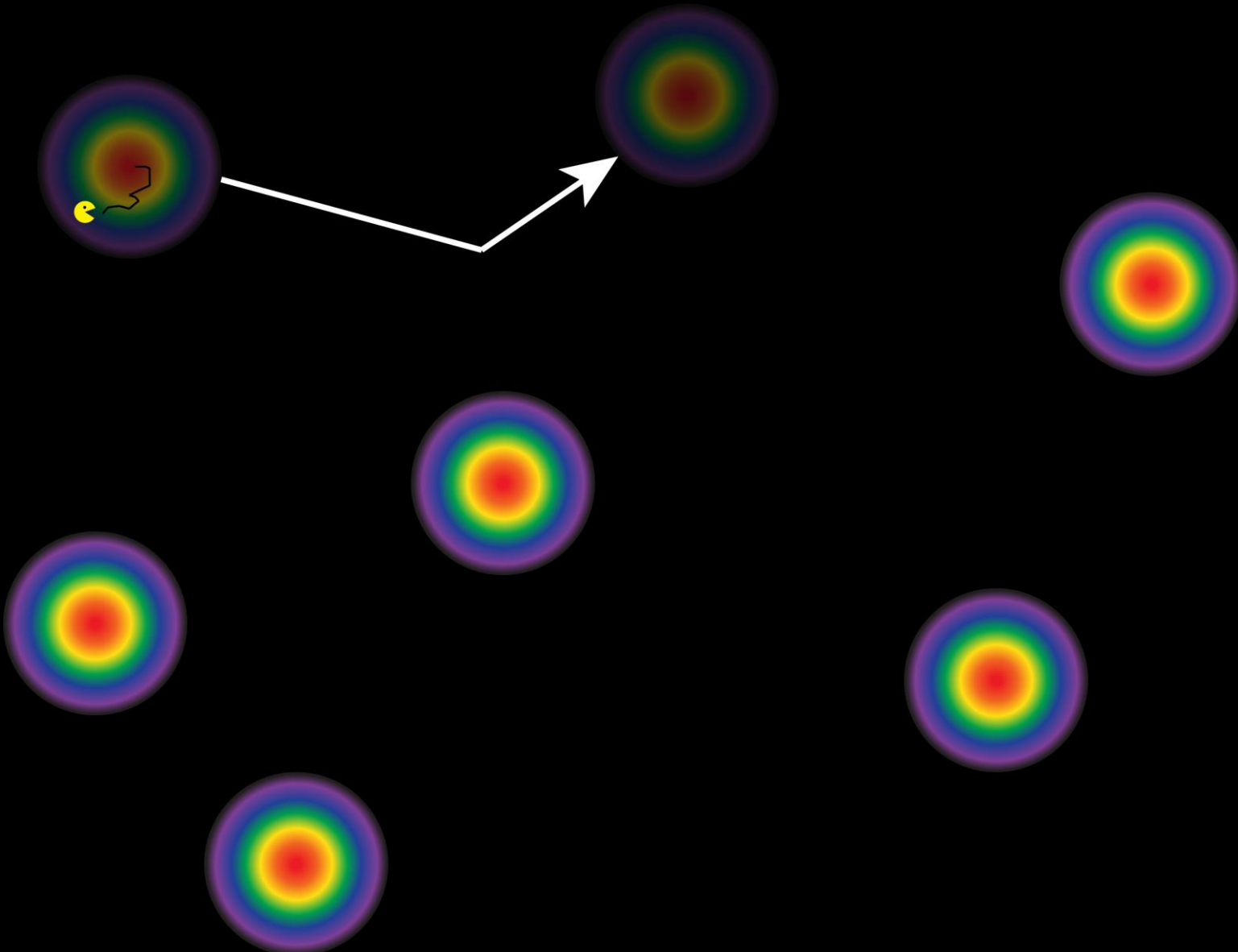


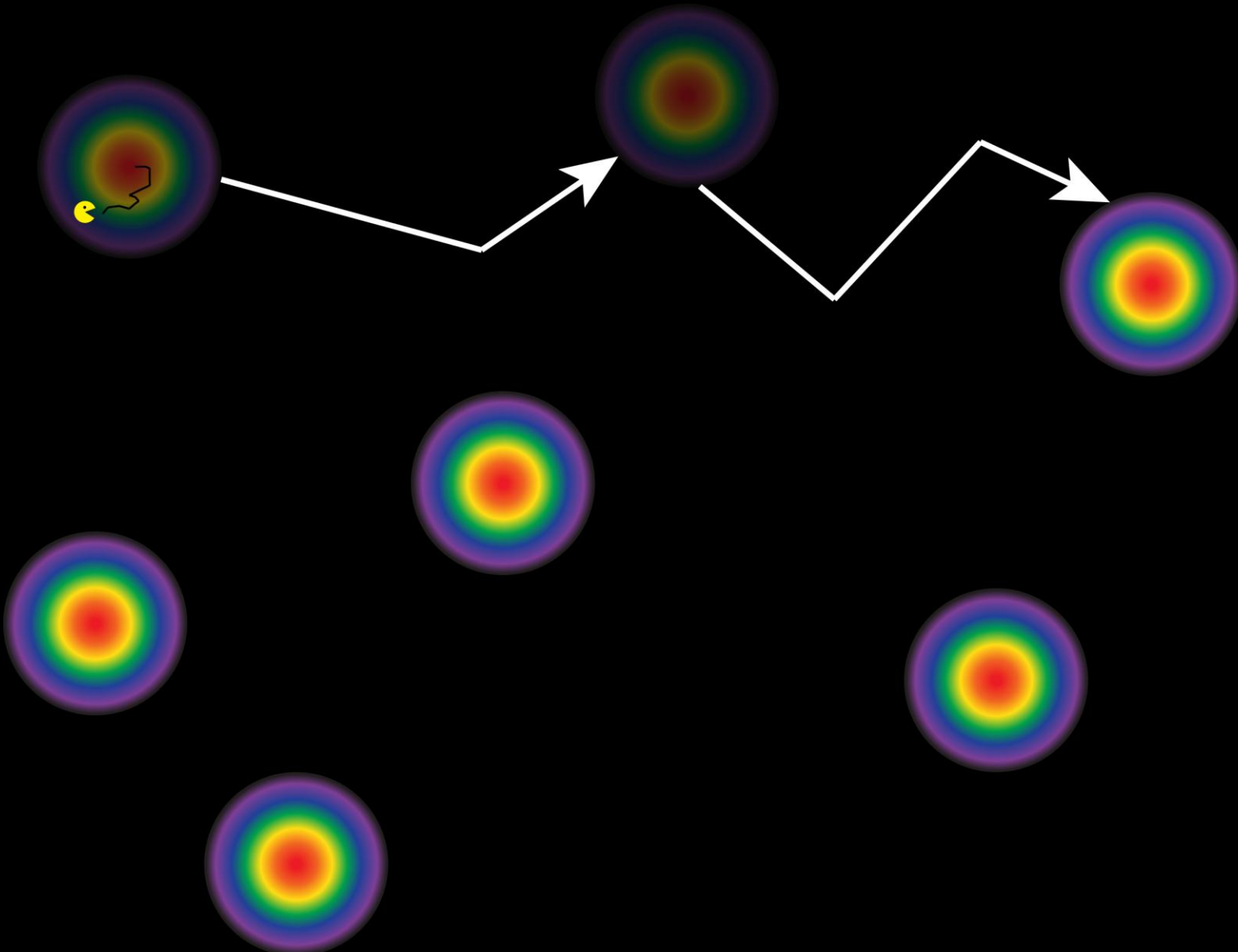












Questions

- What is an optimum foraging strategy?
- How is this strategy encoded?
- How is this strategy implemented?

Marginal Value Theorem

THEORETICAL POPULATION BIOLOGY 9, 129-136 (1976)

Optimal Foraging, the Marginal Value Theorem

ERIC L. CHARNOV*

*Center for Quan. Science in Forestry, Fisheries, and Wildlife,
University of Washington, Seattle, Washington 98195; and
Institute of Animal Resource Ecology UBC, Vancouver 8, Canada*

Received December 26, 1974

Marginal Value Theorem

THEORETICAL POPULATION BIOLOGY 9, 129–136 (1976)

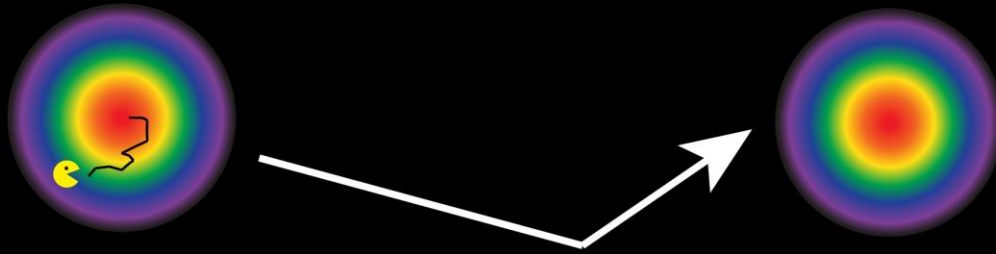
Optimal Foraging, the Marginal Value Theorem

ERIC L. CHARNOV*

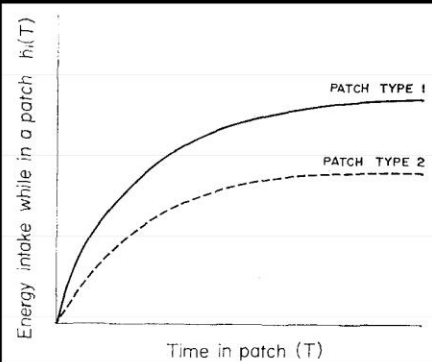
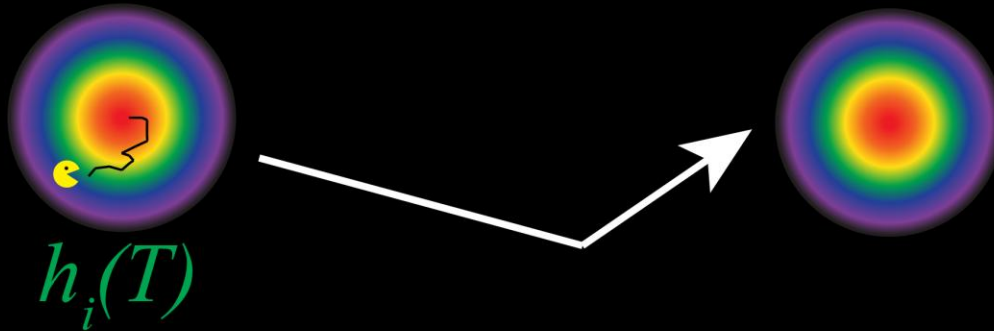
*Center for Quan. Science in Forestry, Fisheries, and Wildlife,
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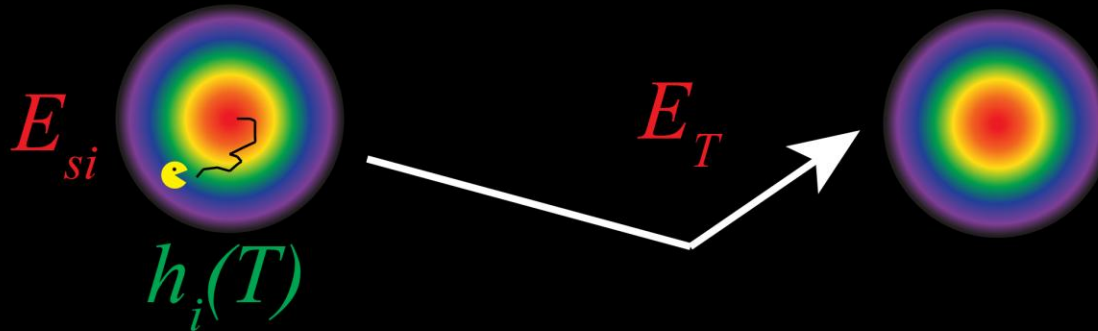
Marginal Value Theorem



Marginal Value Theorem



Marginal Value Theorem

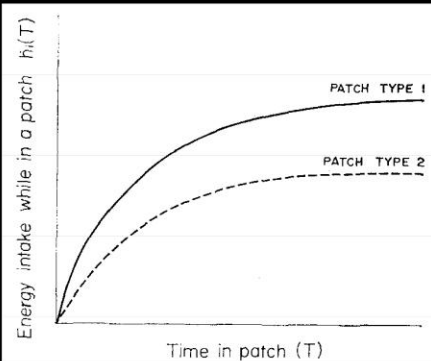


P_i = proportion of the visited patches that are of type i ($i = 1, 2, \dots, k$).
 E_T = energy cost per unit time in traveling between patches.
 E_{si} = energy cost per unit time while searching in a patch of type i .
 $h_i(T)$ = assimilated energy from hunting for T time units in a patch of type i minus all energy costs except the cost of searching.
 $g_i(T) = h_i(T) - E_{si} \cdot T$ = assimilated energy corrected for the cost of searching.

$$T_u = t + \sum P_i \cdot T_i.$$

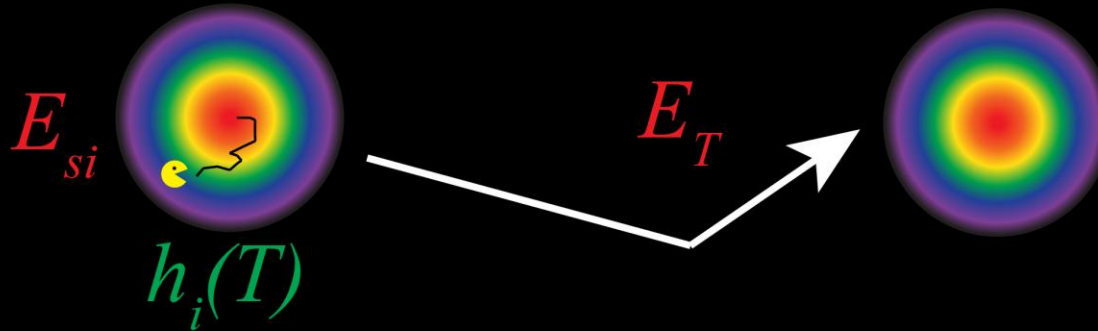
$$E_e = \sum P_i \cdot g_i(T_i).$$

$$E_n = \frac{E_e - t \cdot E_T}{T_u}.$$



$$E_n = \frac{E_e - t E_T}{T_u}$$

Marginal Value Theorem

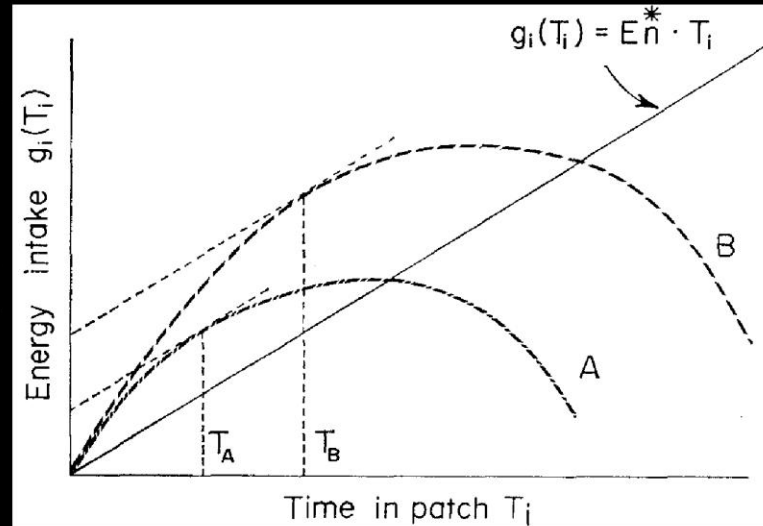
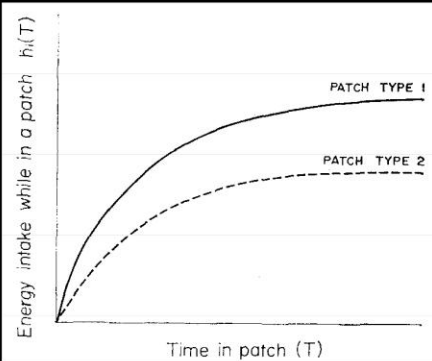


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$$T_u = t + \sum P_i \cdot T_i.$$

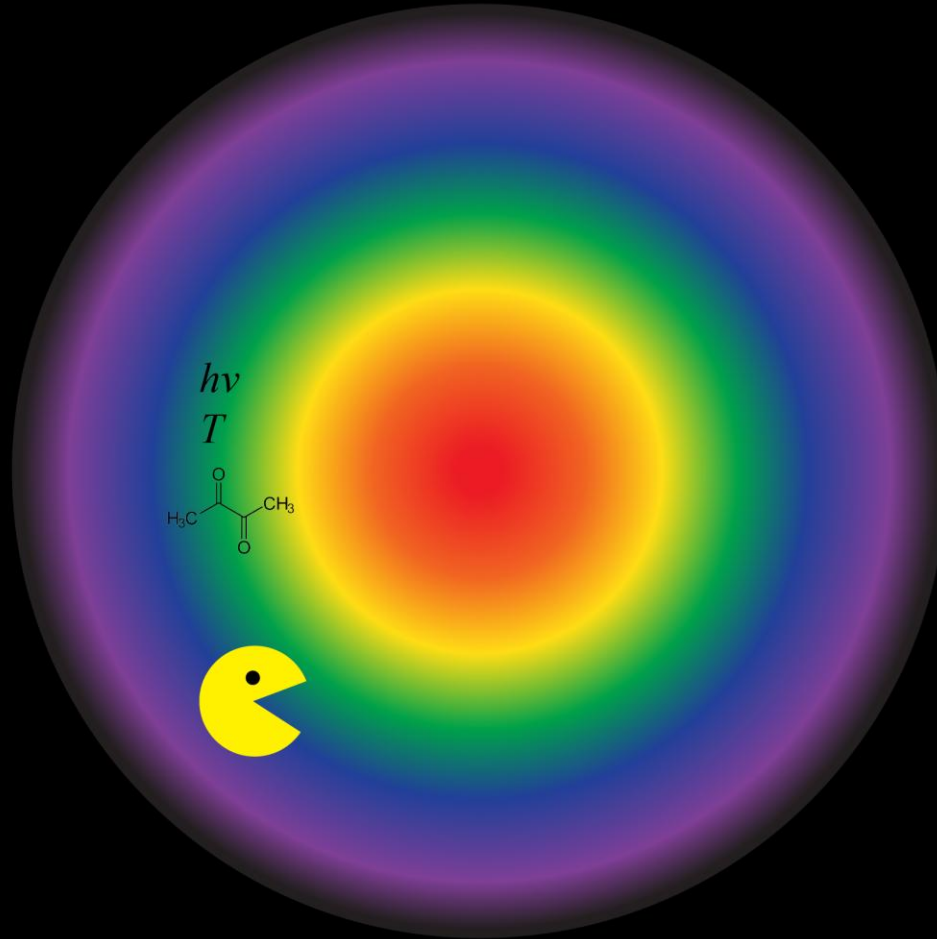
$$E_e = \sum P_i \cdot g_i(T_i).$$

$$E_n = \frac{E_e - t \cdot E_T}{T_u}.$$

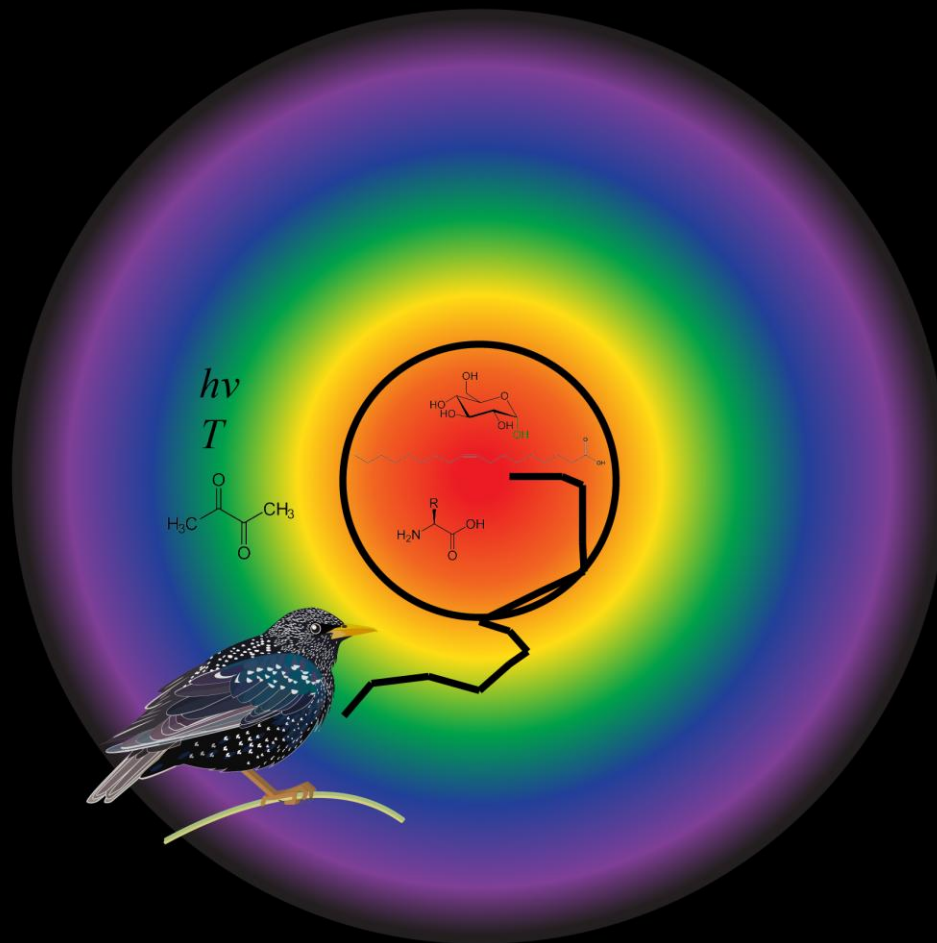


$$E_n = \frac{E_e - t E_T}{T_u}$$

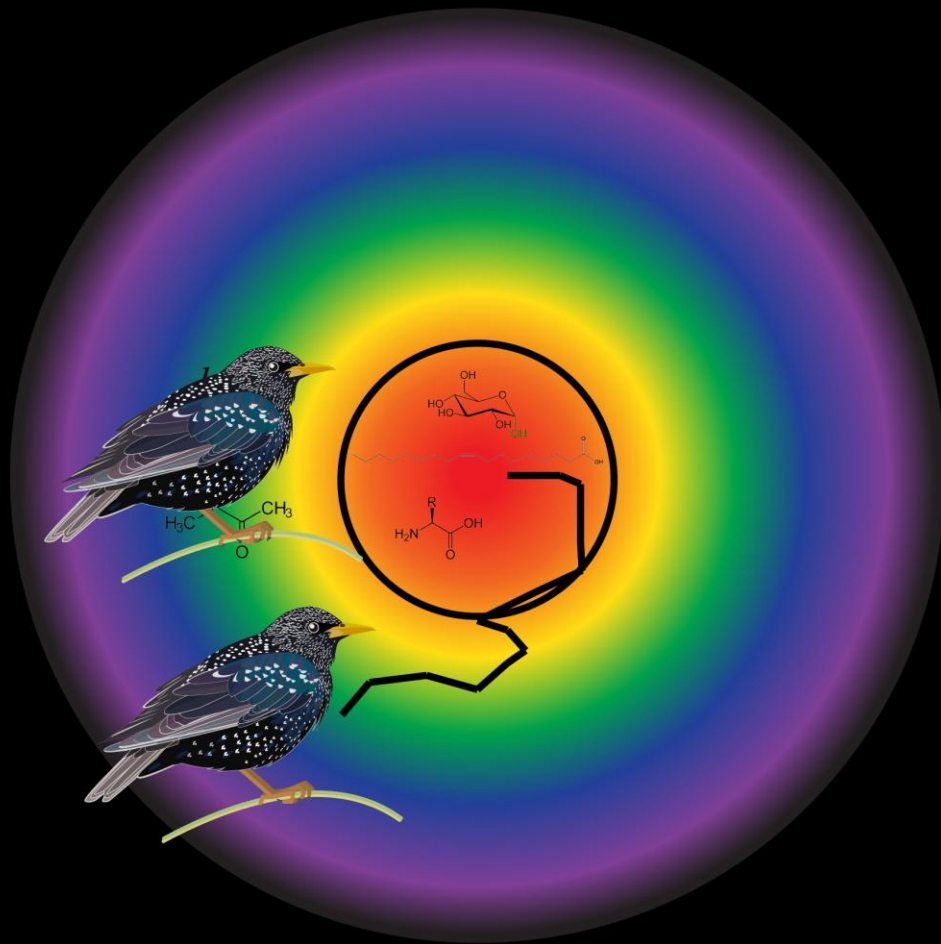
Marginal Value Theorem



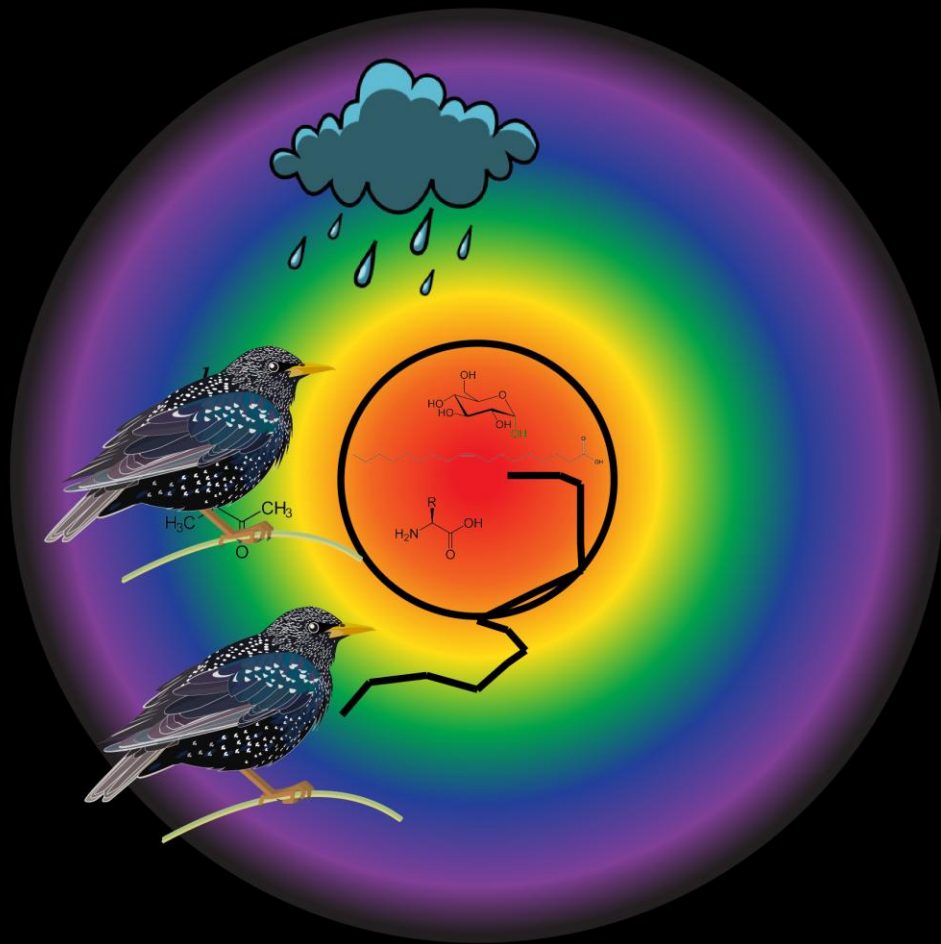
Marginal Value Theorem



Marginal Value Theorem



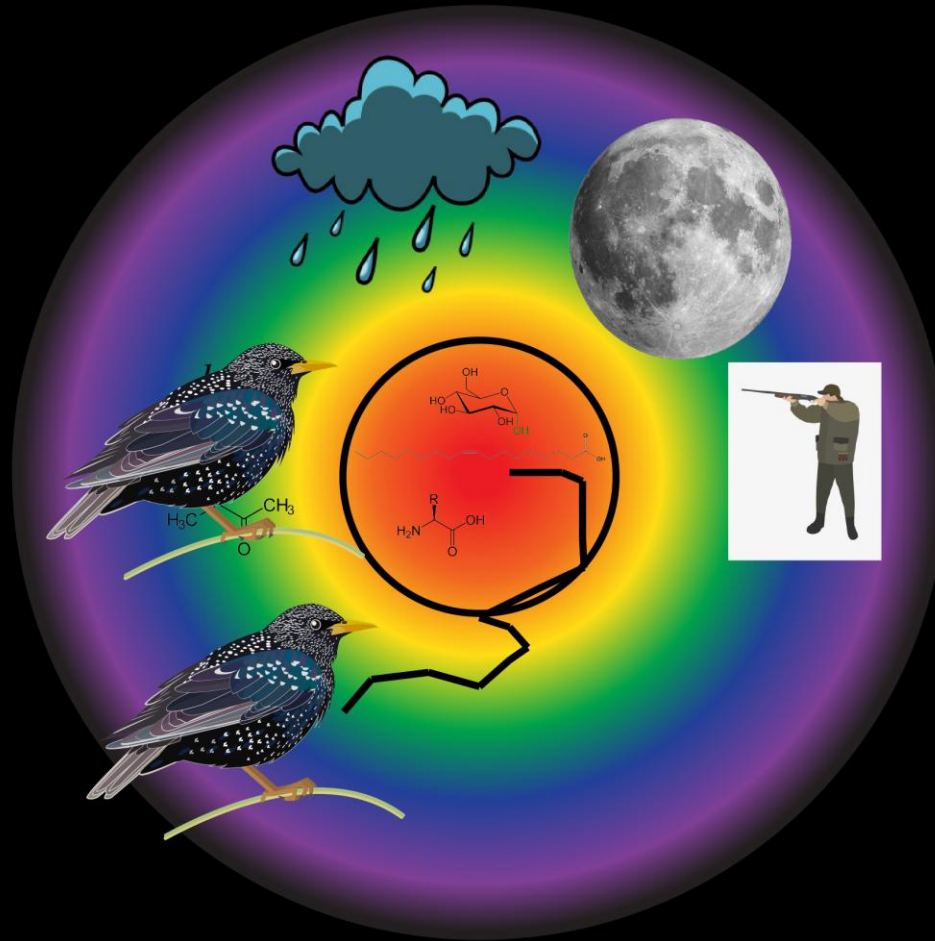
Marginal Value Theorem



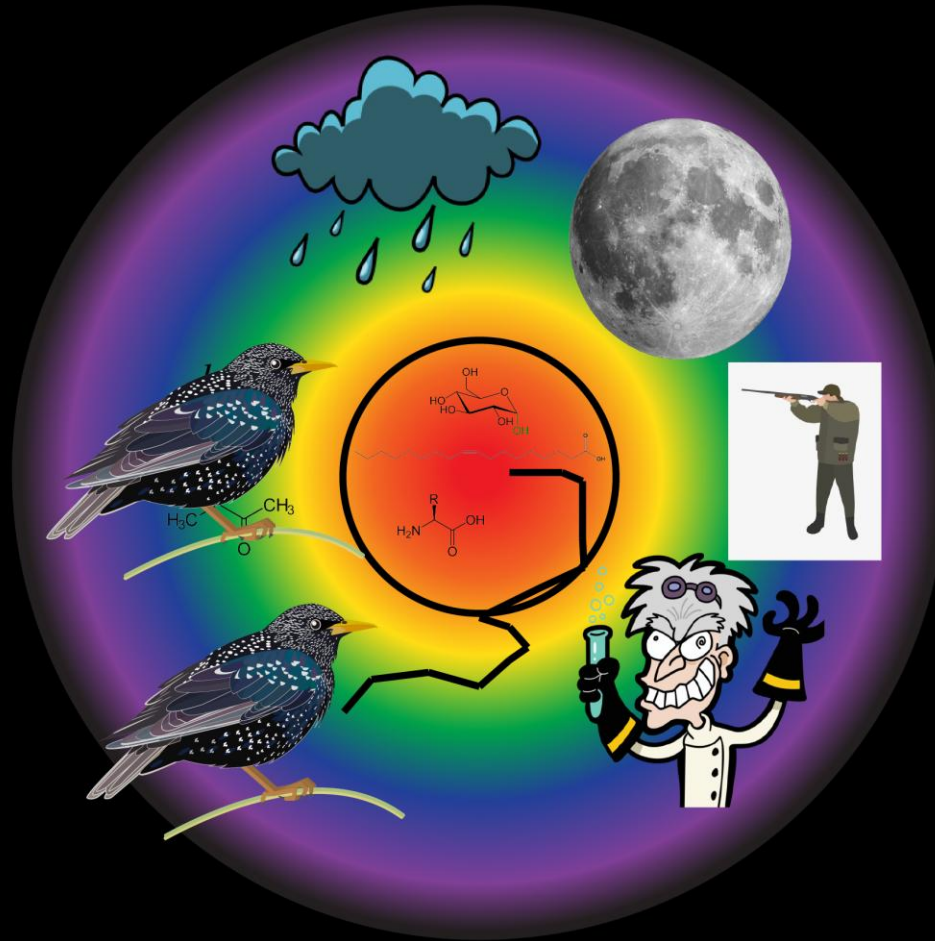
Marginal Value Theorem

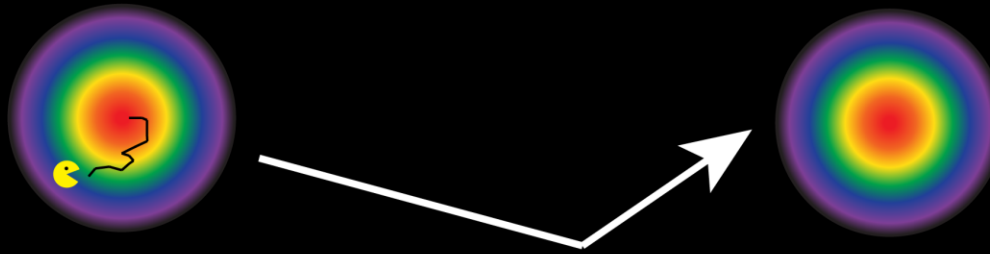


Marginal Value Theorem



Marginal Value Theorem





Foraging Strategies of *Drosophila melanogaster*: A Chromosomal Analysis

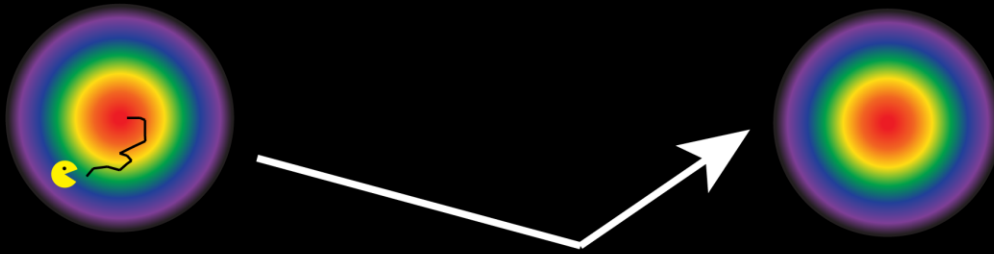
Marla B. Sokolowski¹

Behavior Genetics, Vol. 10, No. 3, 1980

Natural Behavior Polymorphism Due to a cGMP-Dependent Protein Kinase of *Drosophila*

K. A. Osborne, A. Robichon, E. Burgess, S. Butland,*
R. A. Shaw, A. Coulthard, H. S. Pereira[†], R. J. Greenspan,[‡]
M. B. Sokolowski[§]

SCIENCE • VOL. 277 • 8 AUGUST 1997



Foraging Strategies of *Drosophila melanogaster*: A Chromosomal Analysis

Marla B. Sokolowski¹

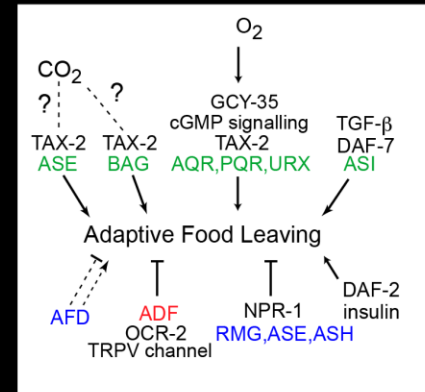
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Natural Behavior Polymorphism Due to a cGMP-Dependent Protein Kinase of *Drosophila*

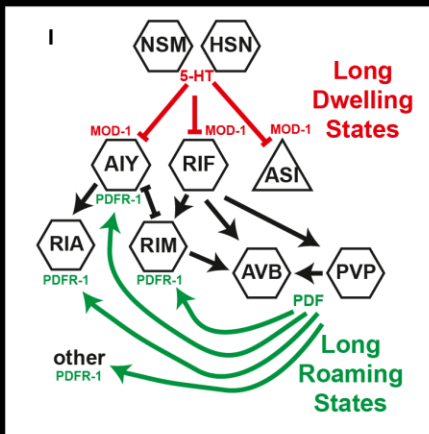
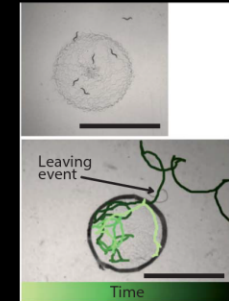
K. A. Osborne, A. Robichon, E. Burgess, S. Butland,*
R. A. Shaw, A. Coulthard, H. S. Pereira†, R. J. Greenspan,‡

M. B. Sokolowski§

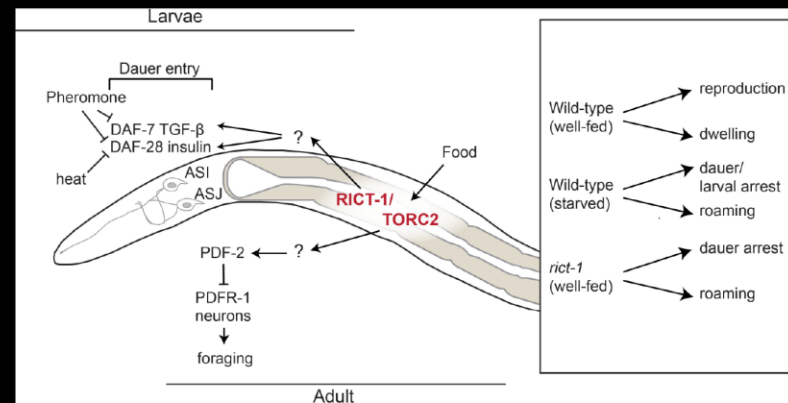
SCIENCE • VOL. 277 • 8 AUGUST 1997



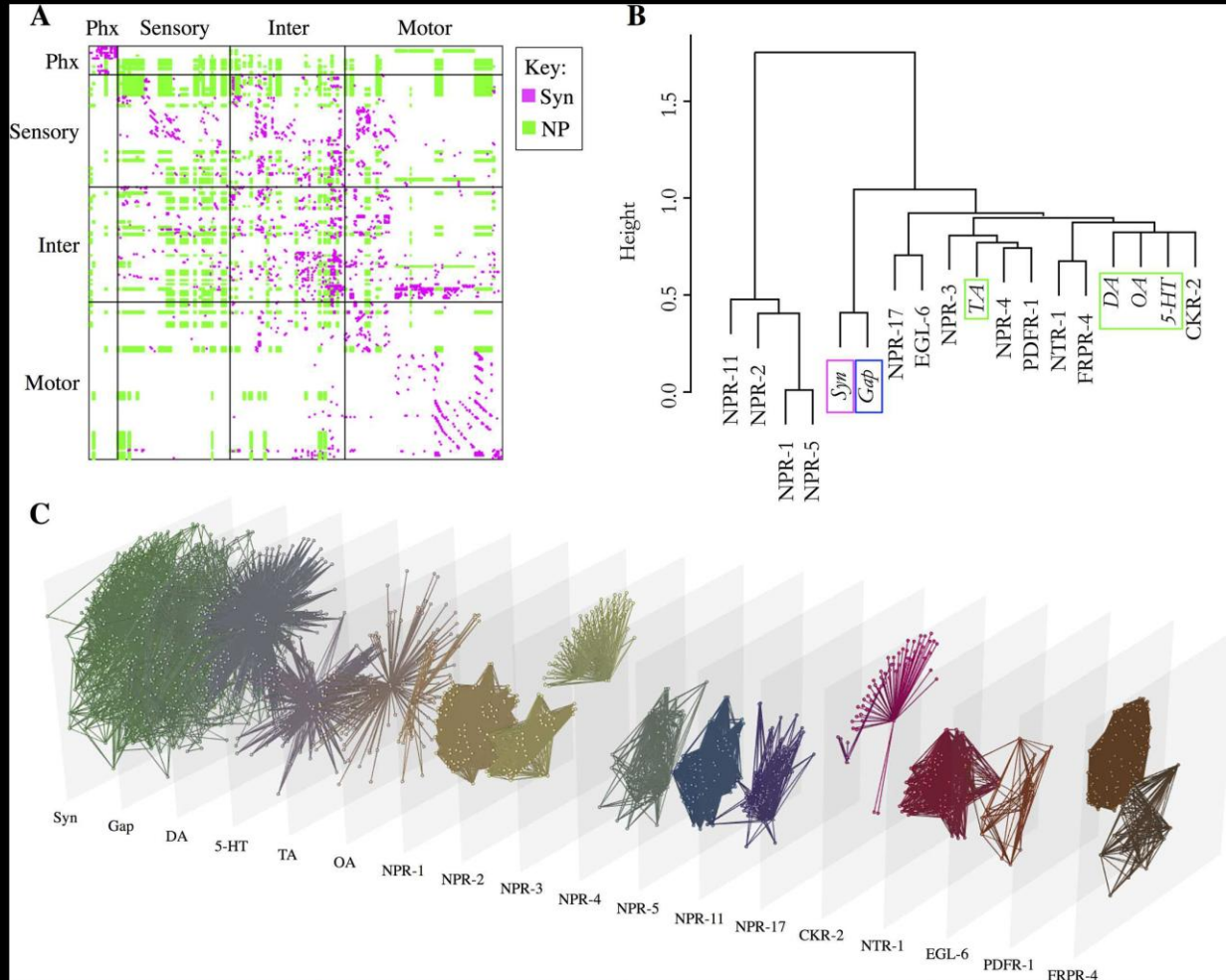
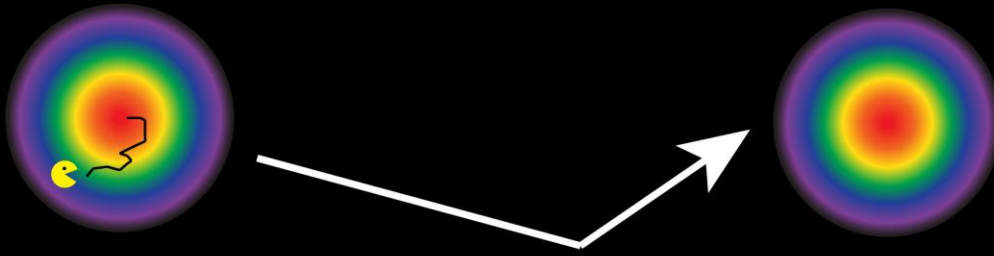
Milward et. al., PNAS, 2011



Flavell et. al., Cell, 2013



O'Donnell et. al., PLOS Gen., 2018



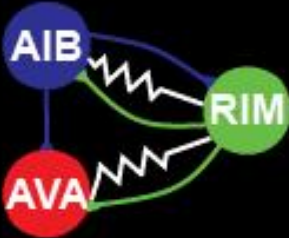
Questions

- What is an optimum foraging strategy?
- How is this strategy encoded?
 - Neuromodulators acting extra-synaptically
- How is this strategy implemented?

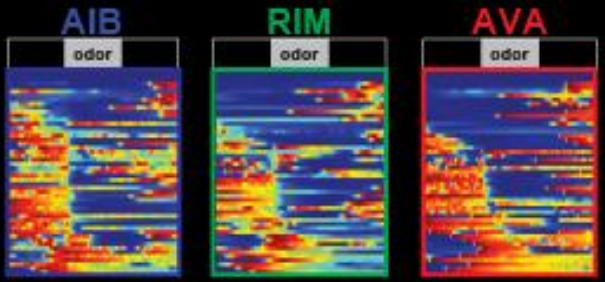
Environmental Input



Neuronal Circuit State



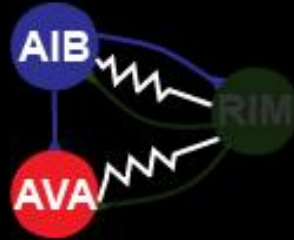
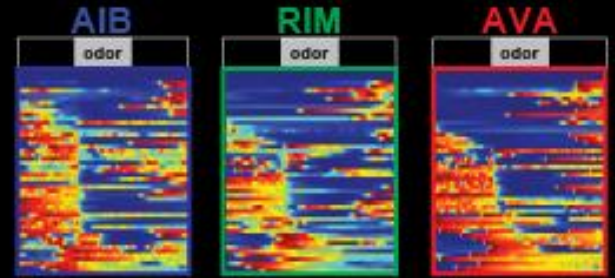
Circuit Output Probabilistic



Environmental Input

Neuronal Circuit State

Circuit Output Probabilistic



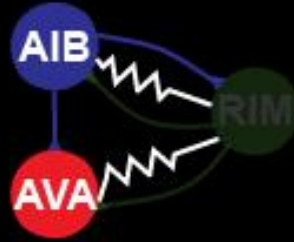
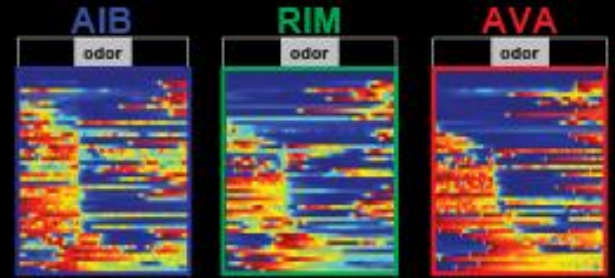
Reliable



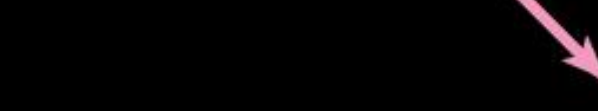
Environmental Input

Neuronal Circuit State

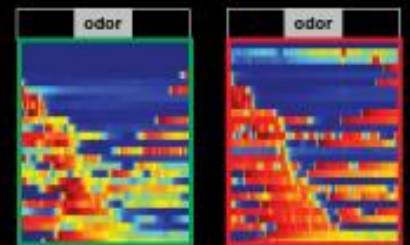
Circuit Output Probabilistic



Reliable



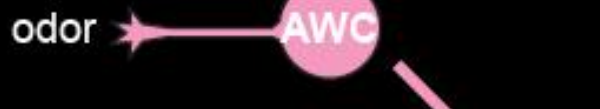
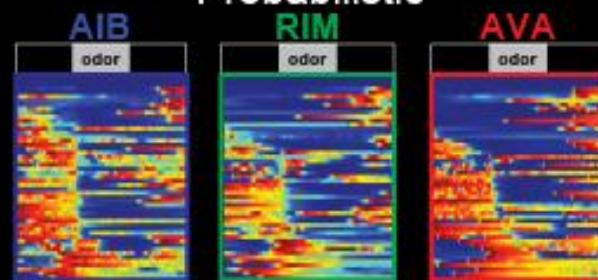
Probabilistic



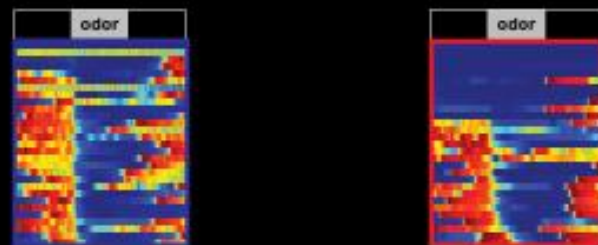
Environmental Input

Neuronal Circuit State

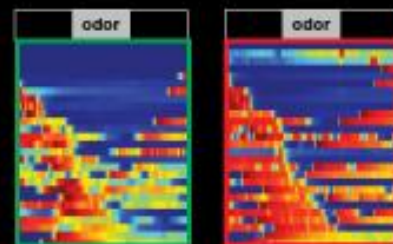
Circuit Output Probabilistic



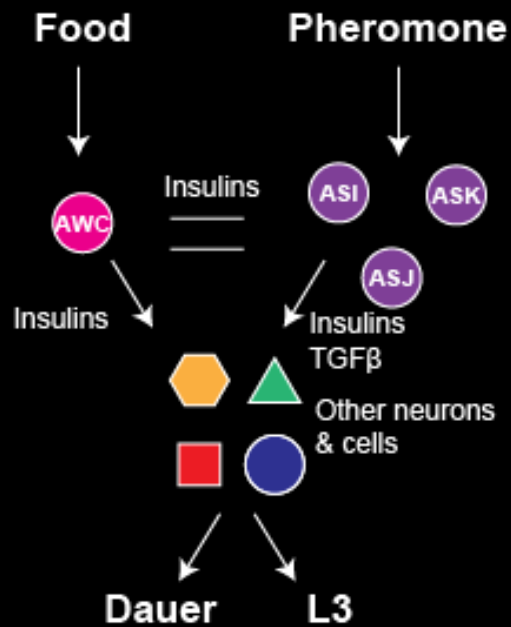
Reliable



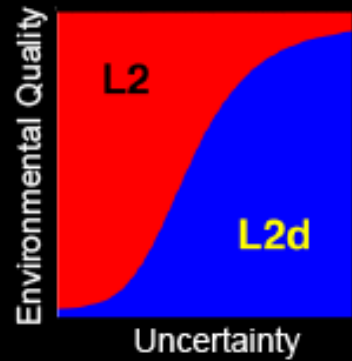
Probabilistic



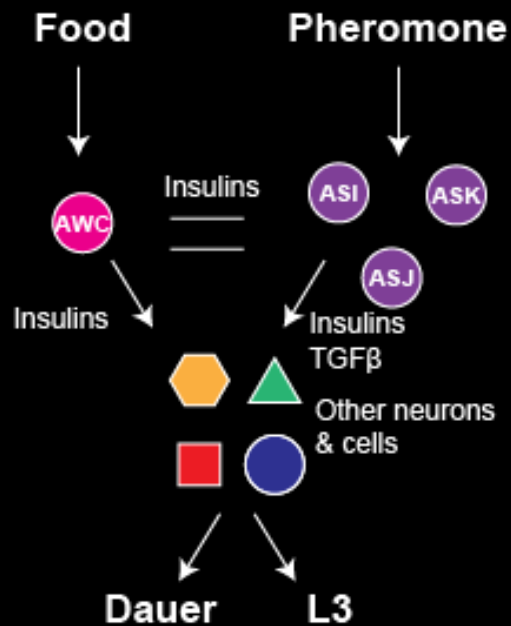
Confidence in Dauer Decision



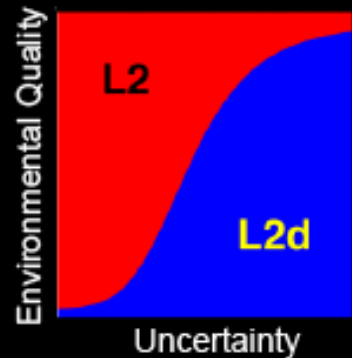
Confidence in Dauer Decision



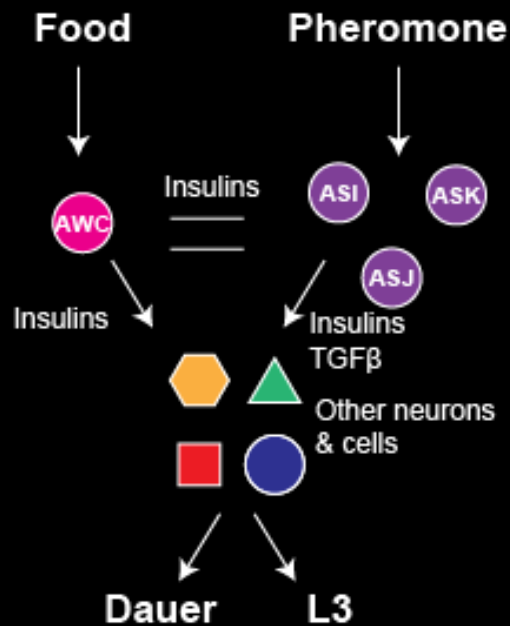
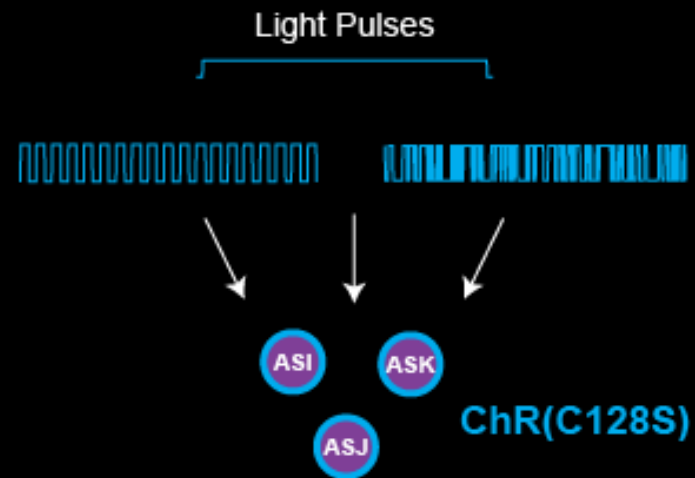
L. Avery, *PLOS One*, (2014)



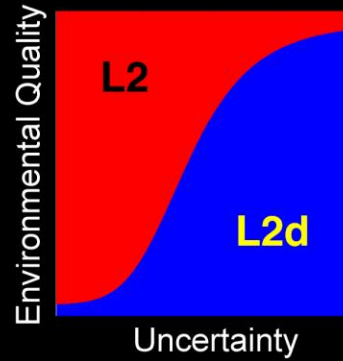
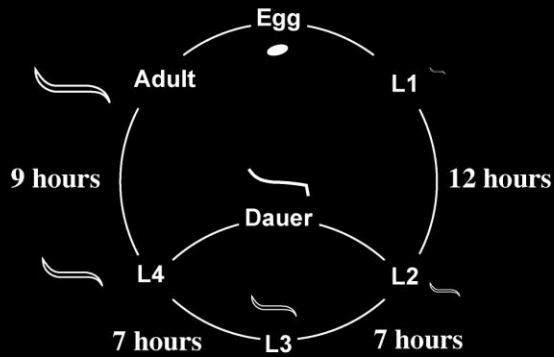
Confidence in Dauer Decision



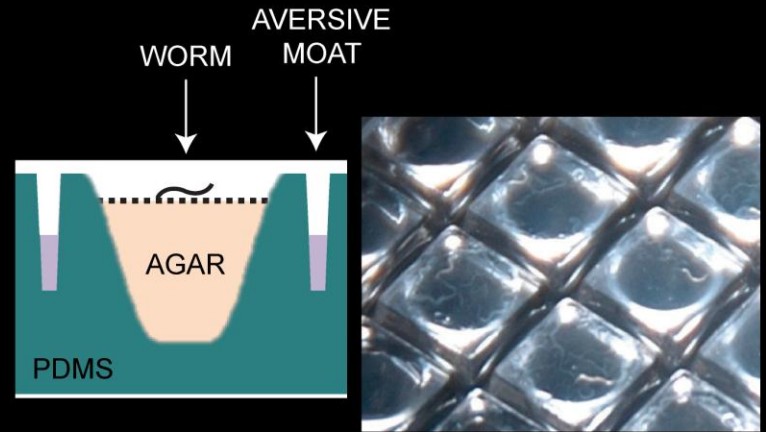
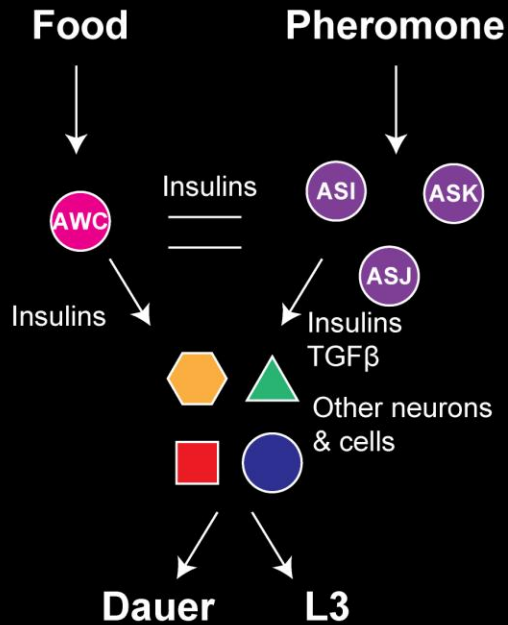
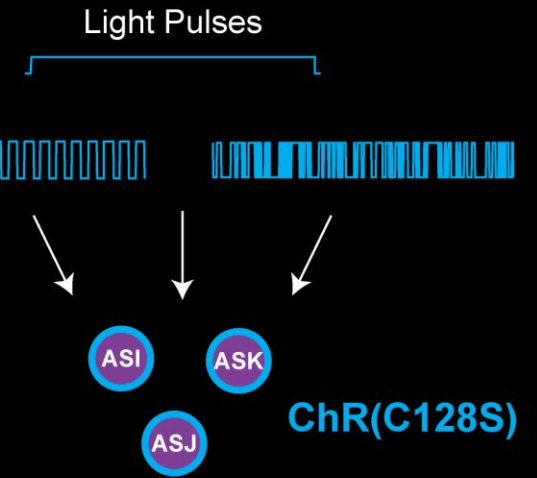
L. Avery, *PLOS One*, (2014)



Confidence in Dauer Decision

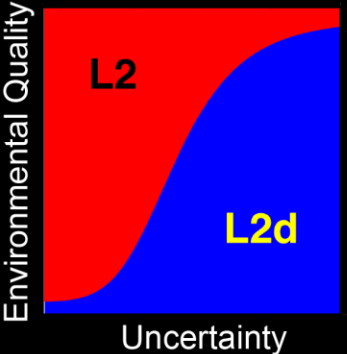
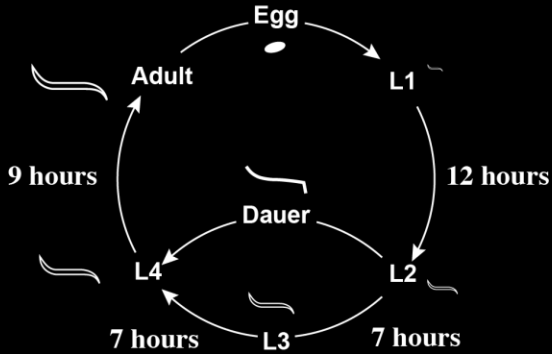


L. Avery, *PLOS One*, (2014)

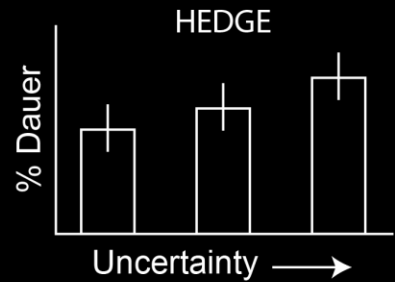
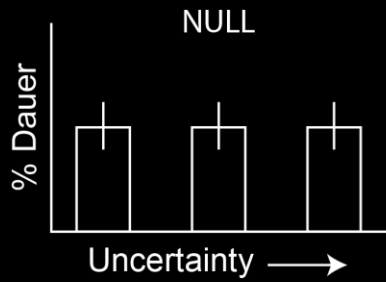
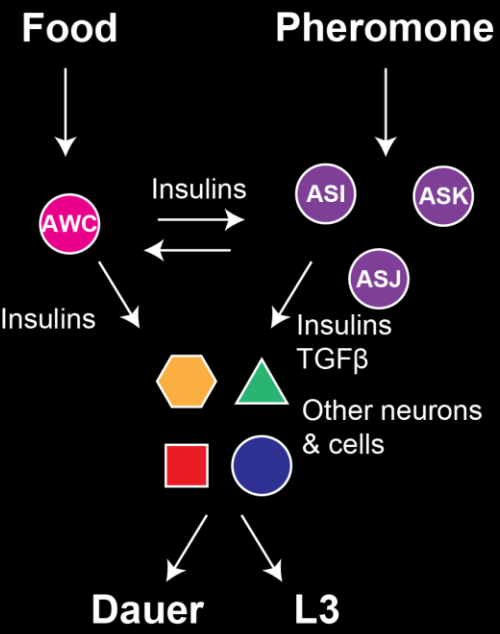
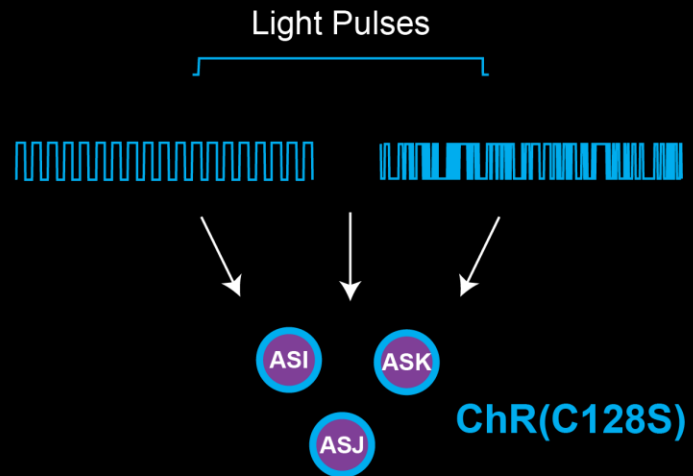


"WorMotel": Churgin *et. al.* *eLife* 2017;6:e26652

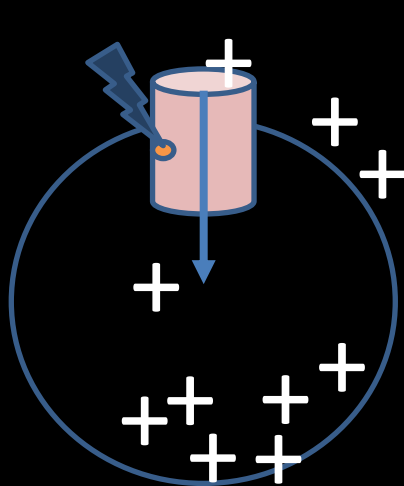
Confidence in Dauer Decision



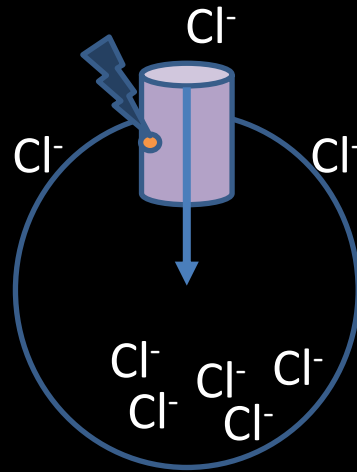
L. Avery, *PLOS One*, (2014)



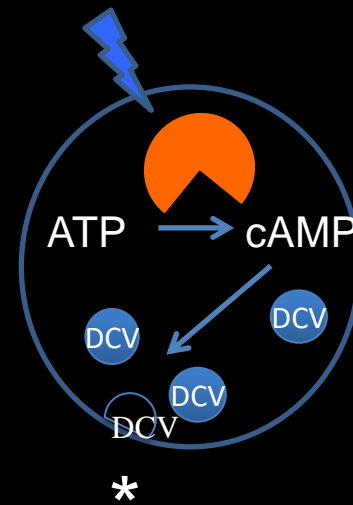
Optogenetics for different signaling modalities



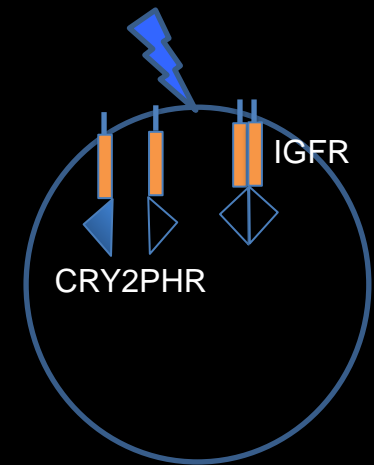
*Cation
Channelrhodopsin*



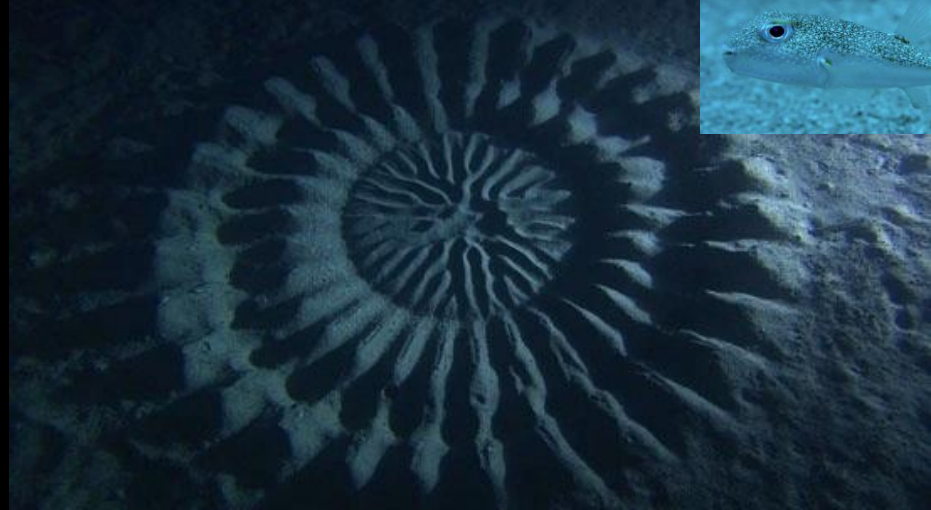
*Anion
Channelrhodopsin*



*BlaC
(Dense core
vesicle release)*



*optoIGFR &
optoTGFR
(RTK activation)*



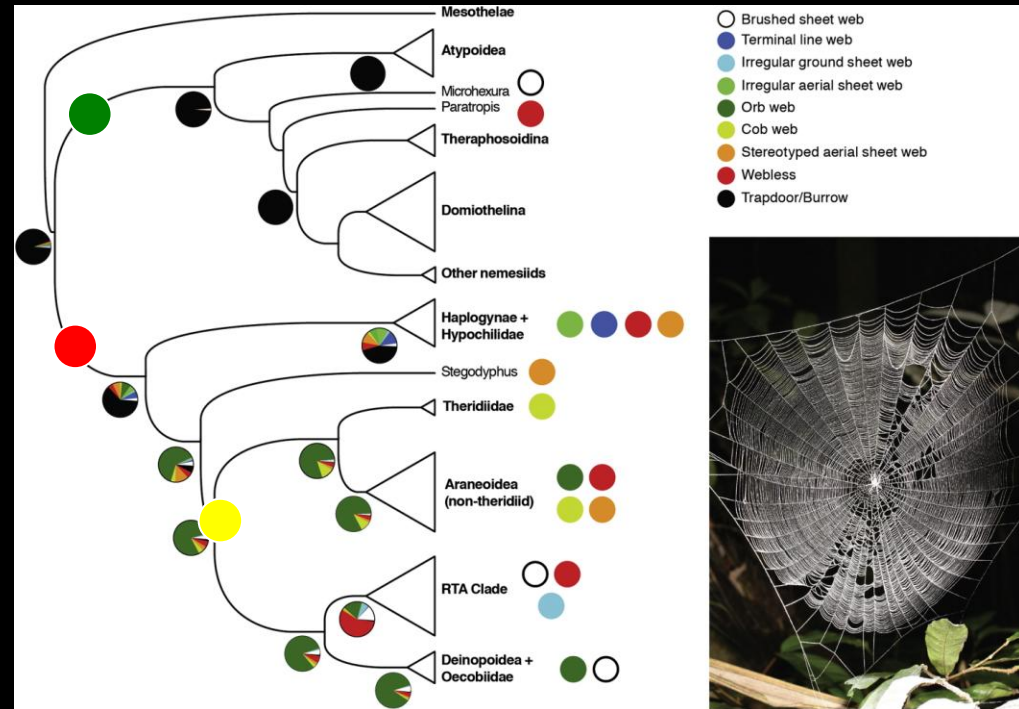
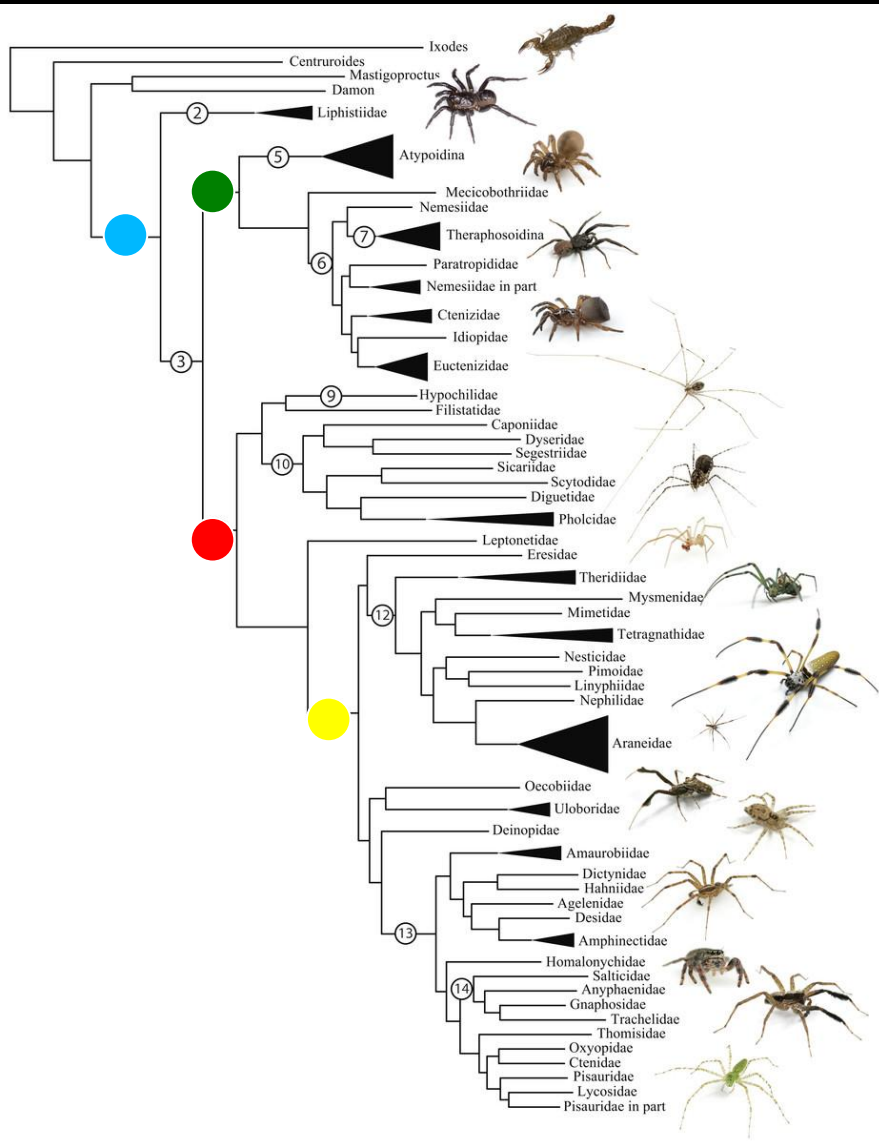
Web Architecture Reflects Behavioral Architecture

- Geometric Structure.
- Genetically Encoded Behavior.
- Requires path integration.
- Performs error correction during construction
- Behavior that is performed multiple times in the lifetime of the organism



Orb-Weaving Evolved Once

- Araneae
- Mygalomorphae
- Araneomorphae
- Orb-weaving



Jason E. Bond, Nicole L. Garrison, Chris A. Hamilton, Rebecca L. Godwin, Marshal Hedin, Ingi Agnarsson
Phylogenomics Resolves a Spider Backbone Phylogeny and Rejects a Prevailing Paradigm for Orb Web Evolution

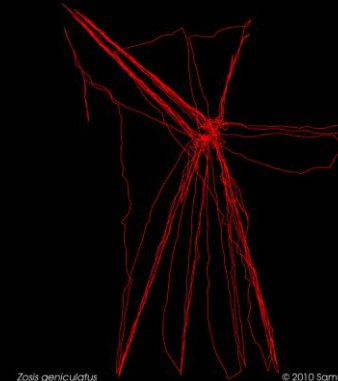
Common Behavioral Strategy

1. Proto-web (red)
2. Radii (yellow)
3. Auxiliary Spiral (white)
4. Sticky Spiral (blue)
5. Eat hub and wait



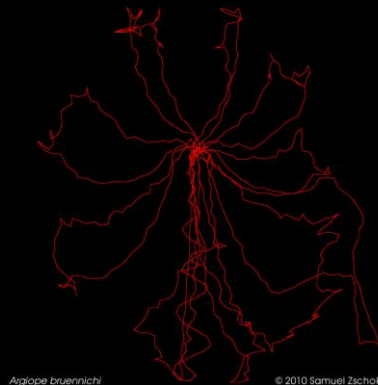
Araneus diadematus © 2010 Samuel Zschokke

Cyclosa insulana



Zosis geniculatus © 2010 Samuel Zschokke

Araneus diadematus



Argiope bruennichi © 2010 Samuel Zschokke

Argiope bruennichi



Zilla diodia © 2010 Samuel Zschokke

Zilla diodia

Common Behavioral Strategy

Proto-web (red)



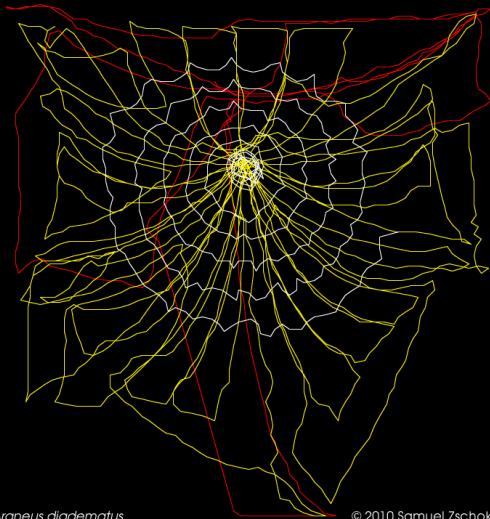
Araneus diadematus © 2010 Samuel Zschokke

Radii (yellow)



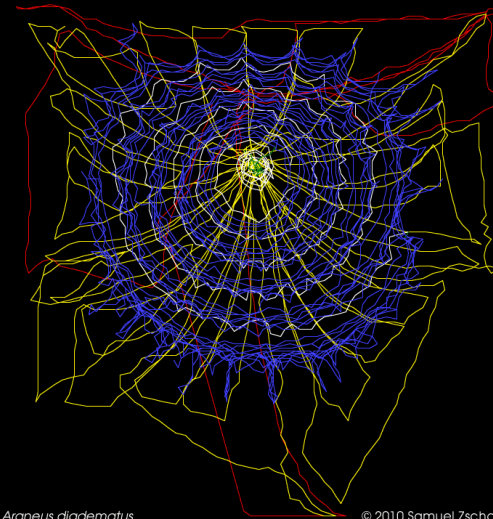
Araneus diadematus © 2010 Samuel Zschokke

Auxiliary web (white)



Araneus diadematus © 2010 Samuel Zschokke

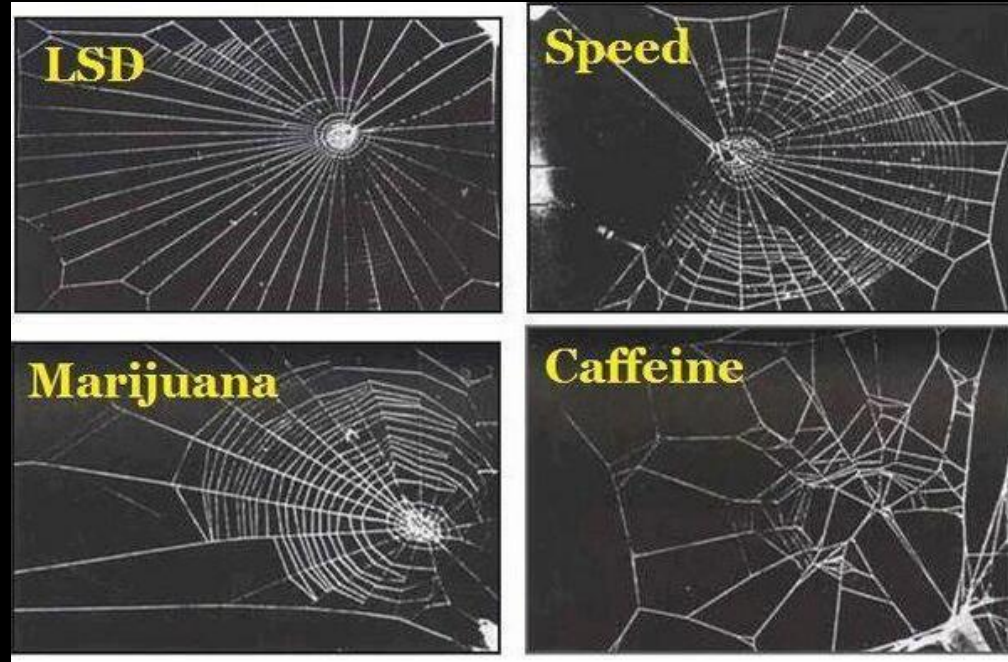
Sticky spiral (blue)



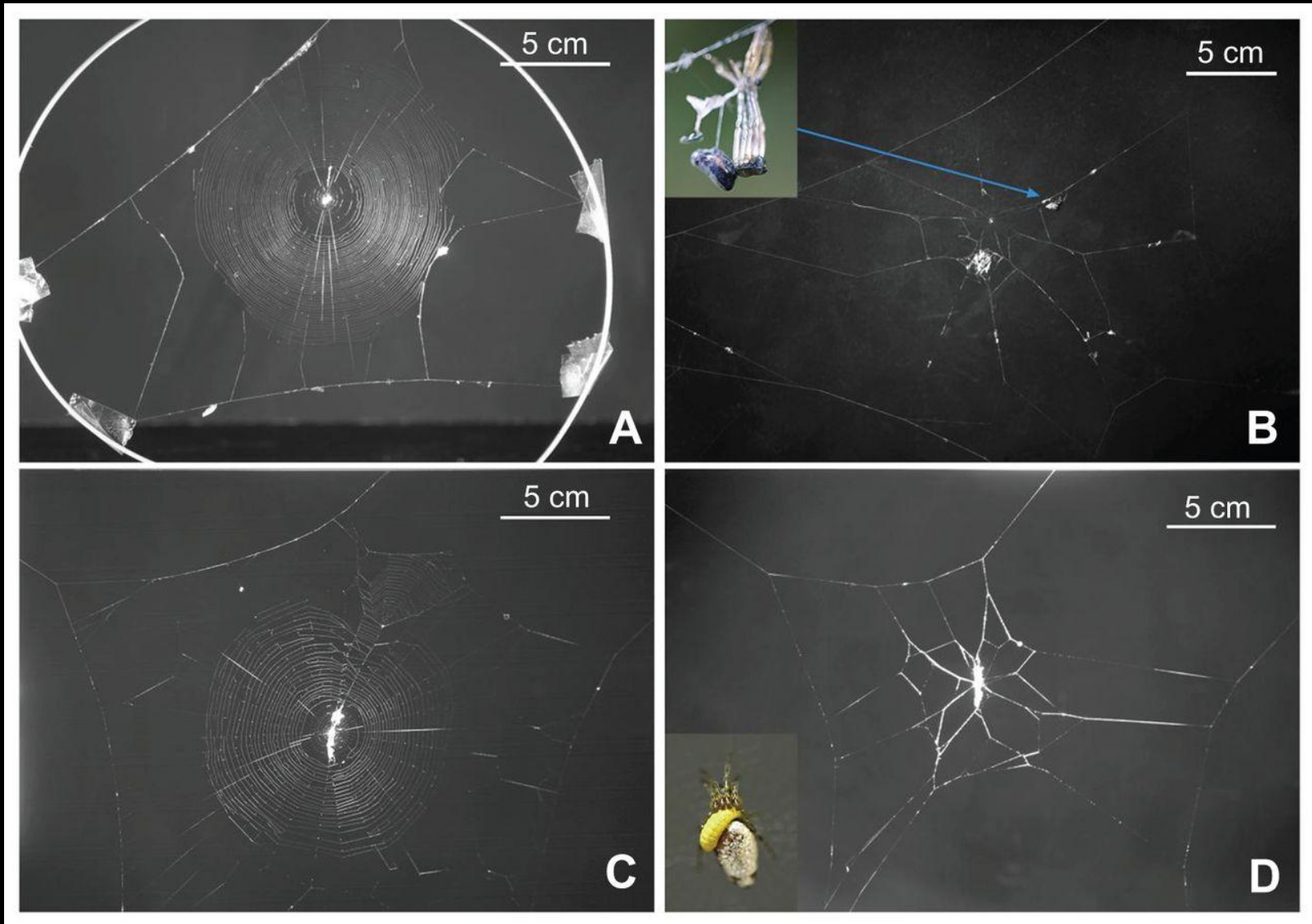
Araneus diadematus © 2010 Samuel Zschokke

Pharmacological Perturbation

















- Effect of drugs on web design investigated.
(P.N. Witt, 1949)



Pharmacological Perturbation (Neuromodulatory)



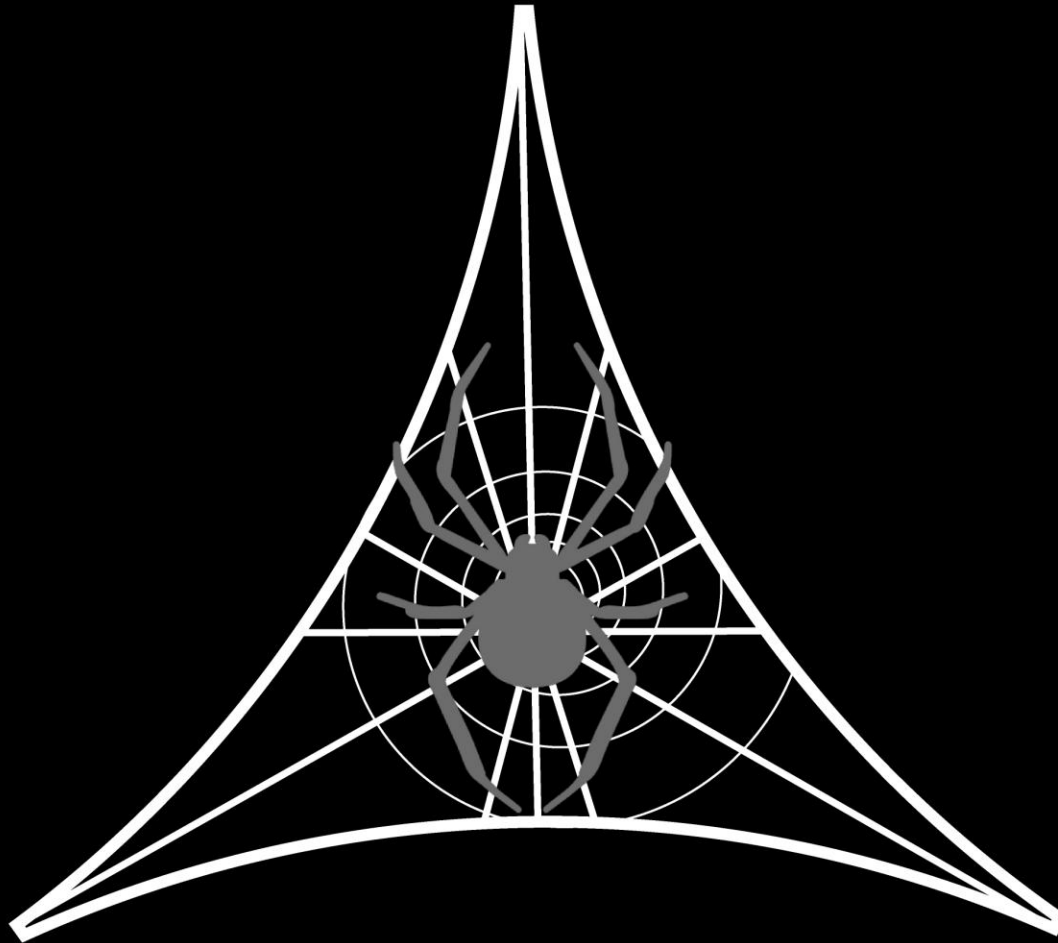
Chemical Perturbation

			Web Feature Affected			
			Proto	Radii	Auxillary*	Sticky
						
Reagent	Target	Ref.				
Chloropromazine	Antagonist Dopamine Receptors	[6]				
Diazepam	Agonist GABA Receptors	[6]				
Pentobarbital	Agonist GABA Receptors	[6]				
Phenobarbital	Agonist GABA Receptors	[6]				
Physostigmine	Inhibitor Acetylcholinesterase	[6]				
Scopolamine	Antagonist mAChR	[6,7]				
<i>Polysphincta janzeni</i> venom	Ecdysone Receptor †	[5]				
Caffeine	Antagonist Adenosine Receptors	[7]				
LSD-25	Agonist 5-HT Receptors	[6]				
Psilocybin	Agonist 5-HT Receptors	[6]				
Dexedrine	Agonist trace amine receptors	[6]				
Methamphetamine	Agonist trace amine receptors	[6,7]				

*The effect on the auxillary spiral was inferred in Ref. 6, but directly observed in Ref. 7

† The target of *P. janzeni* venom is purely speculative at this moment.

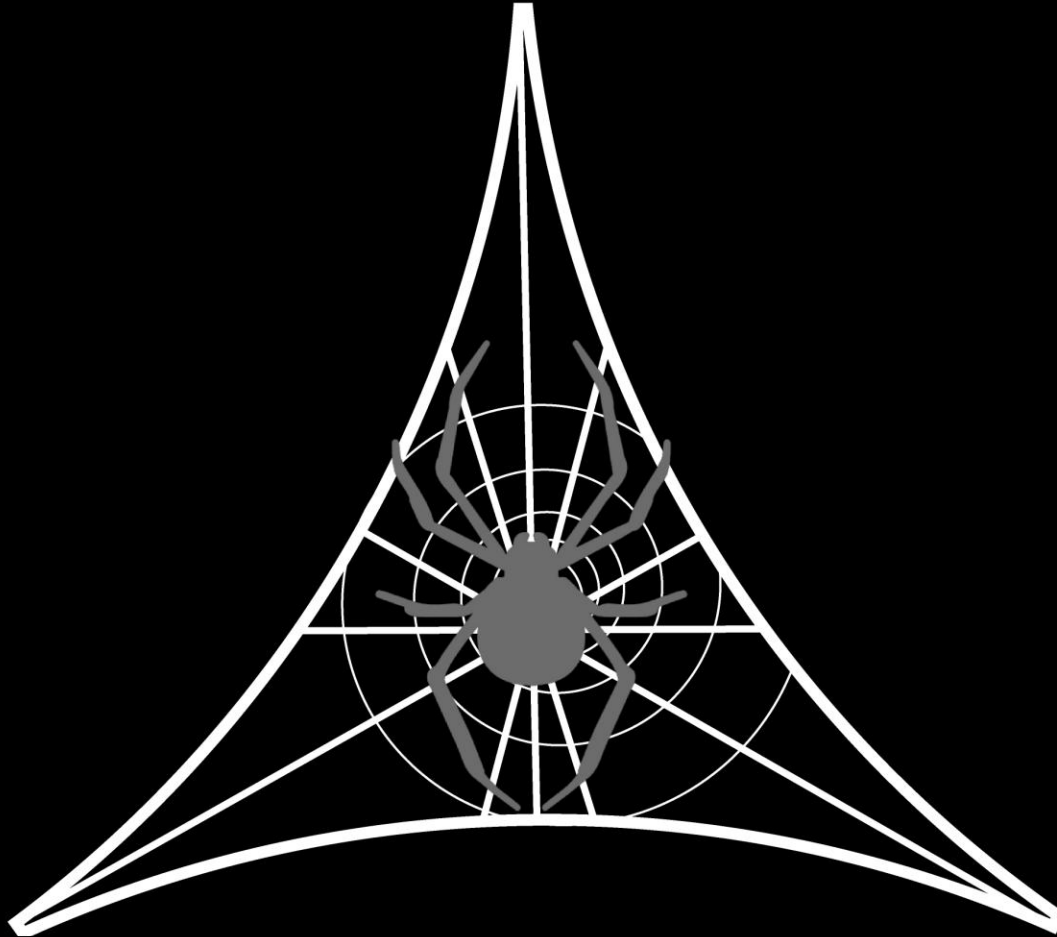
BEHAVIOR



GENETICS

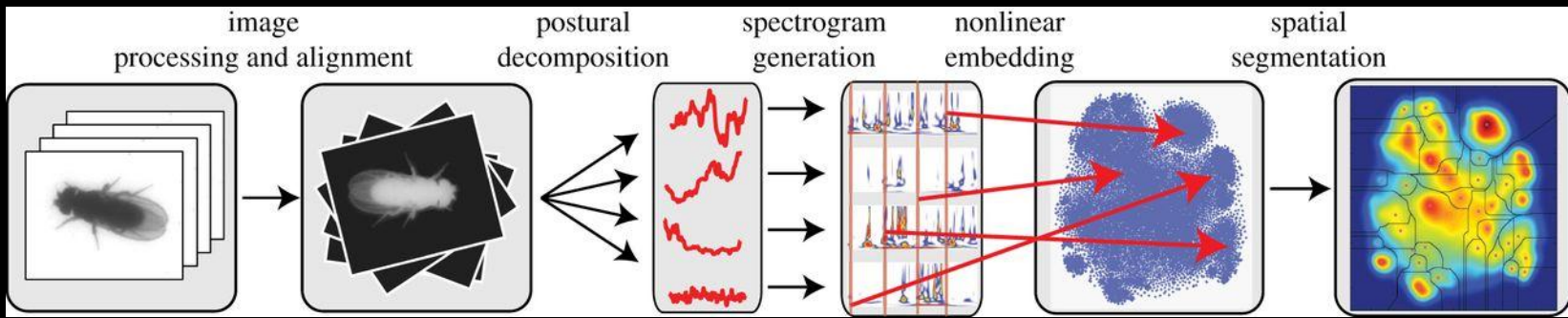
NEURONS

BEHAVIOR



GENETICS

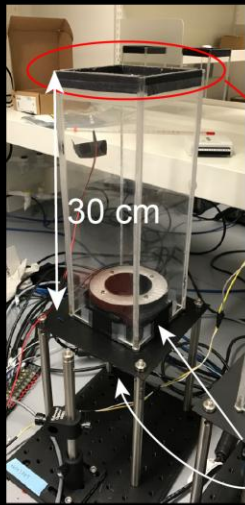
NEURONS



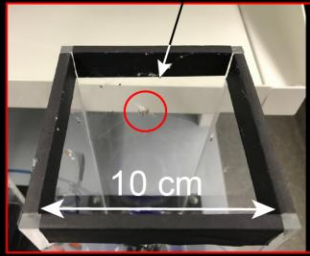
Uloborus diversus

- Small (4-5 mm).
- Short generation time (~1 month).
- Prefers arid, temperate environments.
- Readily builds webs in laboratory conditions.
- Lacks venom glands
 - Neural ganglia are accessible.

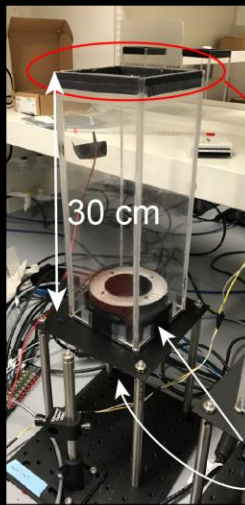




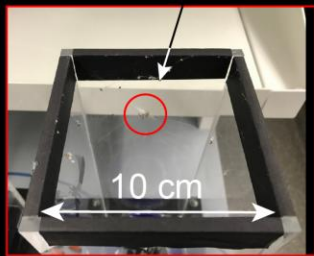
spider



880 nm LED
USB Camera

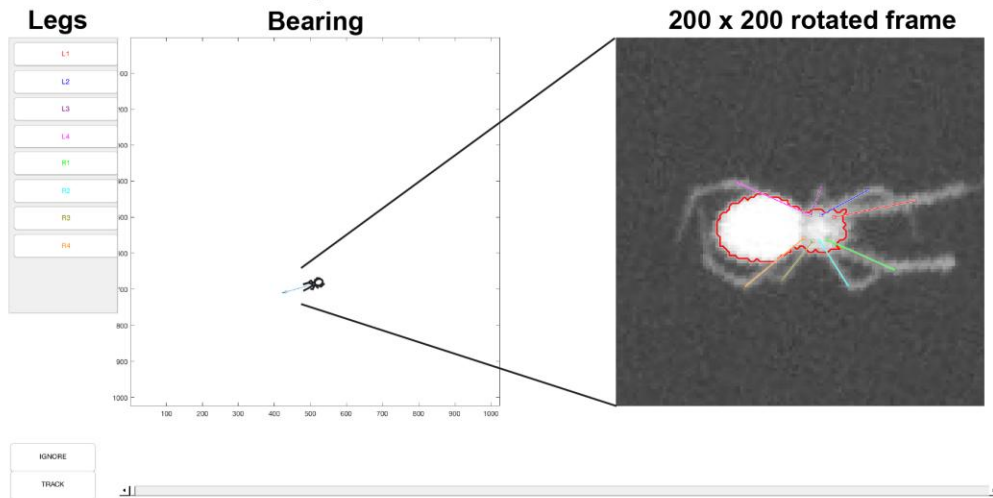


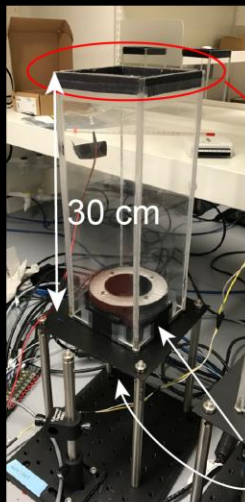
spider



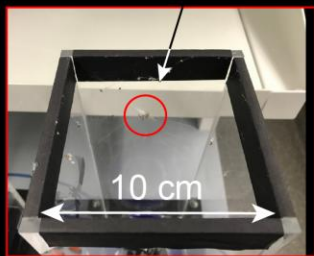
880 nm LED
USB Camera

Spider Location & Bearing

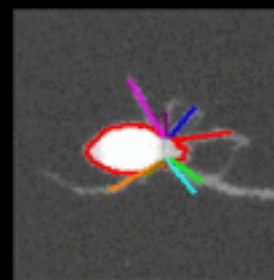
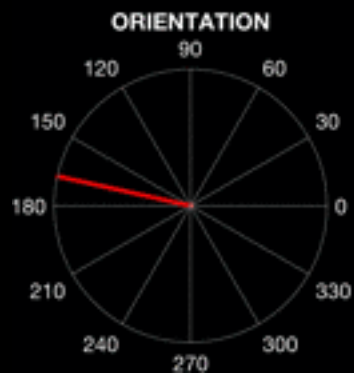
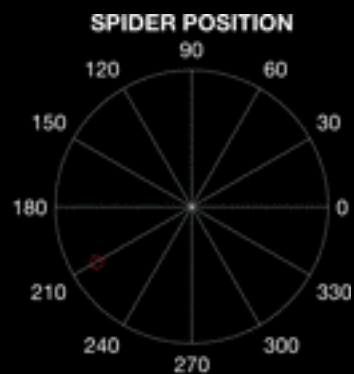
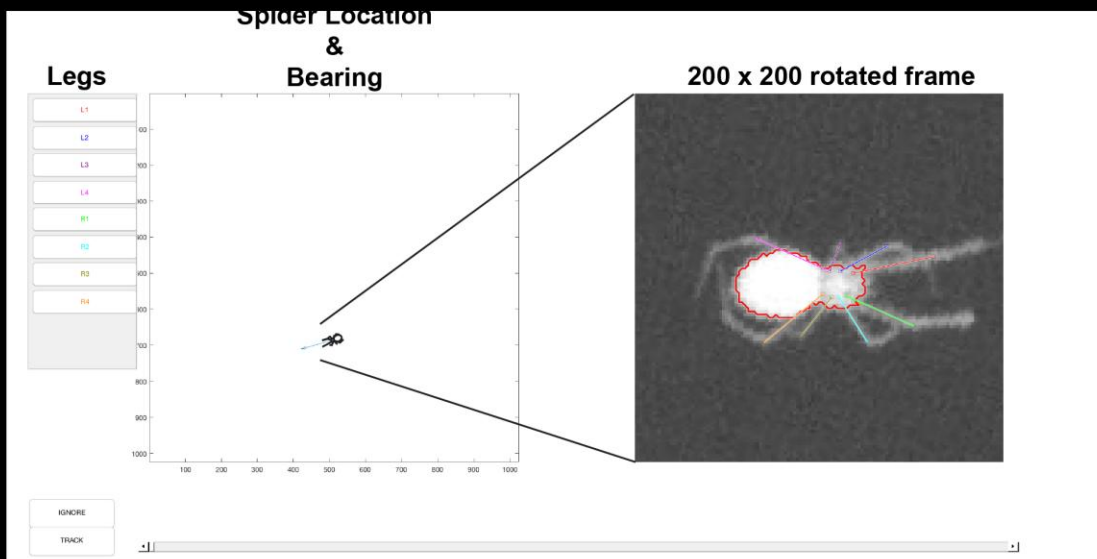




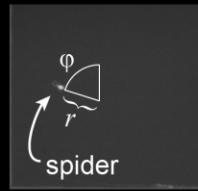
spider



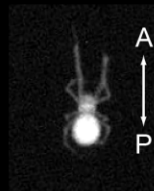
880 nm LED
USB Camera



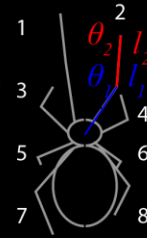
Feature Extraction



center at (r, φ)
& rotate (ψ)



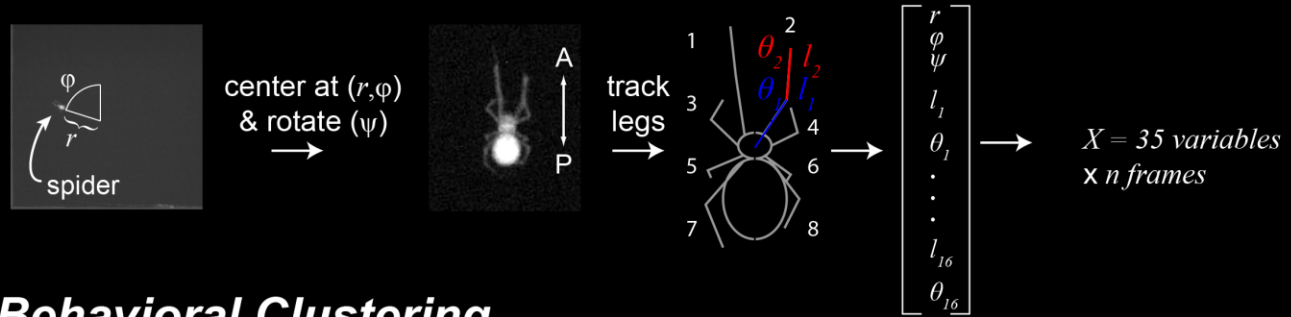
track
legs



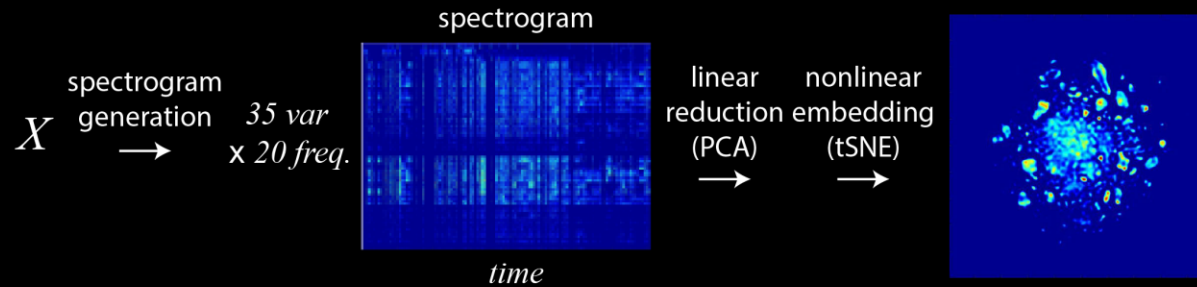
$$\begin{bmatrix} r \\ \varphi \\ \psi \\ l_1 \\ \theta_1 \\ \vdots \\ l_{16} \\ \theta_{16} \end{bmatrix}$$

$X = 35 \text{ variables}$
 $\times n \text{ frames}$

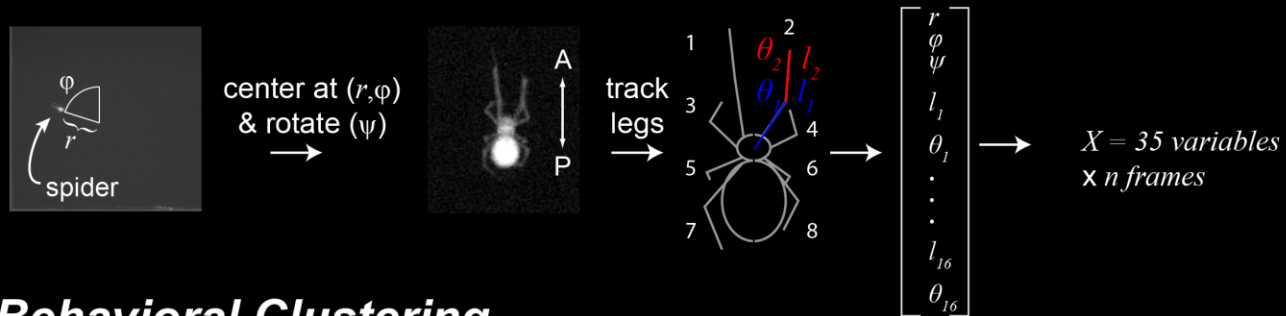
Feature Extraction



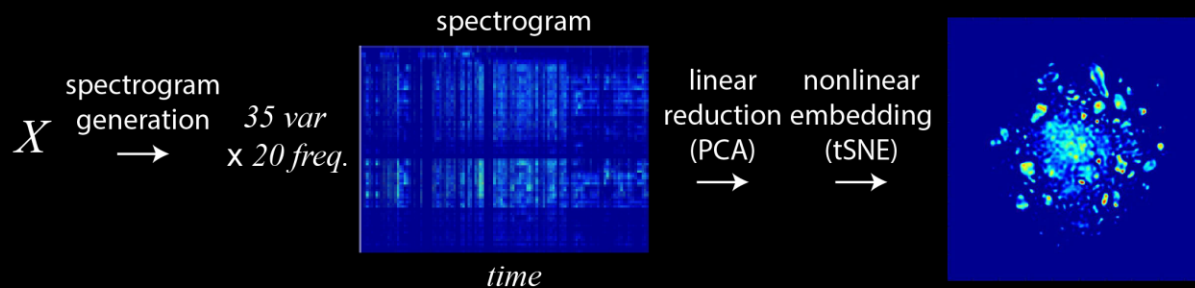
Behavioral Clustering



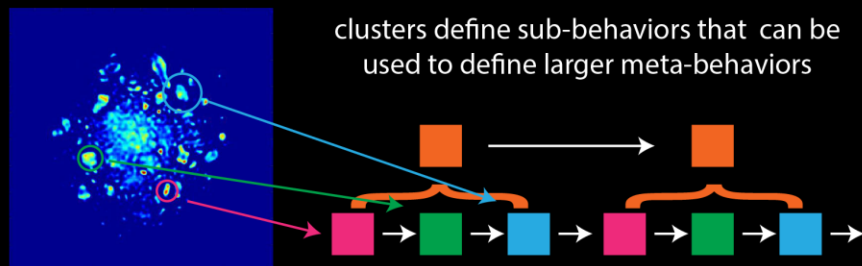
Feature Extraction



Behavioral Clustering



Model Assembly



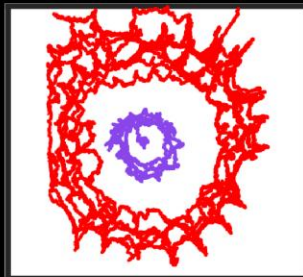
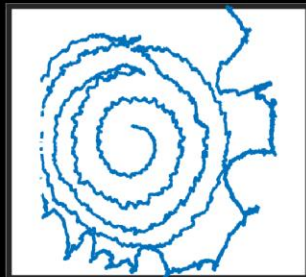
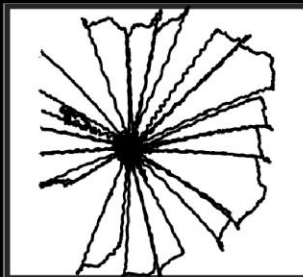
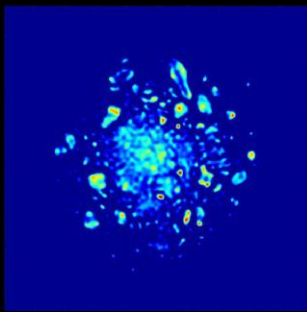
Parameters for inter-web comparisons

Behavioral Density $P(\text{cluster})$

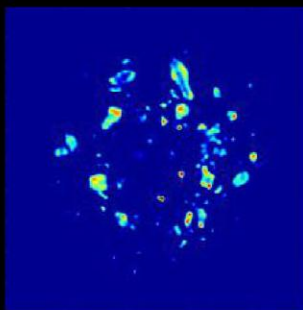
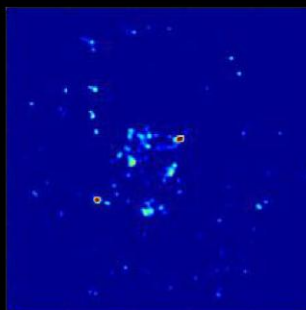
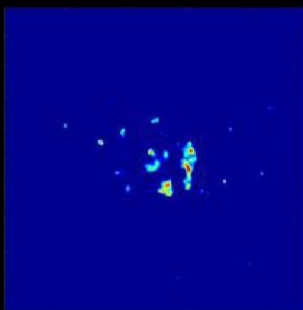
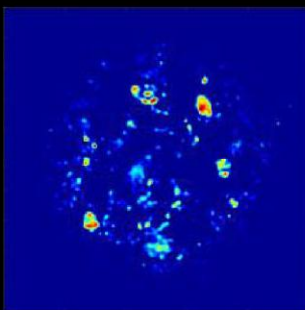
Behavioral Dwell Time $P(\text{pink}(t)), P(\text{green}(t)), \dots P(\text{blue}(t))$

Transitional Probability $P(\text{green} | \text{pink})$

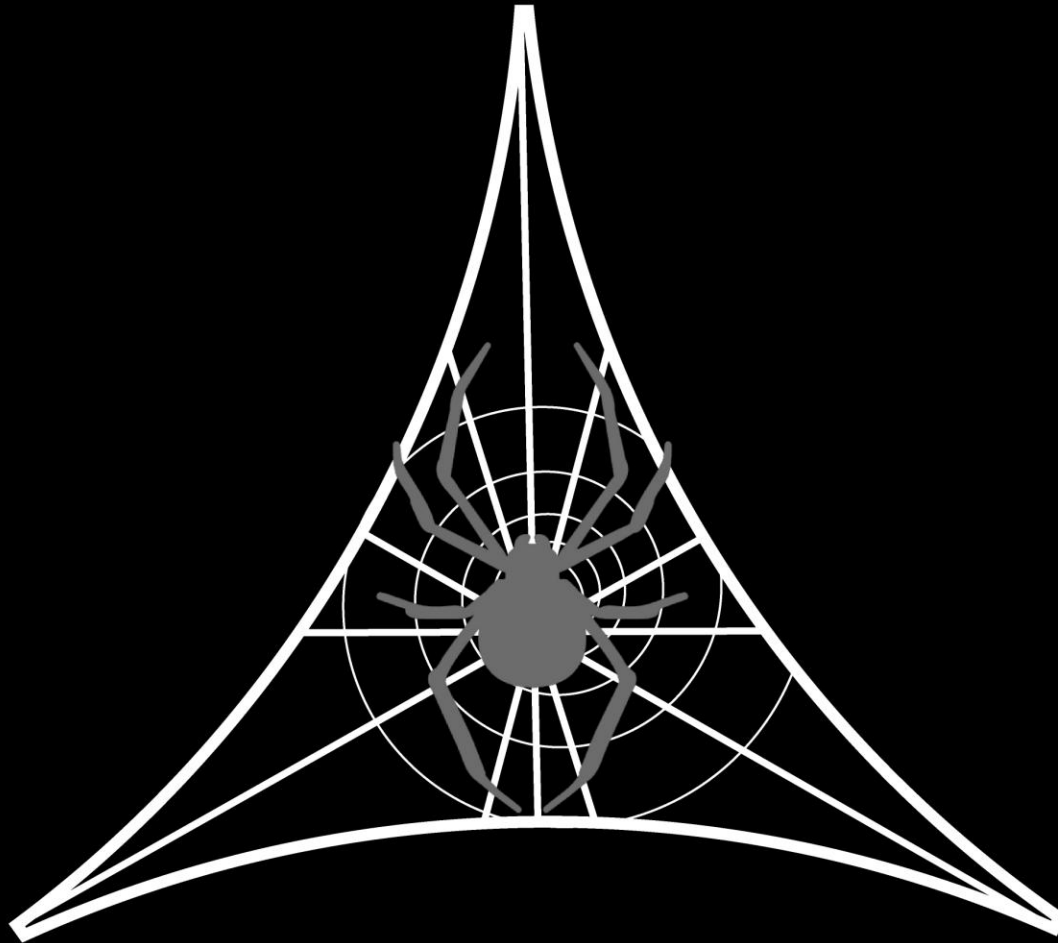
All tSNE-embedded behaviors



tSNE-embedded behaviors parsed by web stage



BEHAVIOR

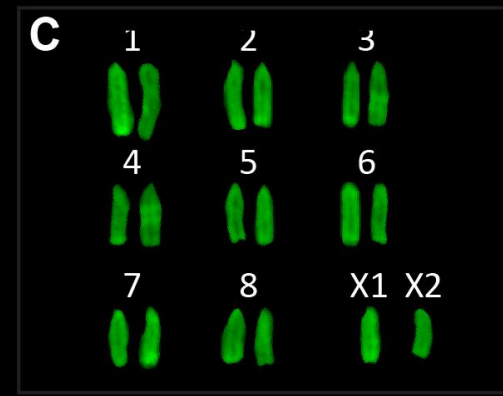
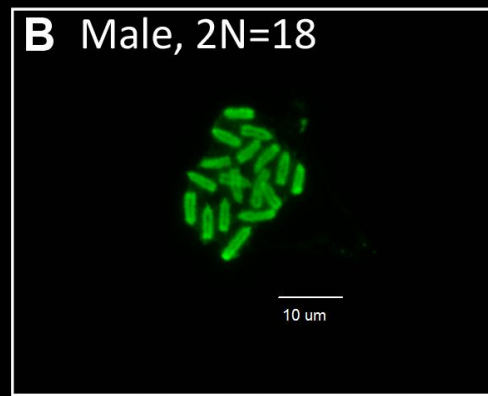
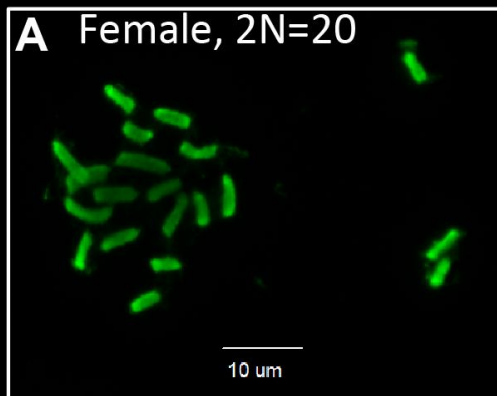


GENETICS

NEURONS

Genetics: So Far


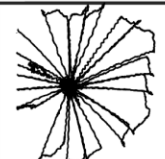
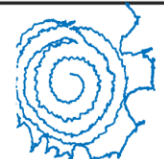
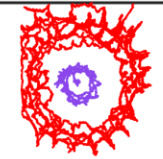
- Illumina library & de novo genome assembly.
 - ~1.7 Gb
- Illumina cDNA sequencing.
 - 121,360 transcripts identified.
 - 30,752 ORFs predicted.



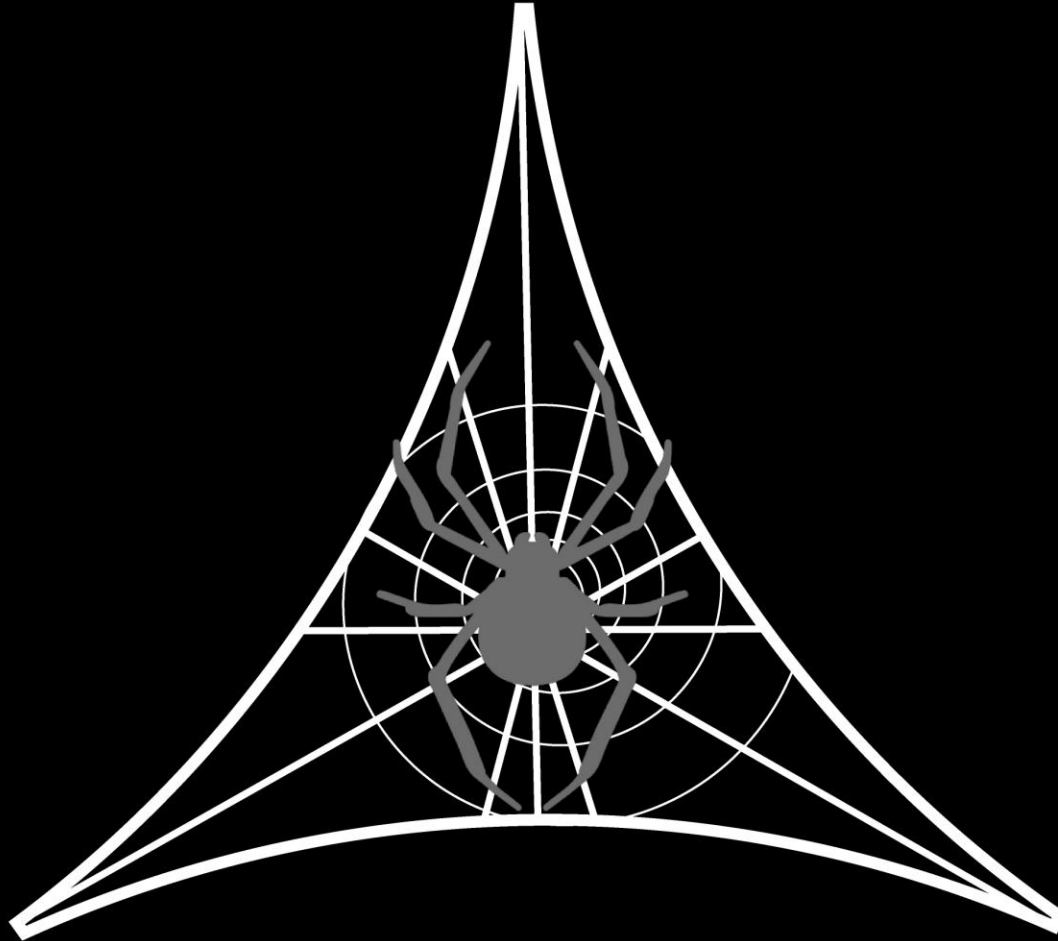
Genetics: Perturbation

- Target neuropeptides and GPCRs for expression knock-down with RNAi and CRISPR-Cas9.
- Introduce transgenics (e.g. GCaMP).

RNAi Targets

		Potential Web Feature Affected			
		Proto	Radii	Auxillary	Sticky
					
<u>Transcripts</u>	<u># Identified</u>				
Receptors					
Dopamine	5				
AMPA-Glutamate	8				
NMDA-Glutamate	7				
nAChR	1				
GABA	10				
mAChR	2				
Ecdysone	1				
Serotonin	7				
Octopamine	1				
Beta-Adrenergic	2	?	?	?	?
Other neuropeptide	20	?	?	?	?
Other hormone	13	?	?	?	?
Other GPCR	22	?	?	?	?
Transporters					
Dopamine	12				
Serotonin	13				

BEHAVIOR



GENETICS

NEURONS

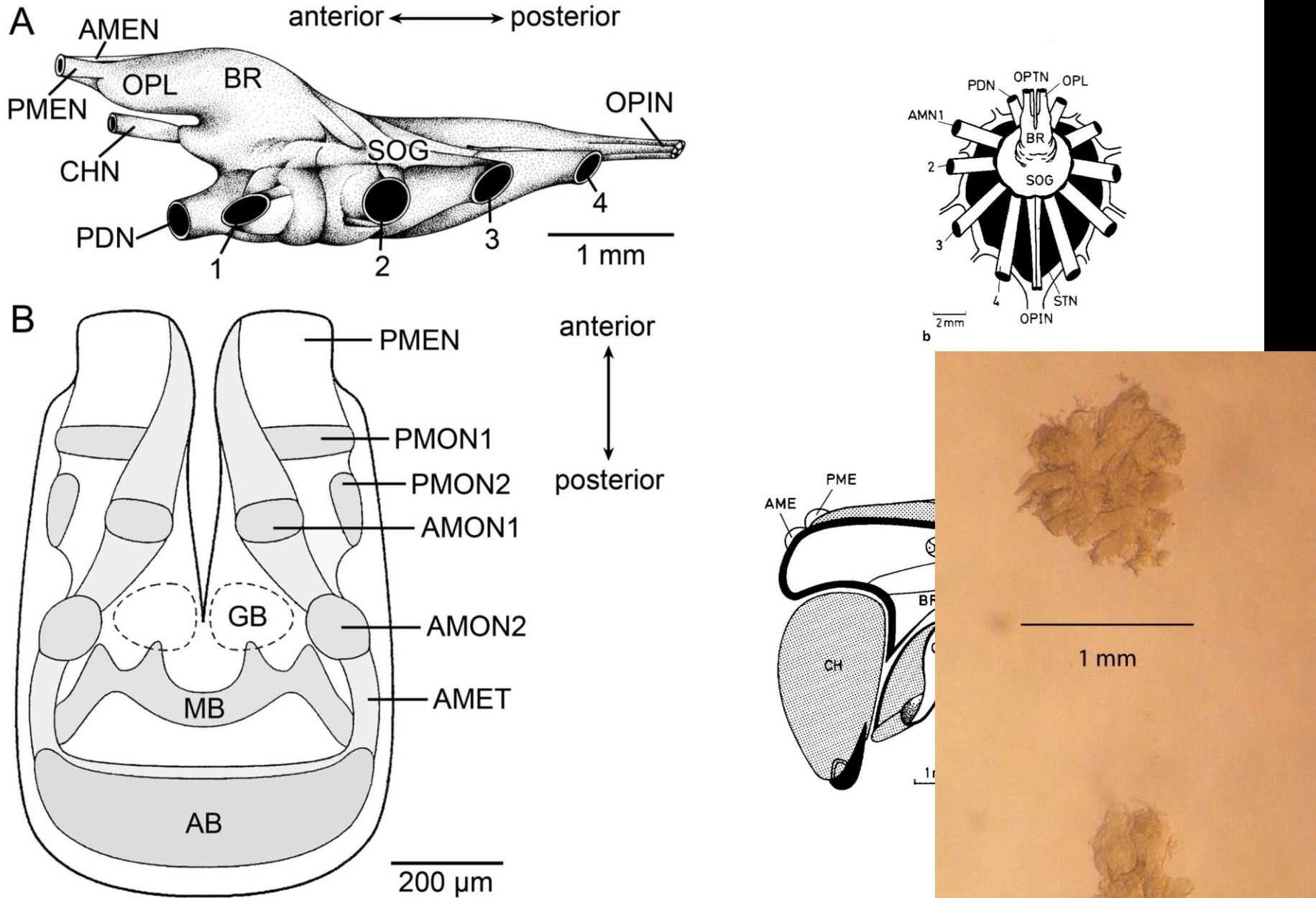
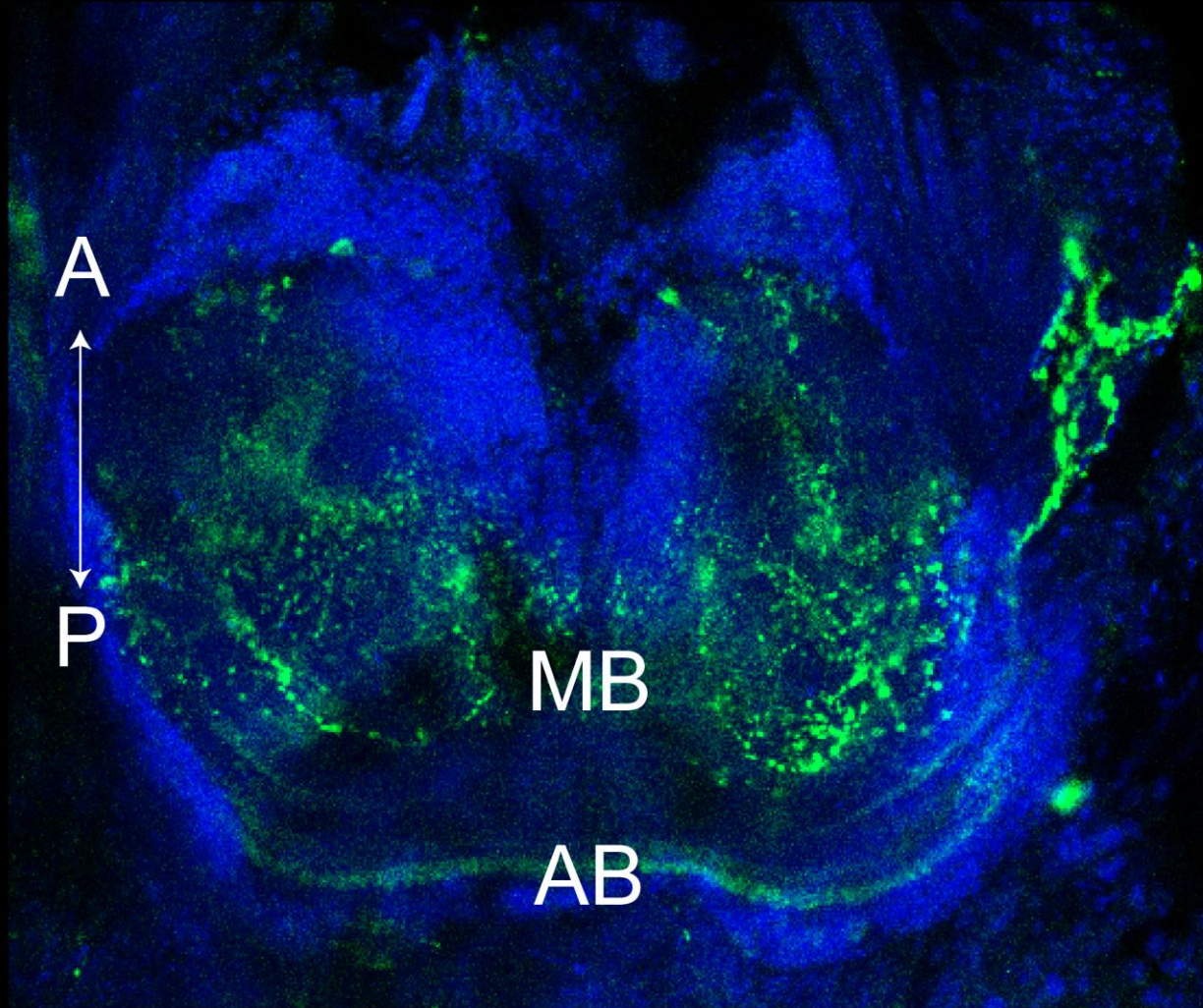
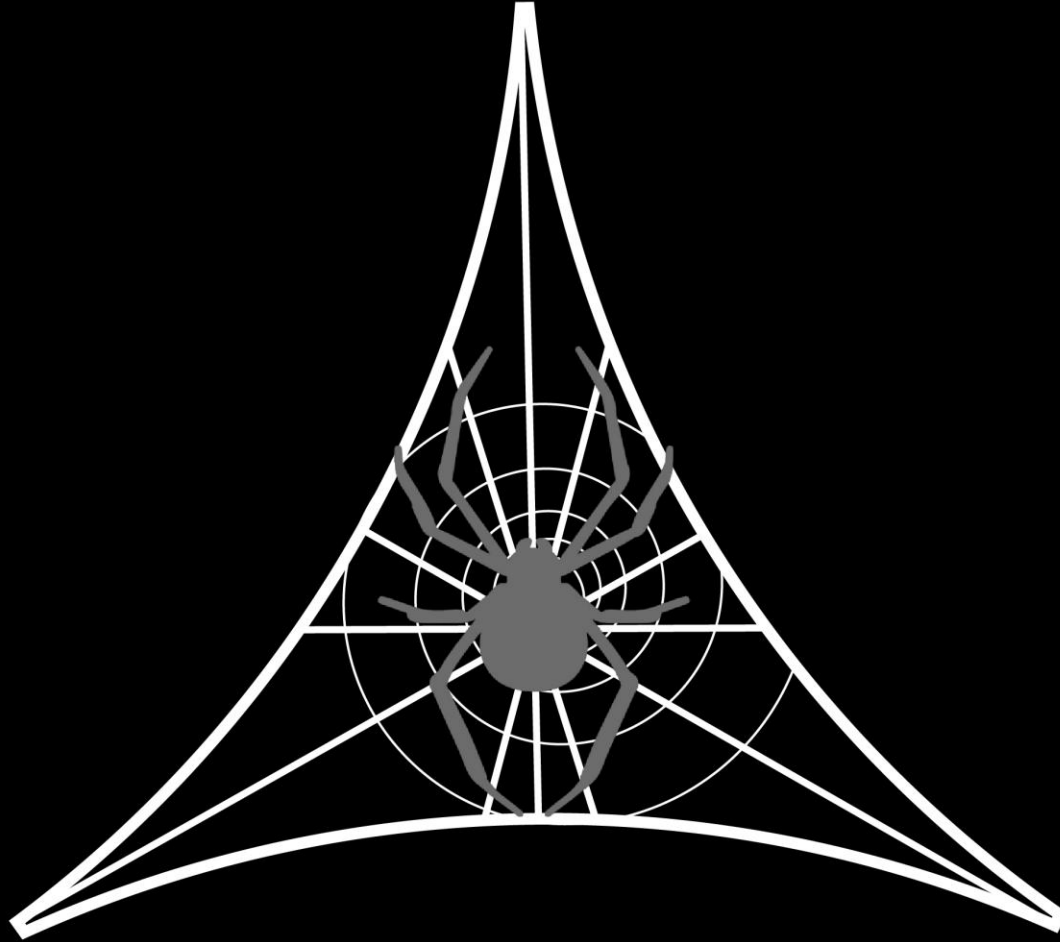


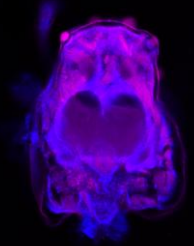
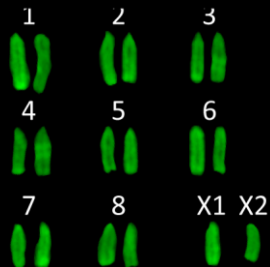
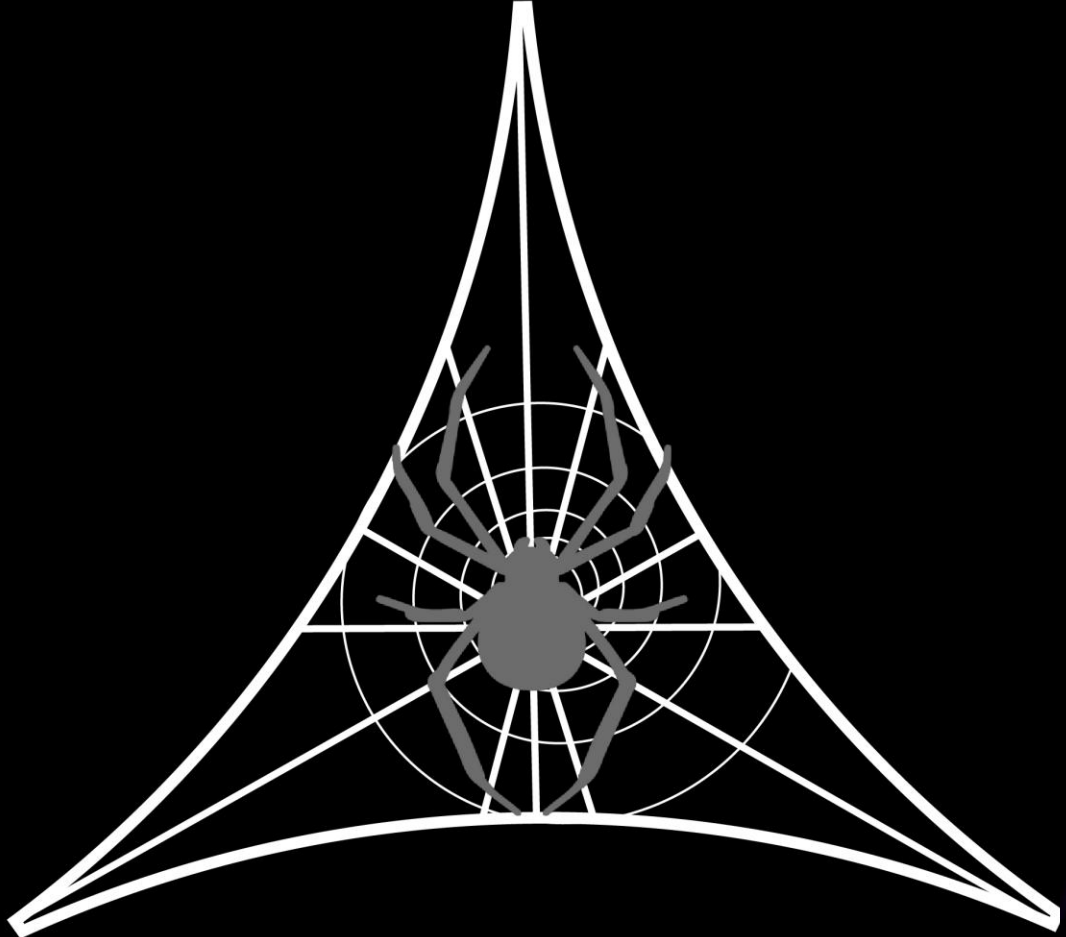
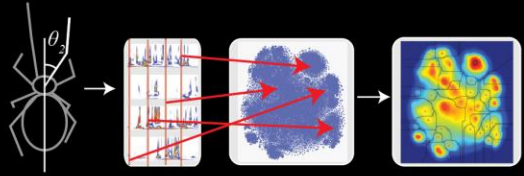
Fig. 1. Gross anatomy of the central nervous system of *Cupiennius salei* (after Babu and Barth, 1984, modi fied). (A) External view of the prosomal ganglion complex as seen from lateral. The supraoesophageal ganglion comprises the optic lobes (OPL) and the brain (BR). Major optic nerves entering the optic lobes are the anterior and the posterior median eye nerves (AMEN and PMEN). The fused subesophageal ganglionic mass (SOG) is innervated by the cheliceral nerves (CHN), the pedipalpal nerves (PDN), the leg nerves (1–4), and the opisthosomal nerve (OPIN). (B) Schematic drawing of the brain and optic lobes as seen from dorsal (adopted from Duncker, 1992, unpublished thesis; summarized in Barth, 2002). Prominent neuropils in the brain are the arcuate body (AB) and the mushroom body (MB). GB, region where the perikarya of globuli cells reside, i.e. neurons that innervate the mushroom bodies. Each of the two optic tracts that originate from the anterior and posterior median eye nerves supply two optic neuropils: AMET, anterior median eye tract (extension of the AMEN into the brain); AMON1 and 2, anterior median optic neuropil 1 and 2; PMON1 and 2, posterior median optic neuropil 1 and 2.

Uloborus diversus: Adult Protocerebrum



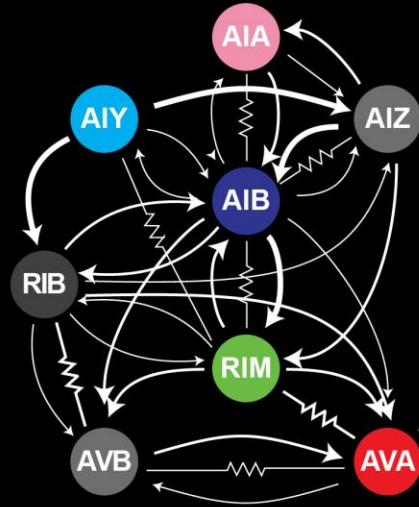
- DAPI
- Anti-Inotocin
- MB: Mushroom Body
- AB: Arcuate Body





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Elana Pyfrom

The Spiders



Jeremiah Miller



Nicolas Wilkerson

