



# Räumliche Orientierung als Fenster in die Funktion des Gehirns

Modellsysteme in der Neurobiologie — NWG Lehrerfortbildung 2017/2018  
Dr. Matthias Wittlinger

## Räumliche Orientierung – Raumsinn oder Richtungssinn

Fähigkeit von Menschen und Tieren, die ihnen hilft, sich im Raum und richtungsbezogen zurechtzufinden und angemessen zu bewegen.



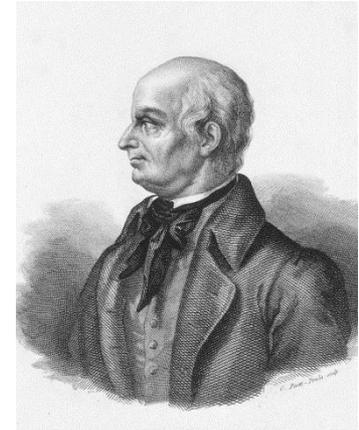
# Heimfindevermögen – homing behavior

## Beispiele im gesamtem Tierreich



## Experimentelle Biologie – Beispiel Echoortung

- 1773 Lazzaro Spallanzani
- 1778 Charles Jurine
- 1938 Robert Galambos und Donald Griffin  
Ultraschalldetektor von William Pierce



Quelle: Wikipedia



## Santschi's Spiegelexperiment *Messor barbatus*

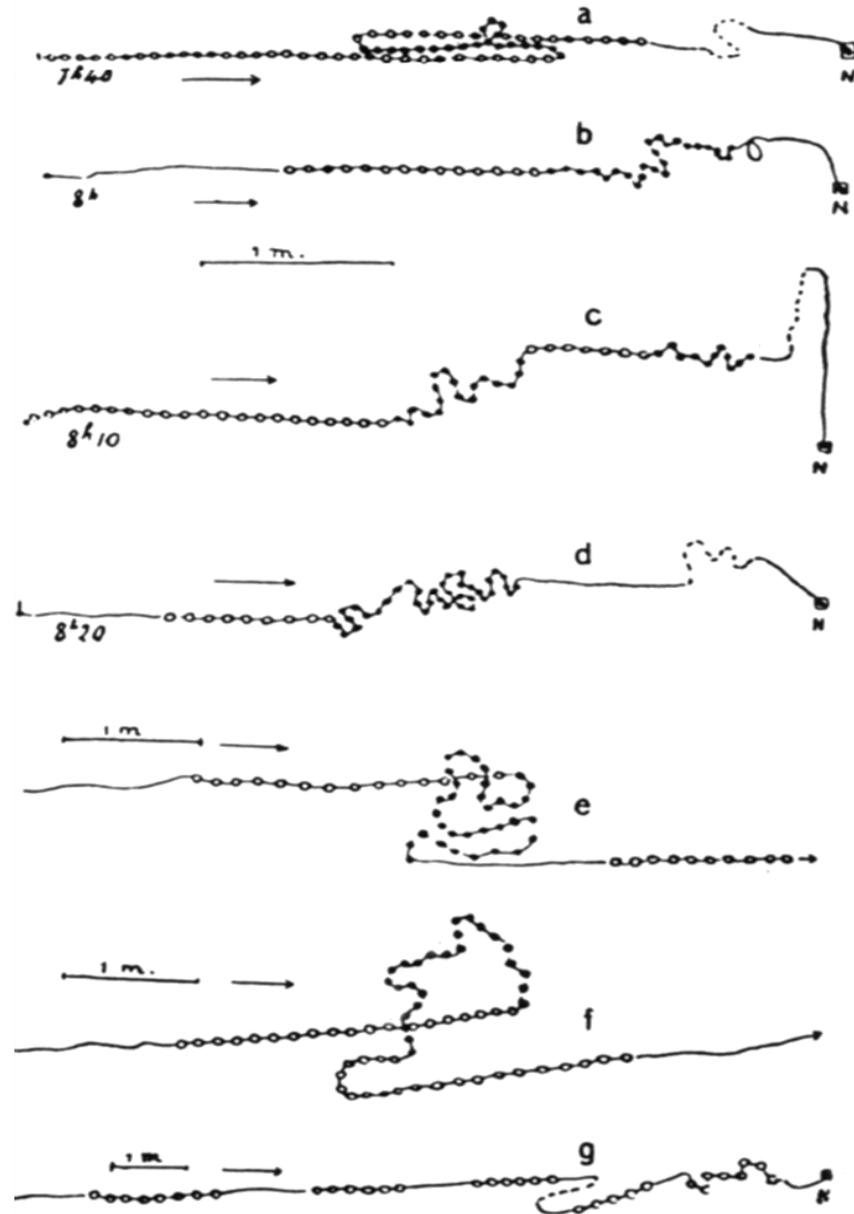
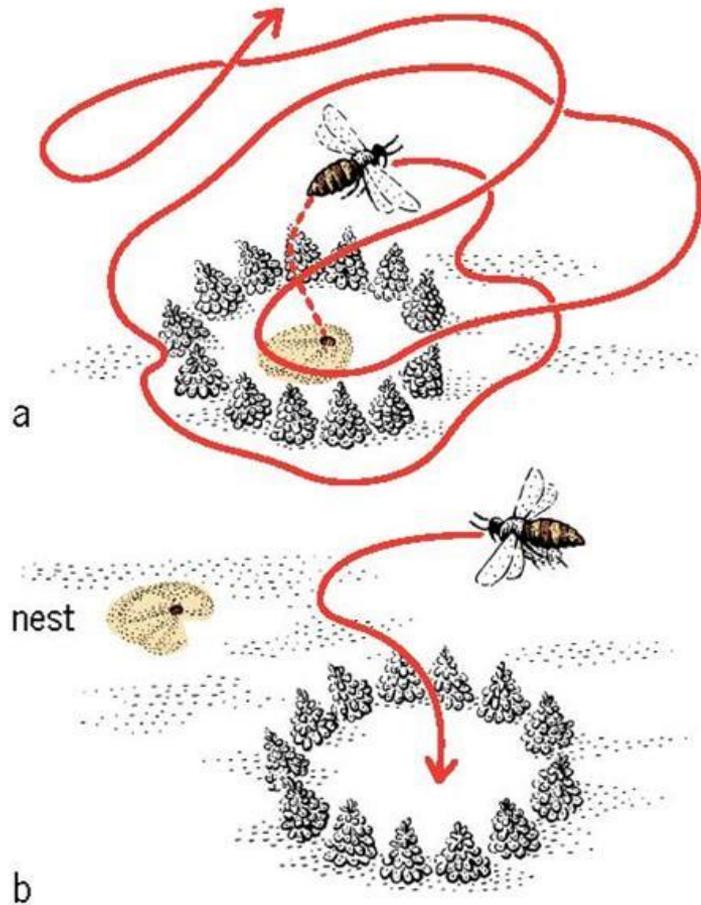
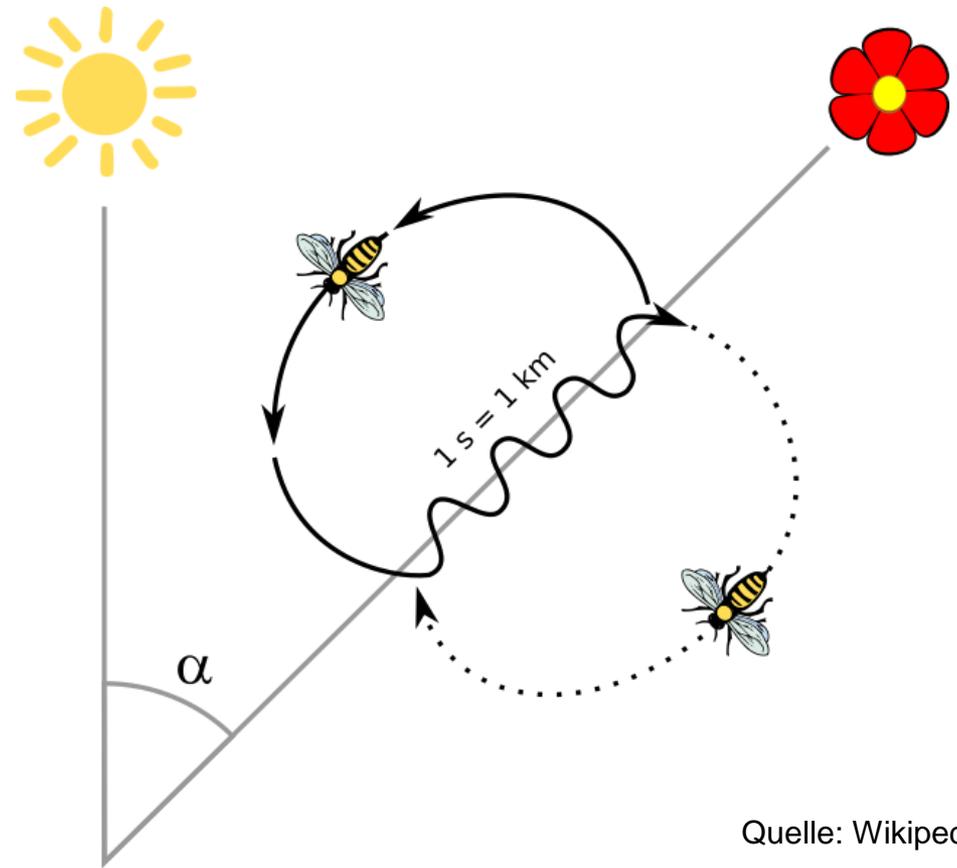


FIG. 2.

Santschi (1911; 1923)



Nikolaas Tinbergen



Quelle: Wikipedia

Karl von Frisch

Nobelpreis 1973: „für ihre Entdeckungen zu Organisation und Auslösung von individuellen und sozialen Verhaltensmustern“



**Warum Forschung an Wüstenameisen?**

landmarkenarm

lebensfeindlich: heiß, trocken, salzig

wenig Nahrung

- keine Duftspuren
- tagaktive Einzelfuragierer
- kein Rekrutieren von Nestgenossen

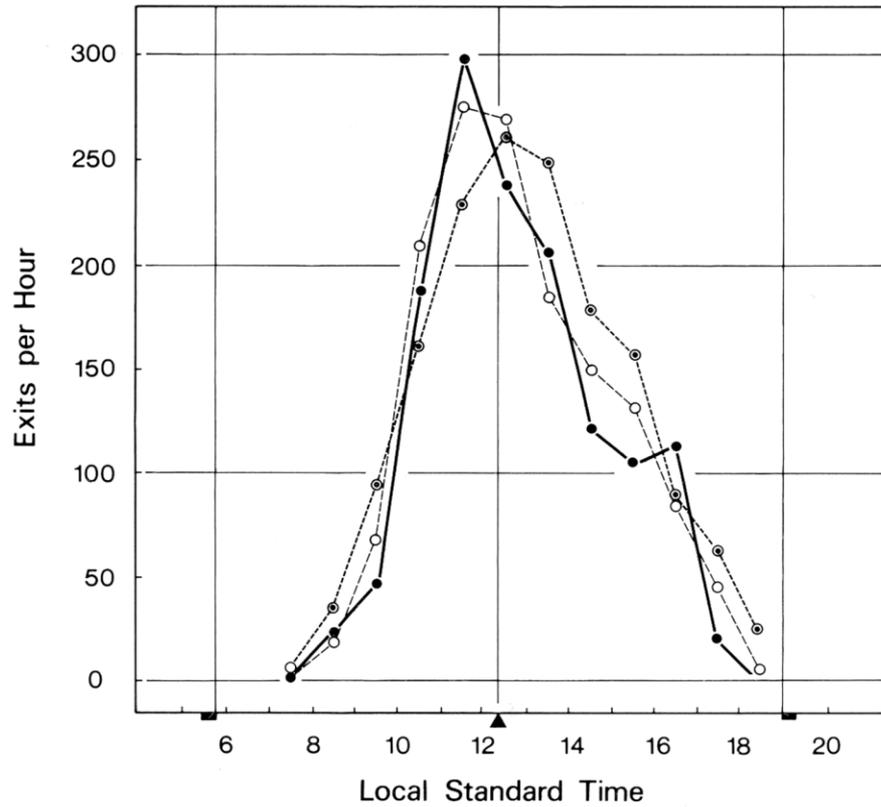


**Lebensraum von *Cataglyphis fortis***



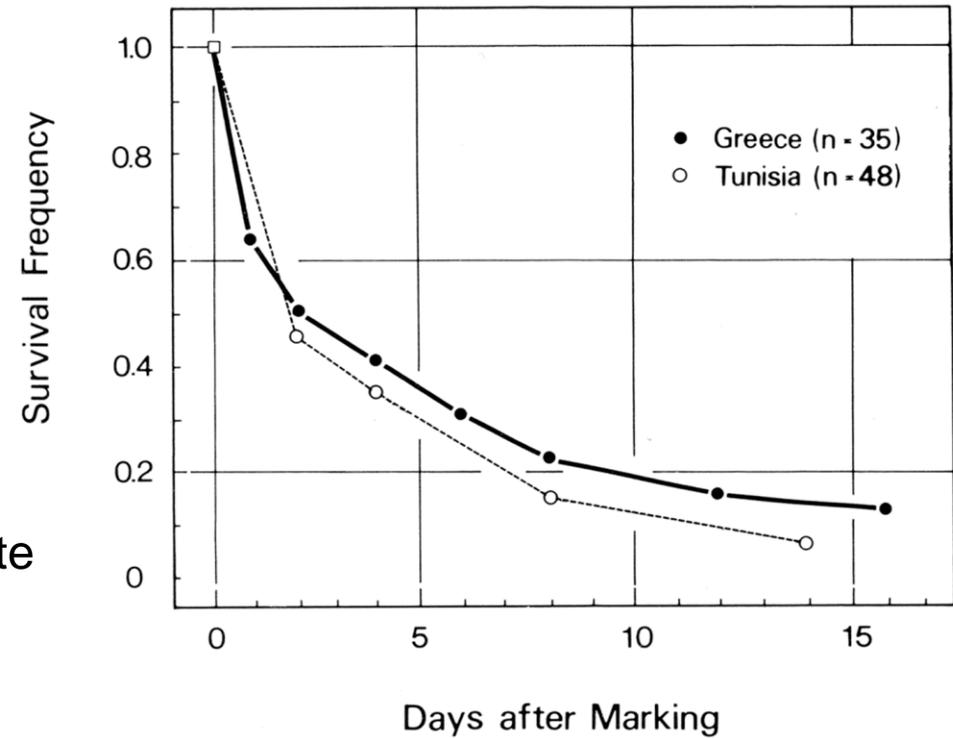
**viele Raubfeinde**





Aktivitätspeak um Mittag

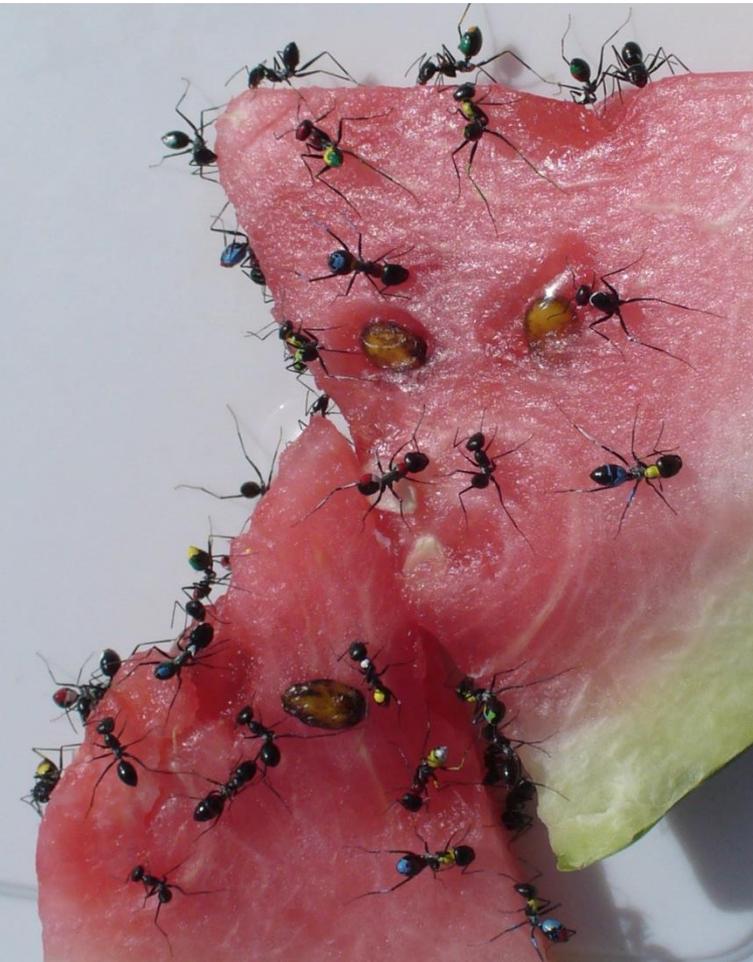
Niedrige Überlebensrate  
(ca. 50% nach 2d)





## Experimentelle Vorteile von *Cataglyphis* Ameisen:

- direkt beobachtbar (cf. Bienen, Tauben, etc.)
- individuelle Identifikation
- einfach zu Manipulieren



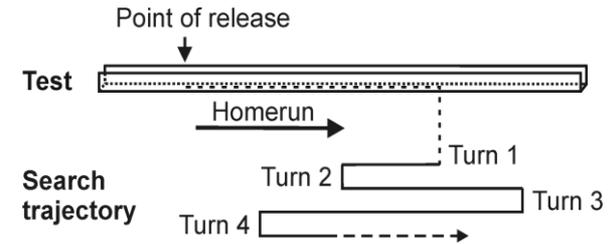
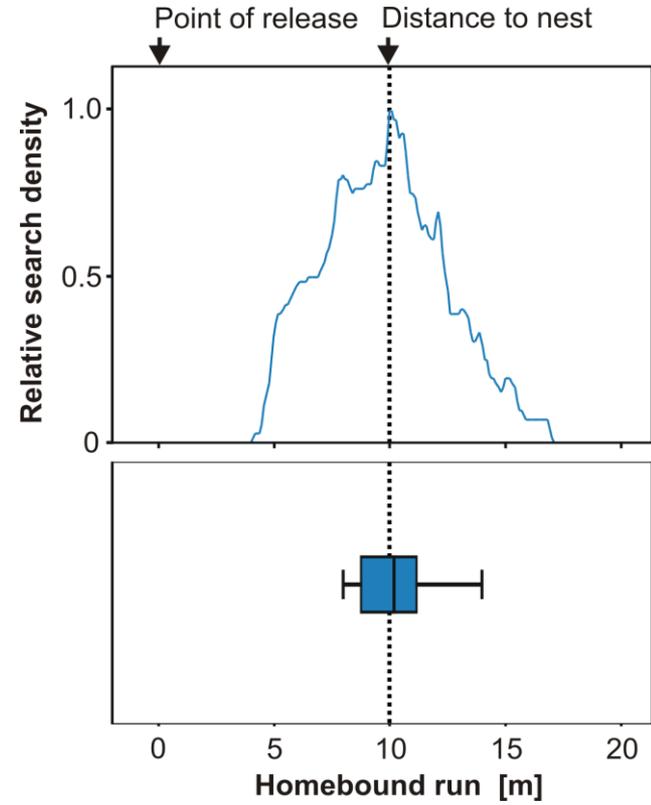
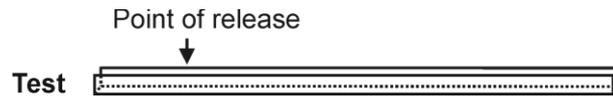
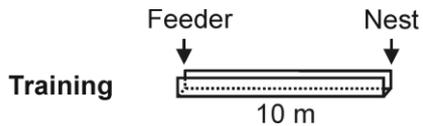
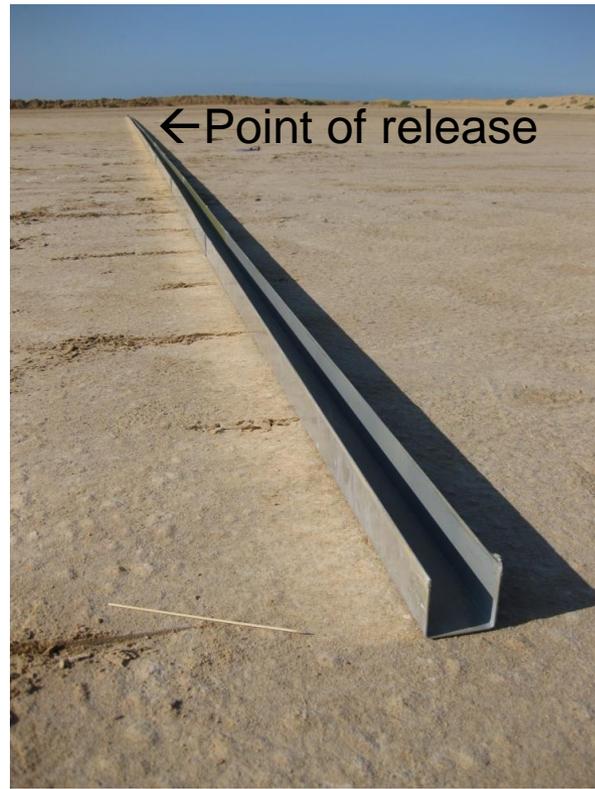
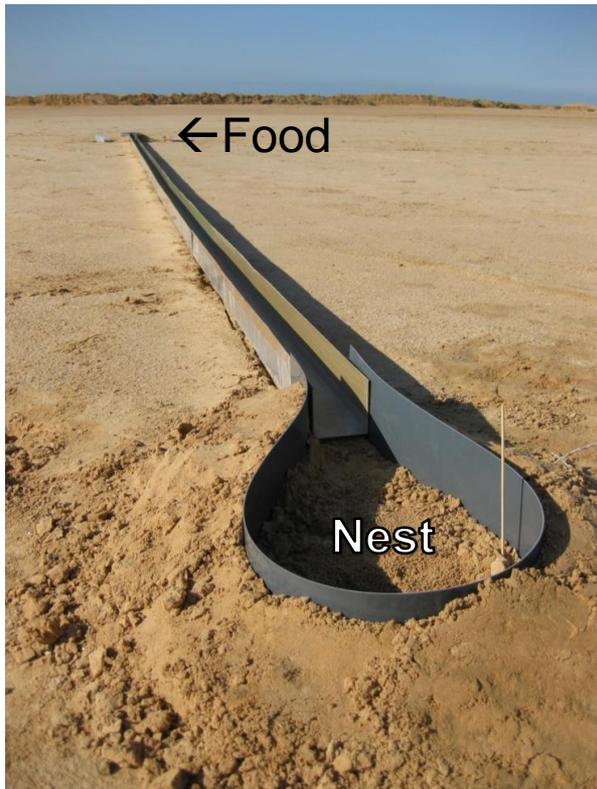


## Landmarkenarme Testfelder

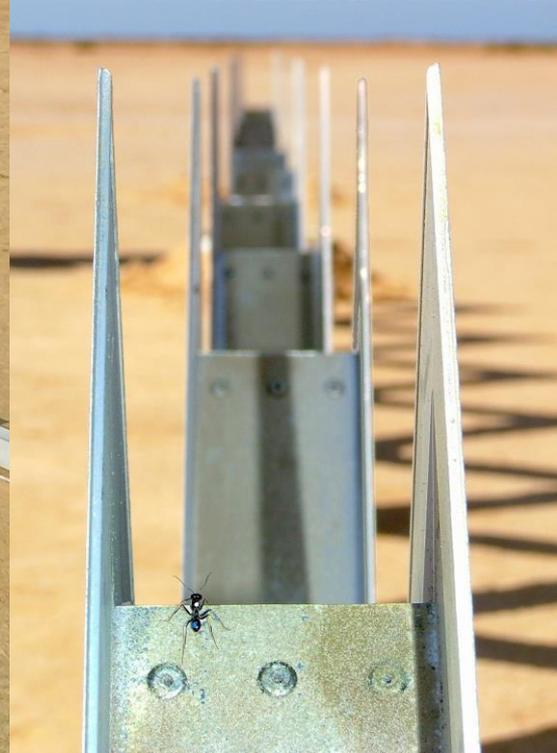
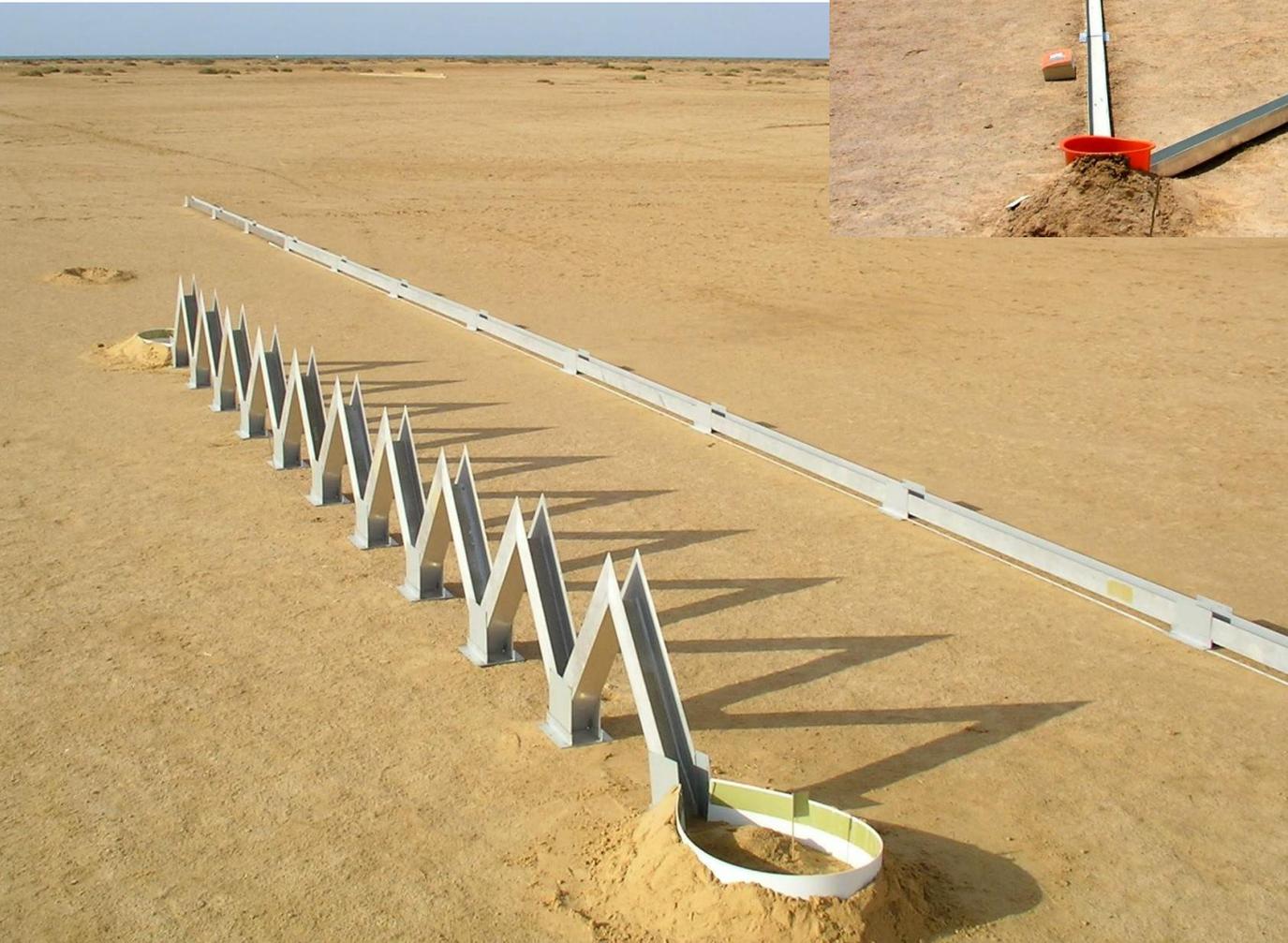


from Wehner 1983

# Kanalexperimente 1D

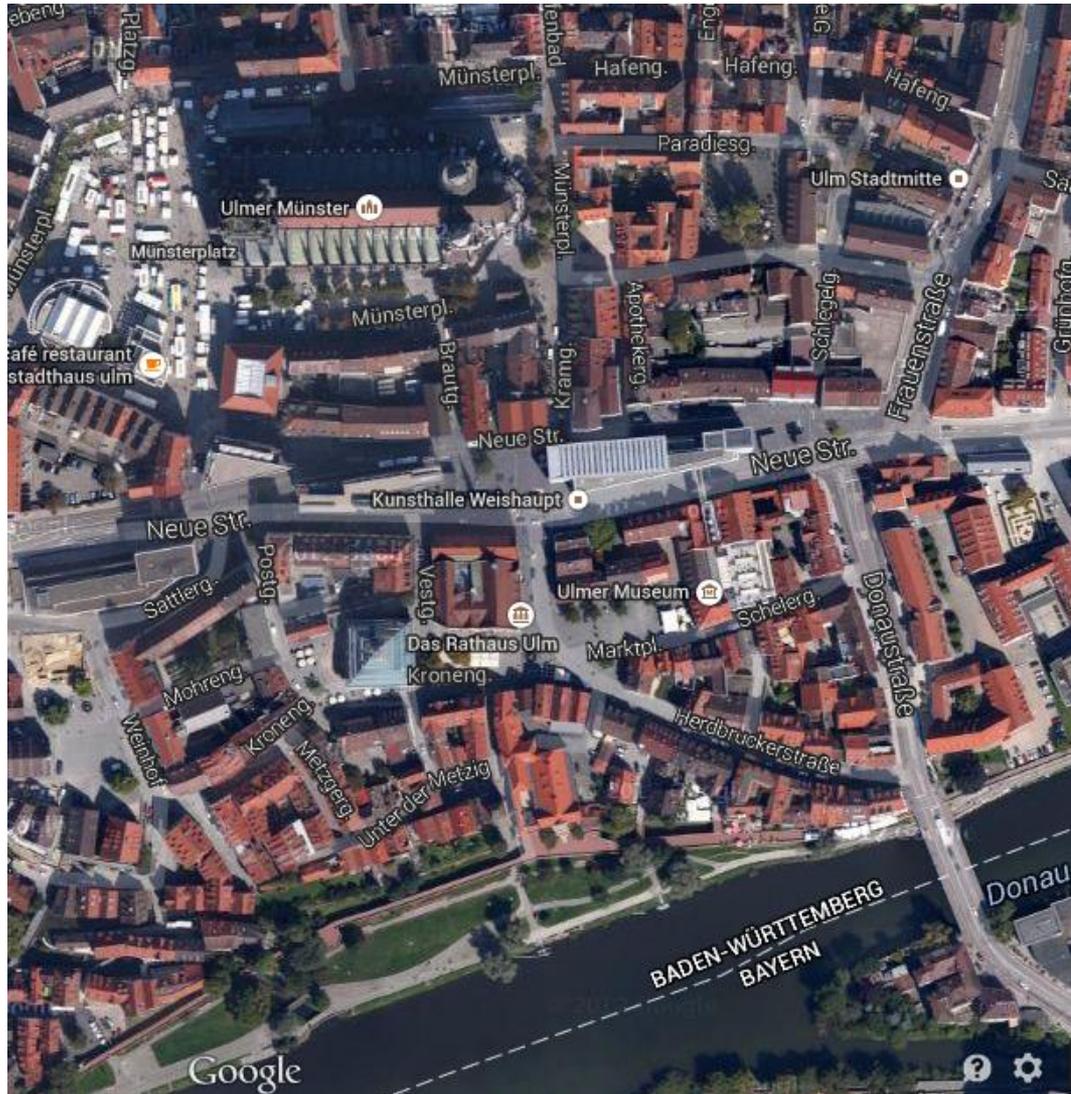


# Kanalexperimente 2D and 3D



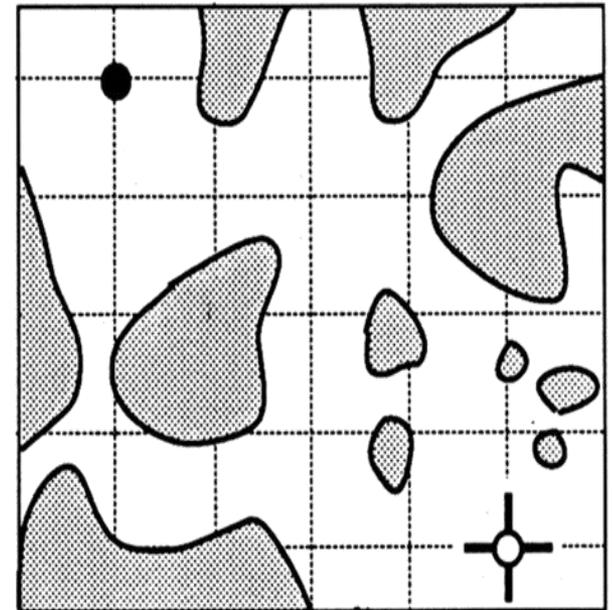


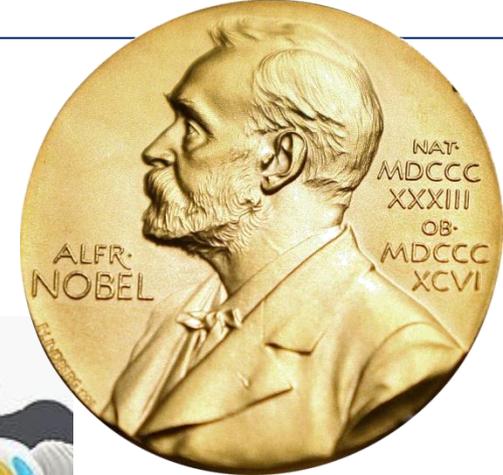
# Grundsätzliche Navigationsstrategien



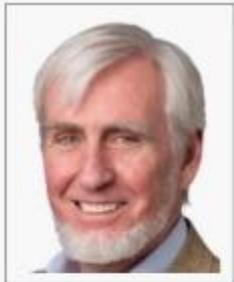
Quelle: <https://www.google.de/maps>

kartenbasierte Systeme

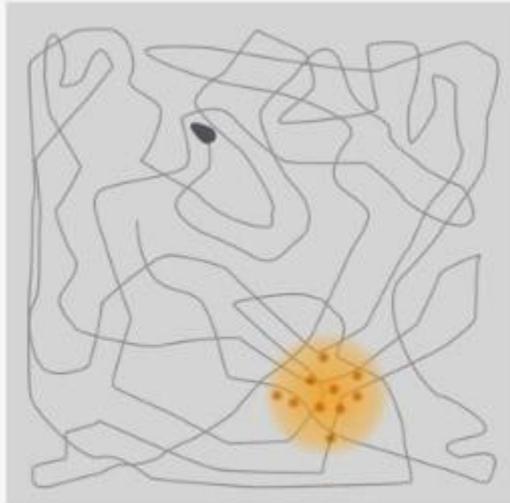




# Nobelpreis für Medizin und Physiologie 2014



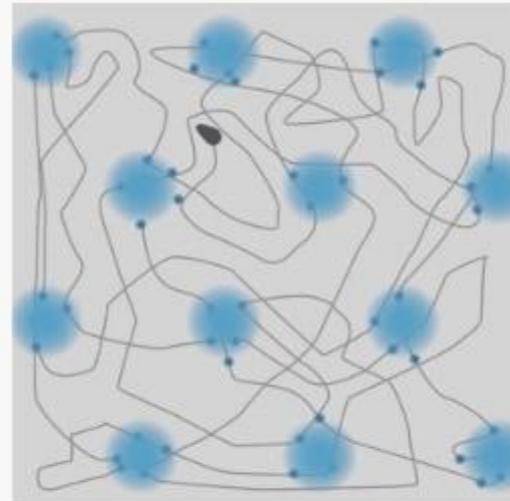
John O'Keefe



May-Britt Moser



Edvard I. Moser



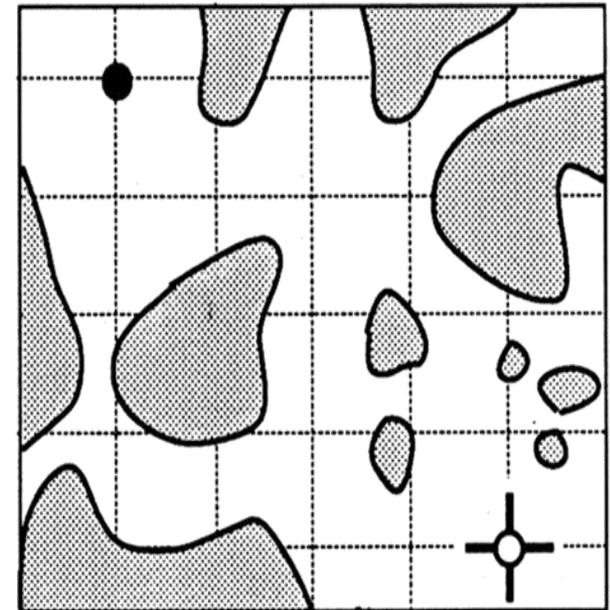
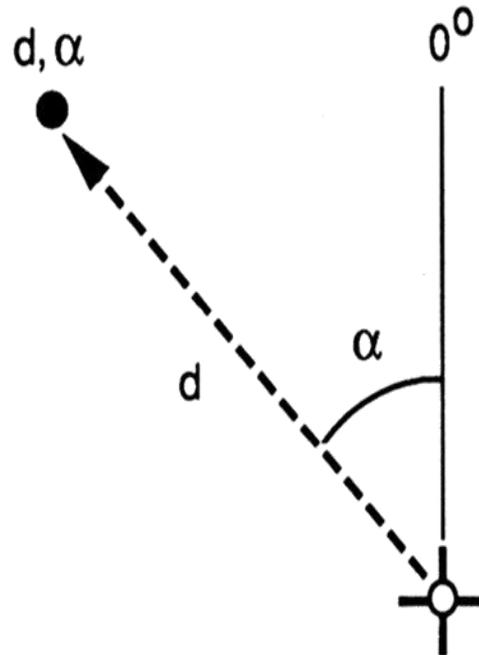
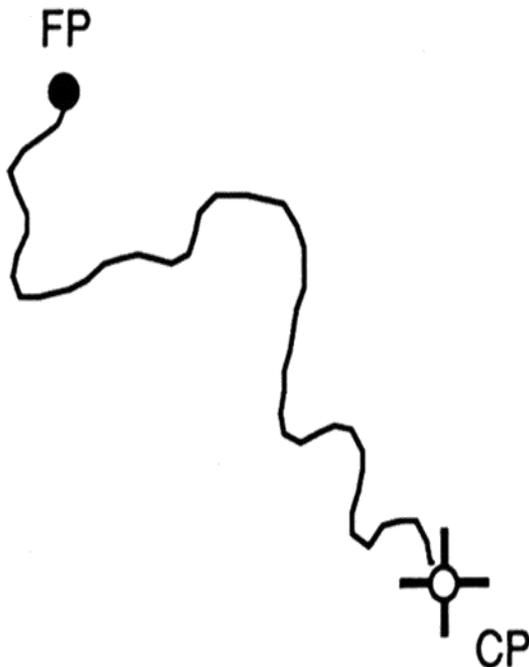
## Grundsätzliche Navigationsstrategien

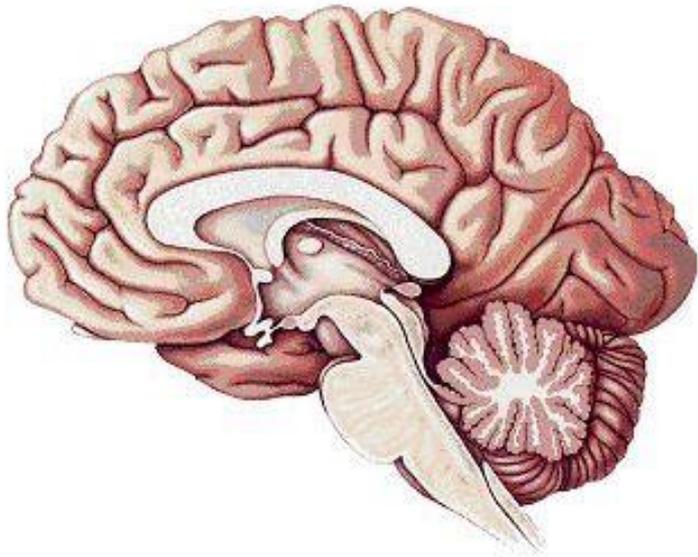
wegebasierte Systeme

kartenbasierte Systeme

dem Weg folgen

Wegintegration



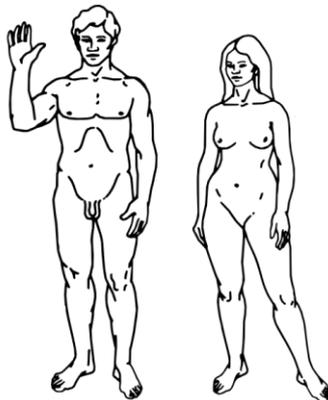


ca. 1,4 kg  
 $10^{11}$  Neuronen



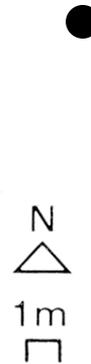
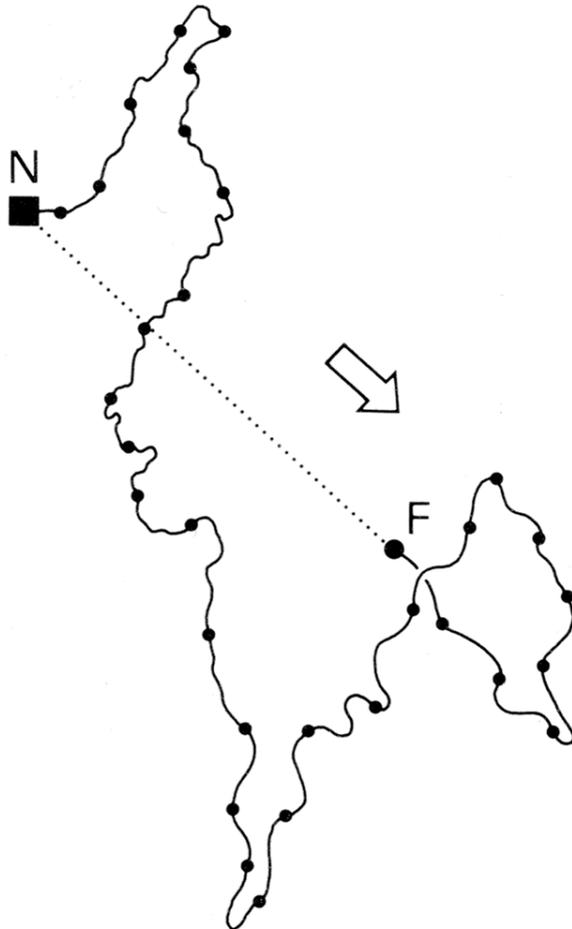
ca. 0,1 mg  
 $10^5$  Neuronen

Wehner 2003



# Versetzungsversuch

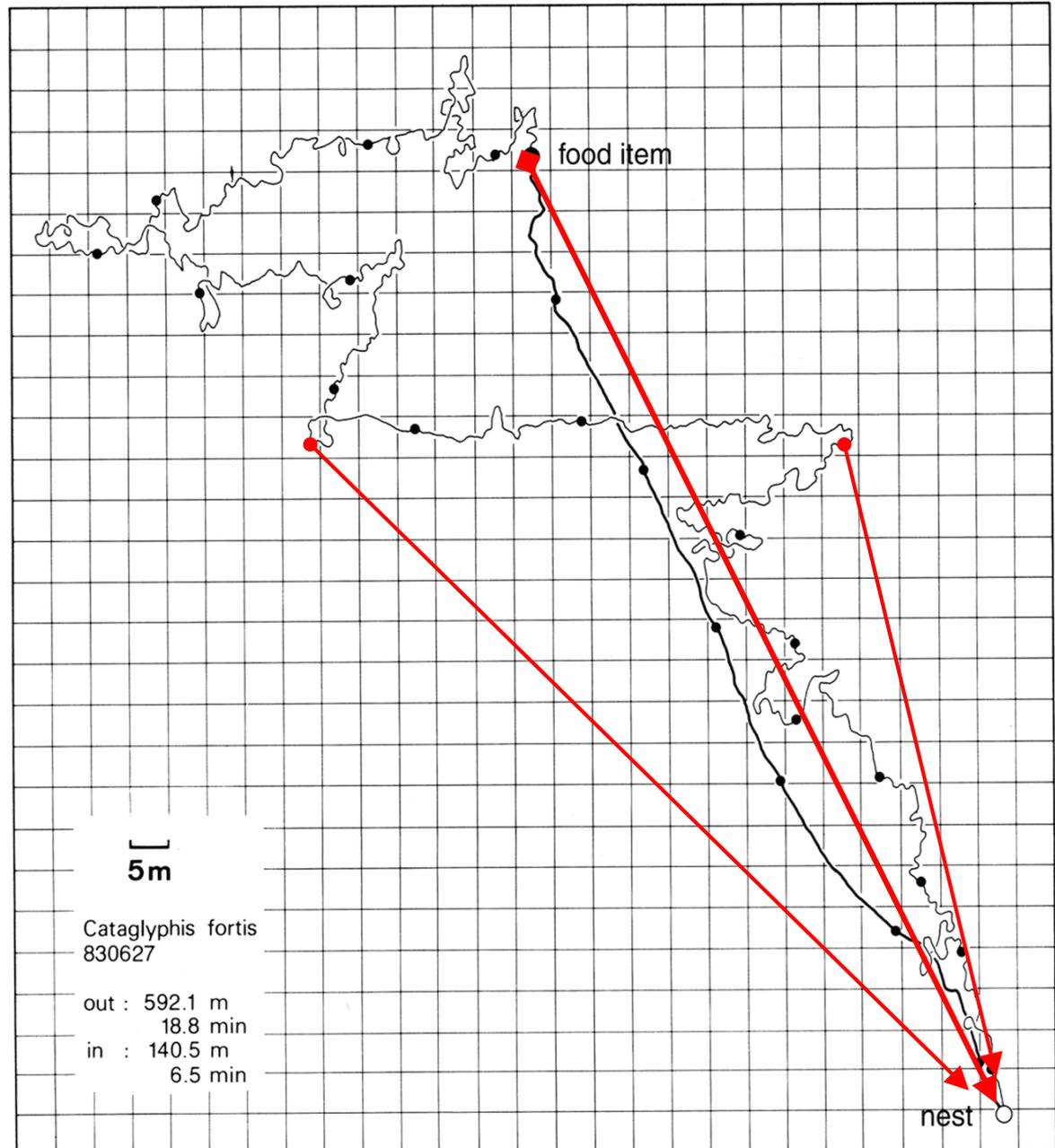
A



## Wegintegration

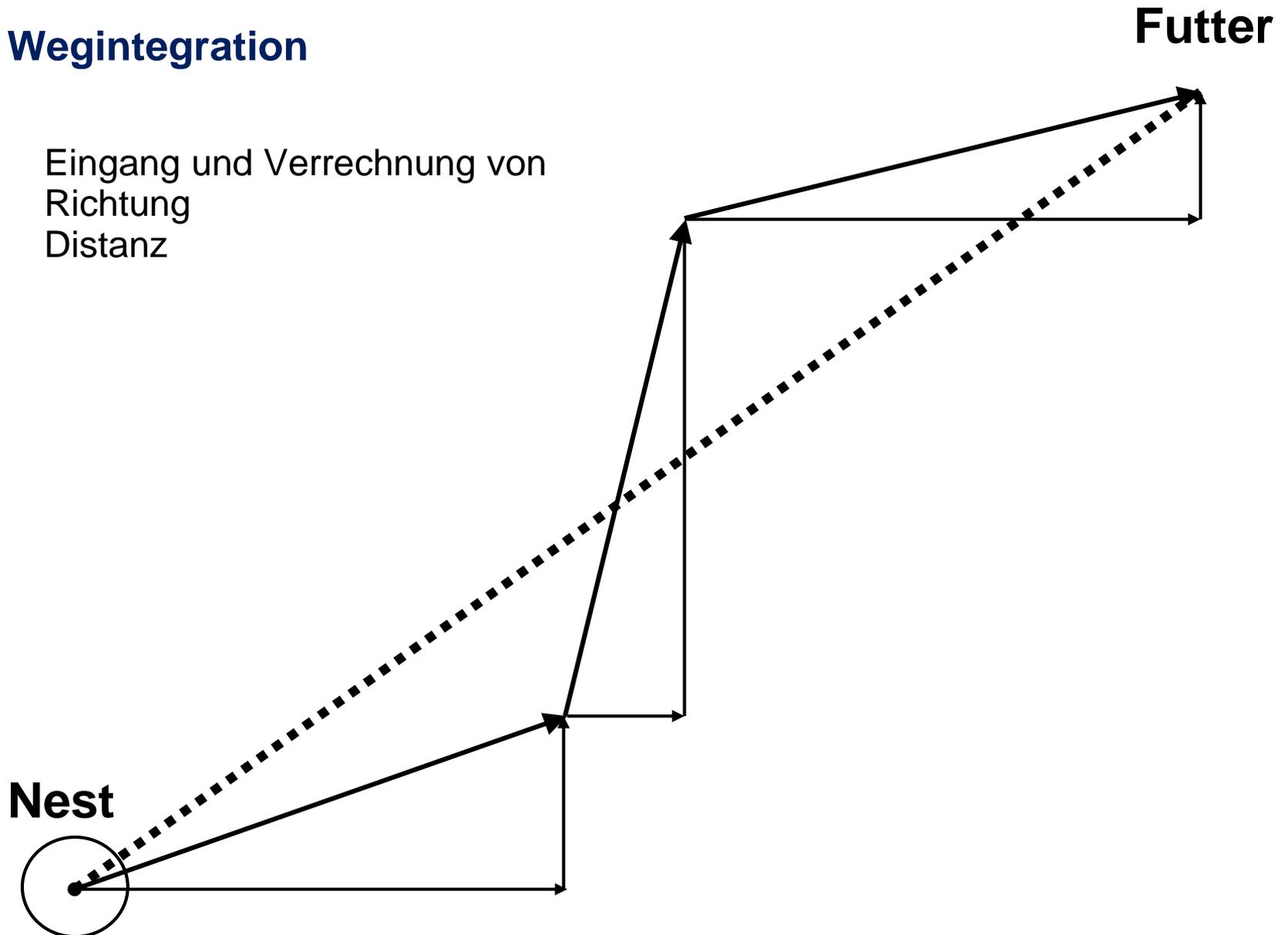
Schritt-für-Schritt  
(angenäherte)  
Vektoraddition

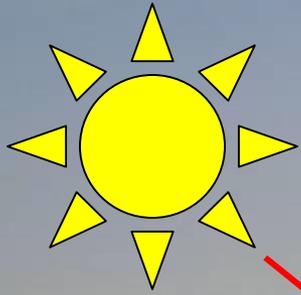
Suche  
Ø 0.52 m/s  
Rückweg  
Ø 0.36 m/s



## Wegintegration

Eingang und Verrechnung von  
Richtung  
Distanz



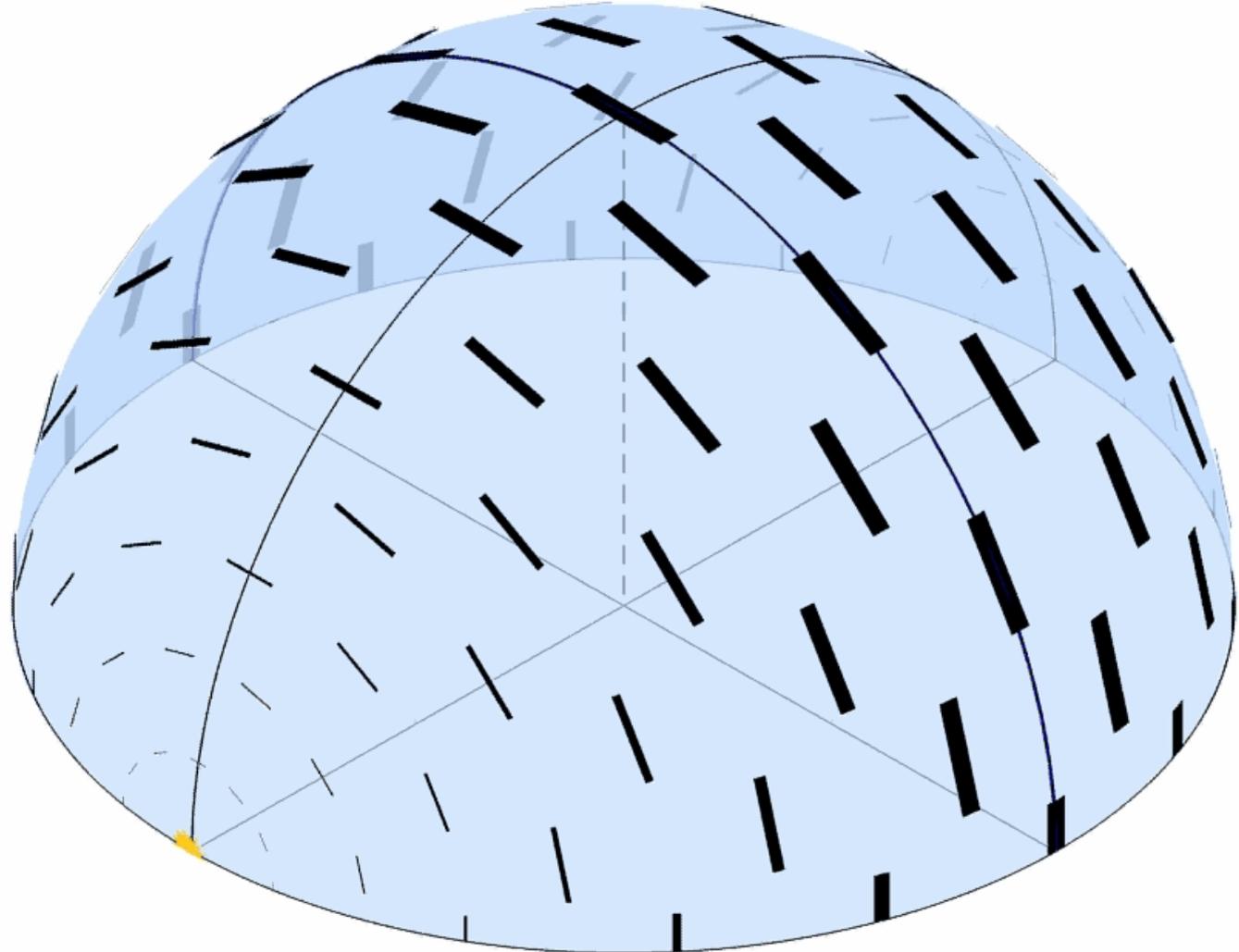


Wie wird die Richtung ermittelt?

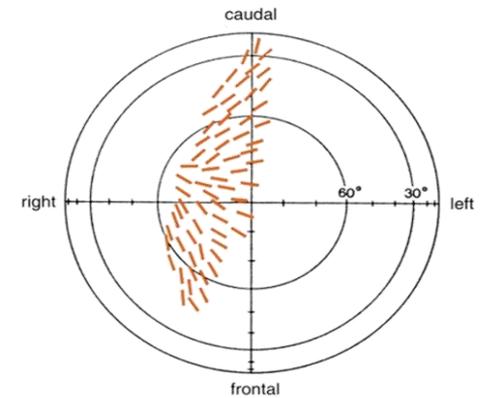
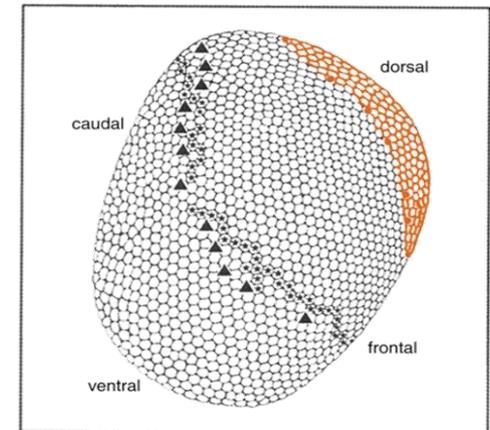
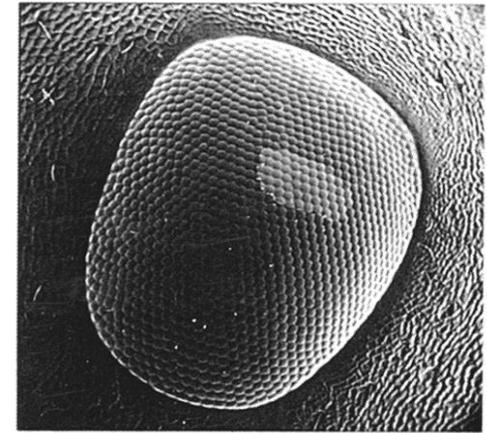
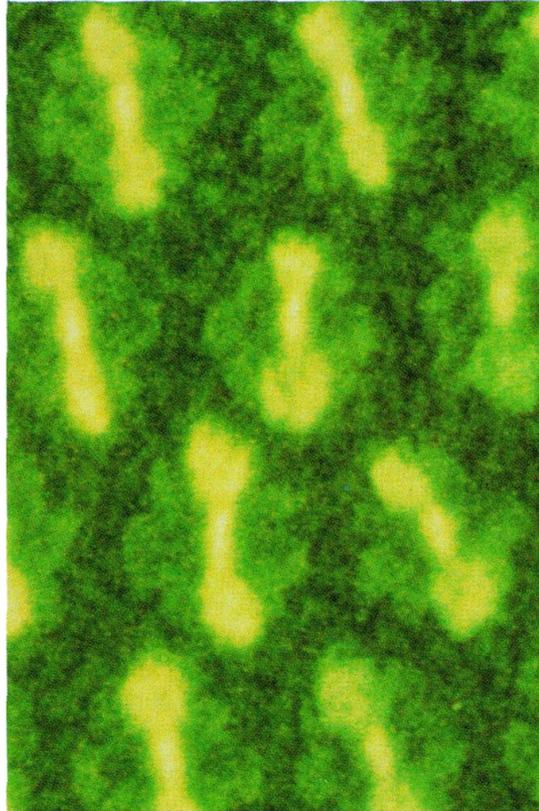
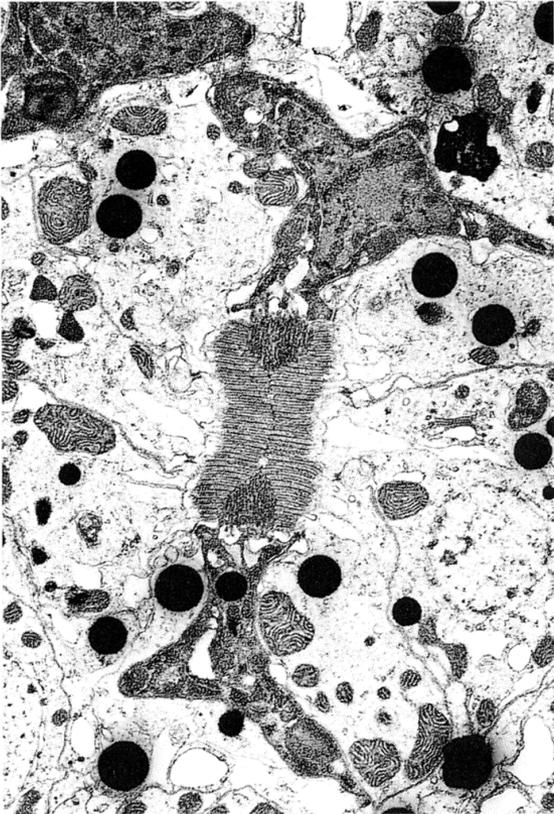
Nest



## Sonnen- und Polarisationskompass



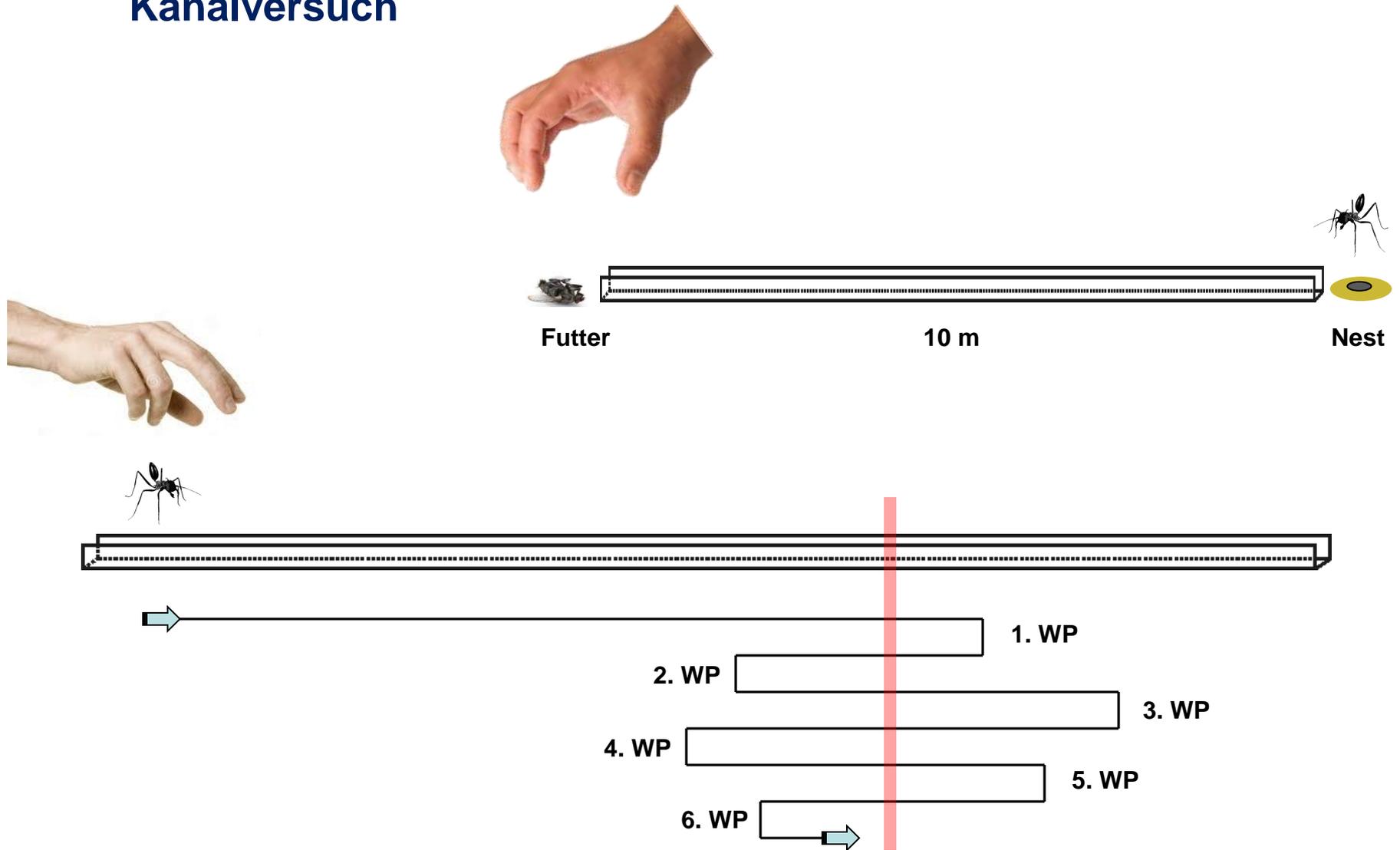
# Filtereigenschaft der Ommatidien dorsalen Augenrand

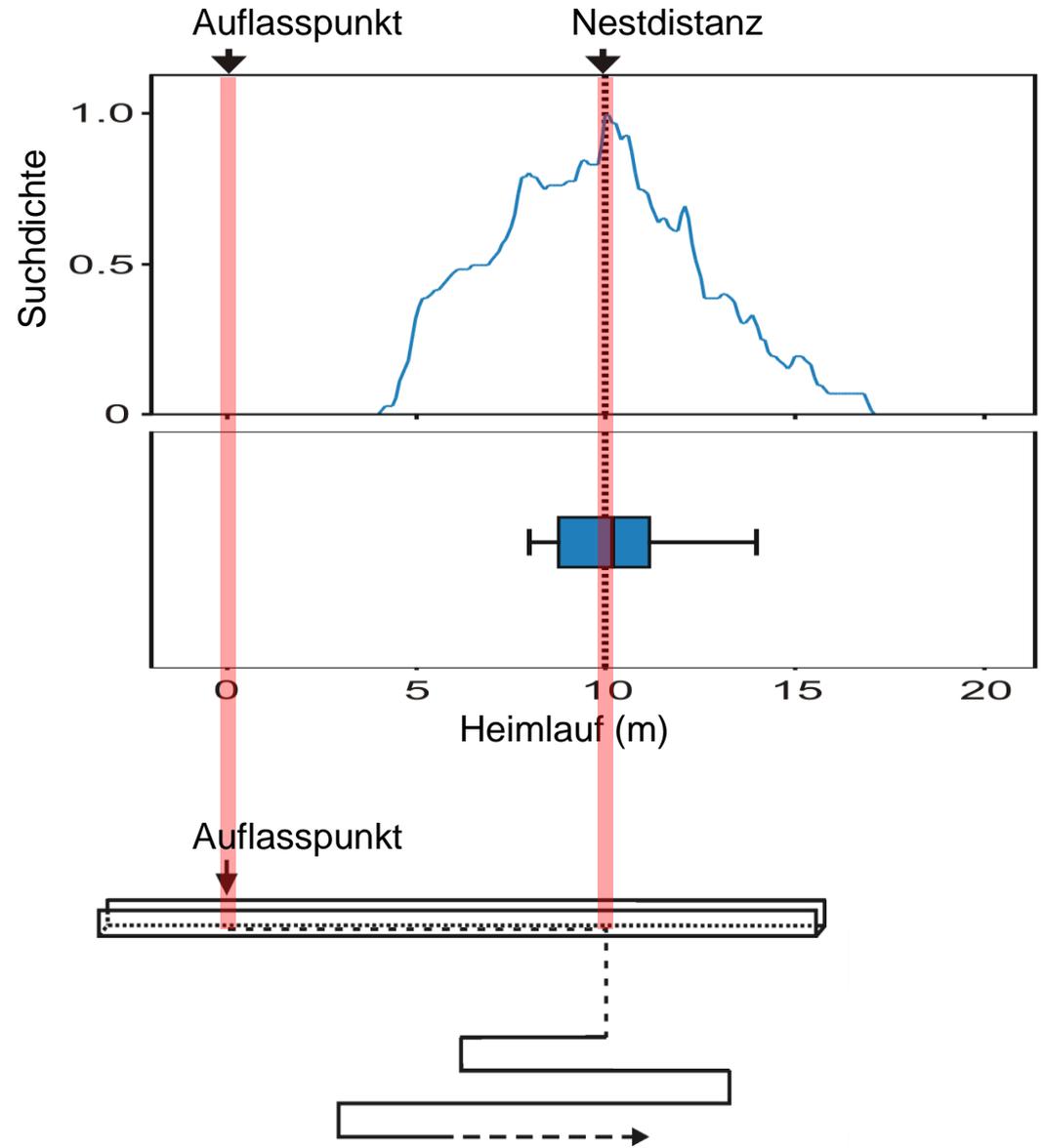
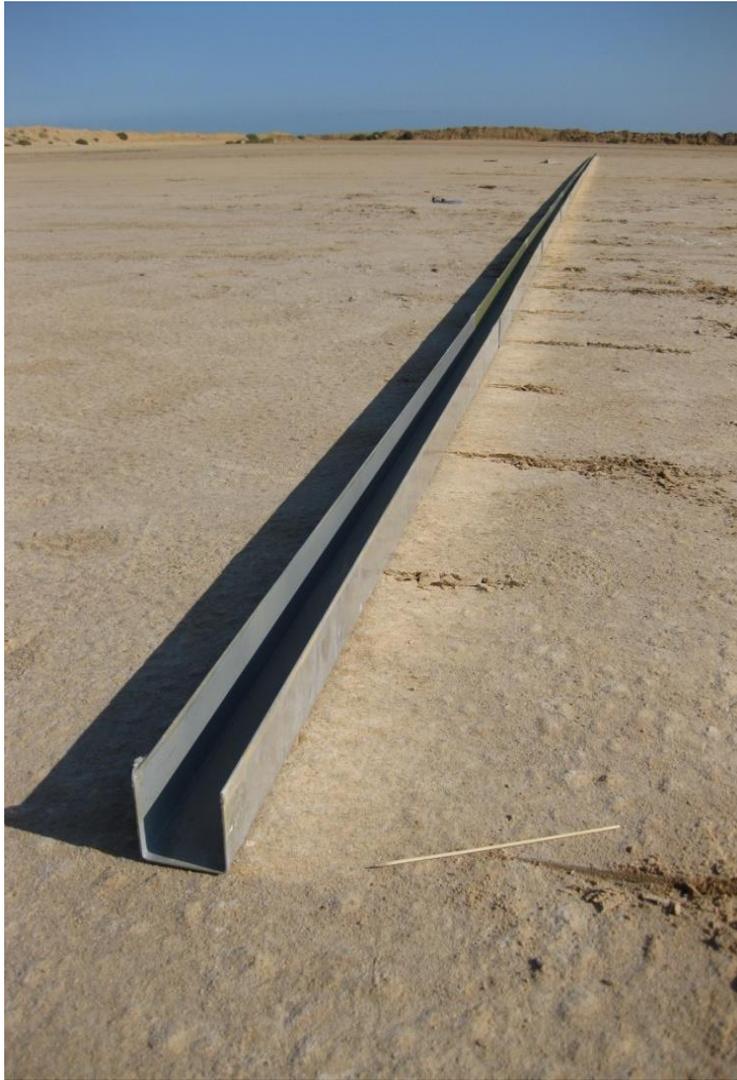


## Distanzmessung Kanalversuch

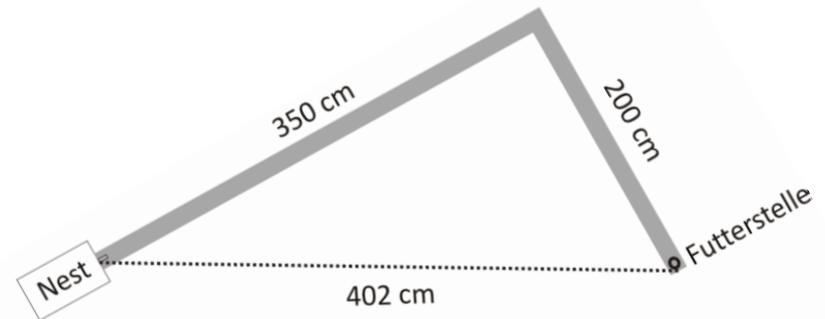
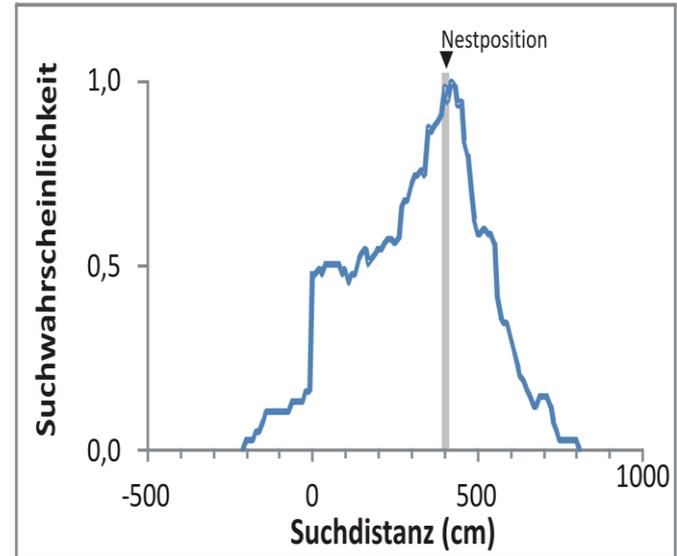


# Distanzmessung Kanalversuch





# Wegintegration Science Camp Sommer 2013



Testkanal

Temperaturen in den Kanälen (14-16 Uhr):  
39,3 - 48,0 °C

## Wie wird die Distanz ermittelt?

### Energieverbrauch ?

Schäfer & Wehner 1993; Wohlgemuth et al. 2002



### Zeitmesser ?

Wohlgemuth et al. 2001; 2002



### Optischer Fluss ?

Ronacher & Wehner 1995; Ronacher et al. 2000



### Schrittintegration ?

Wittlinger et al. 2006; 2007



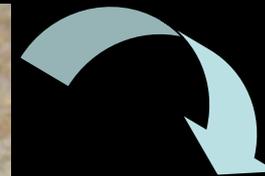
# Beinverlust unterwegs



**Aggression**



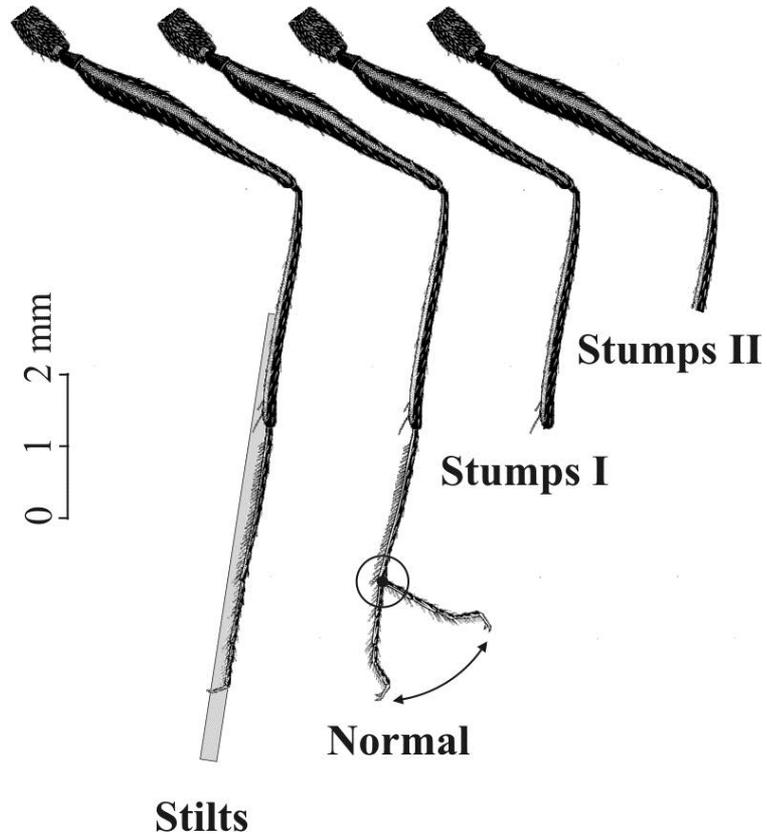
**Kampf**



**“Verlierer”**

**Verlust: 1,5 Beine, 1 Antenne**

## Systematische Beinlängenänderung



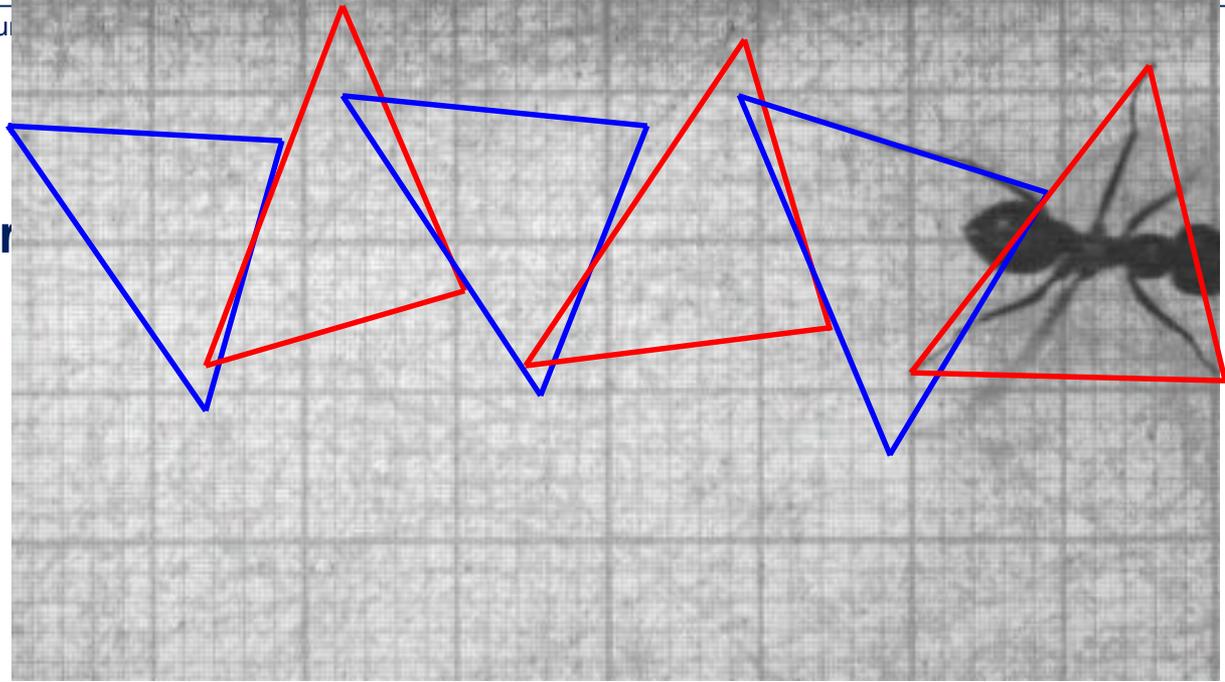




normal

$v = 0,28 \text{ m/s}$

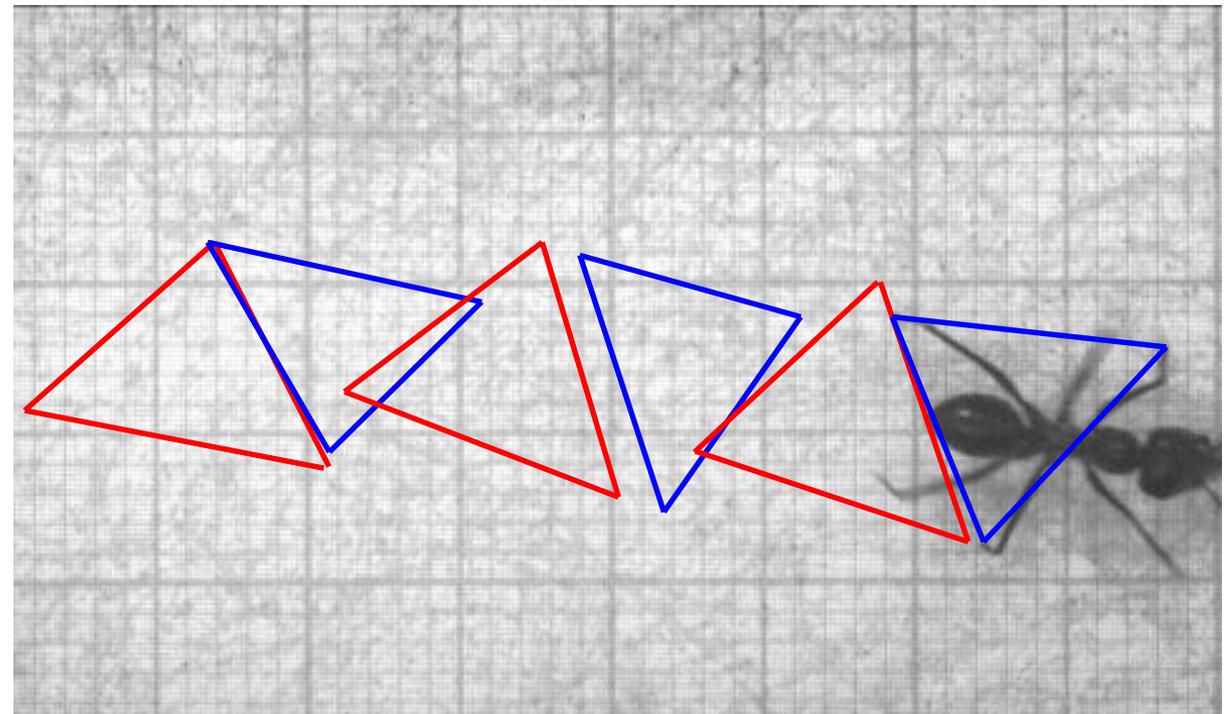
$sl = 14 \text{ mm}$

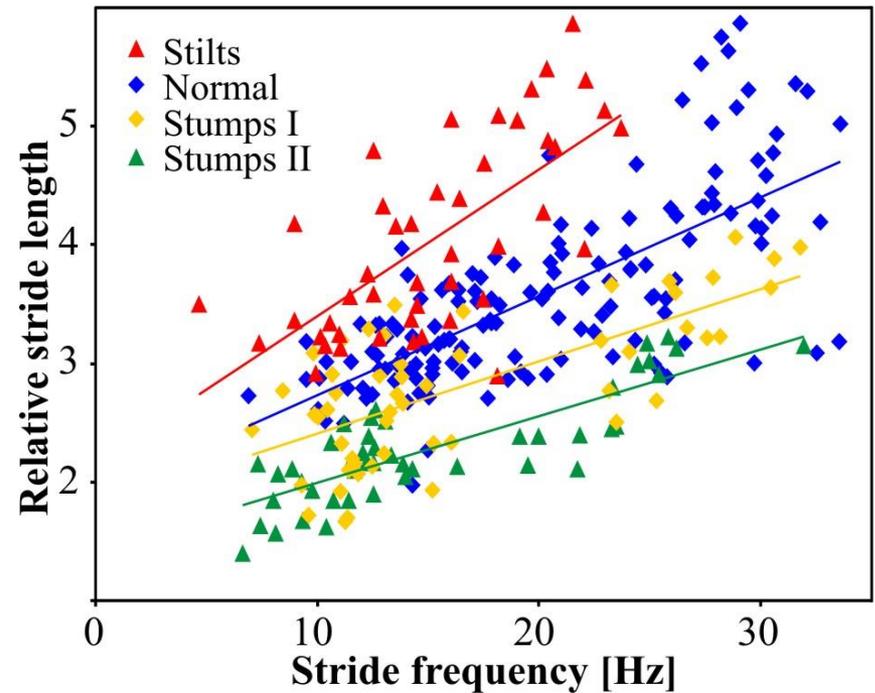
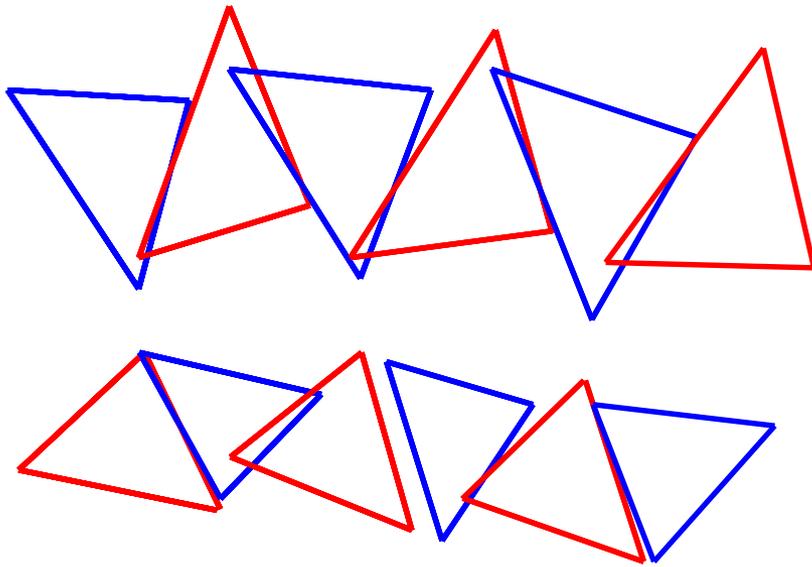


stumps II

$v = 0,27 \text{ m/s}$

$sl = 11 \text{ mm}$



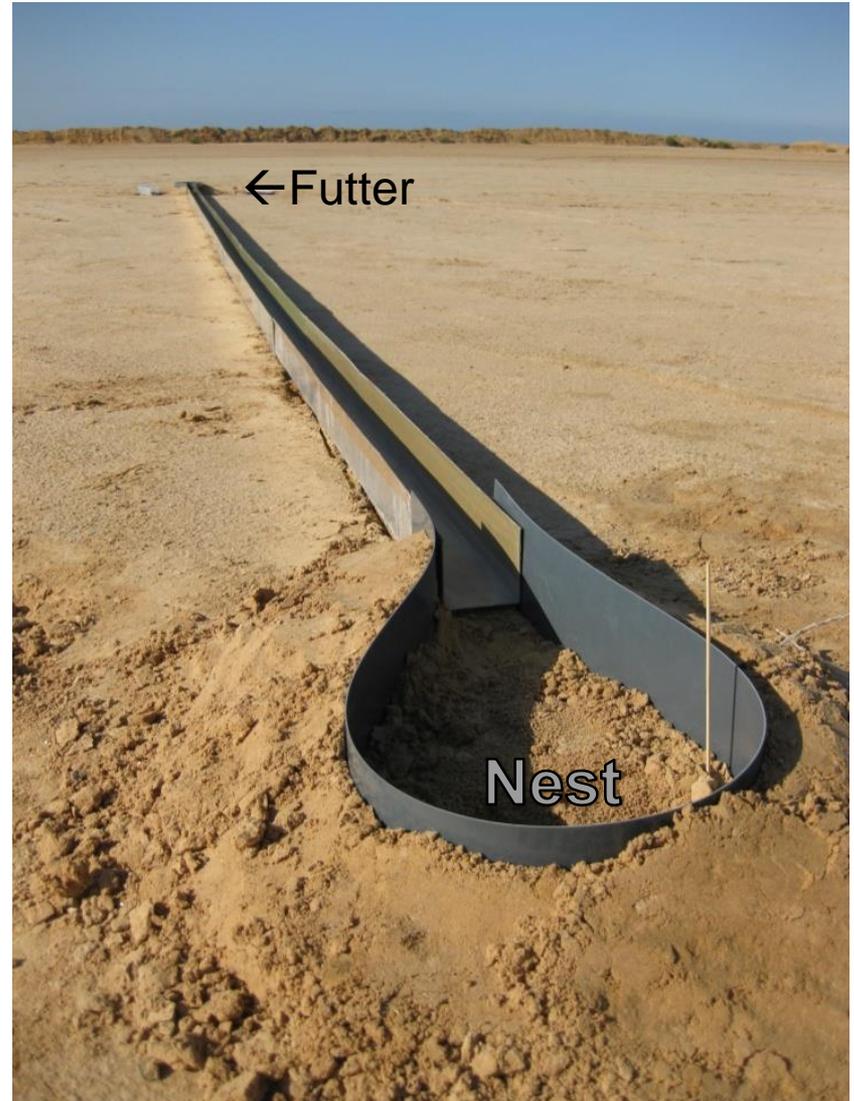


Tripode Gangart bleibt unverändert

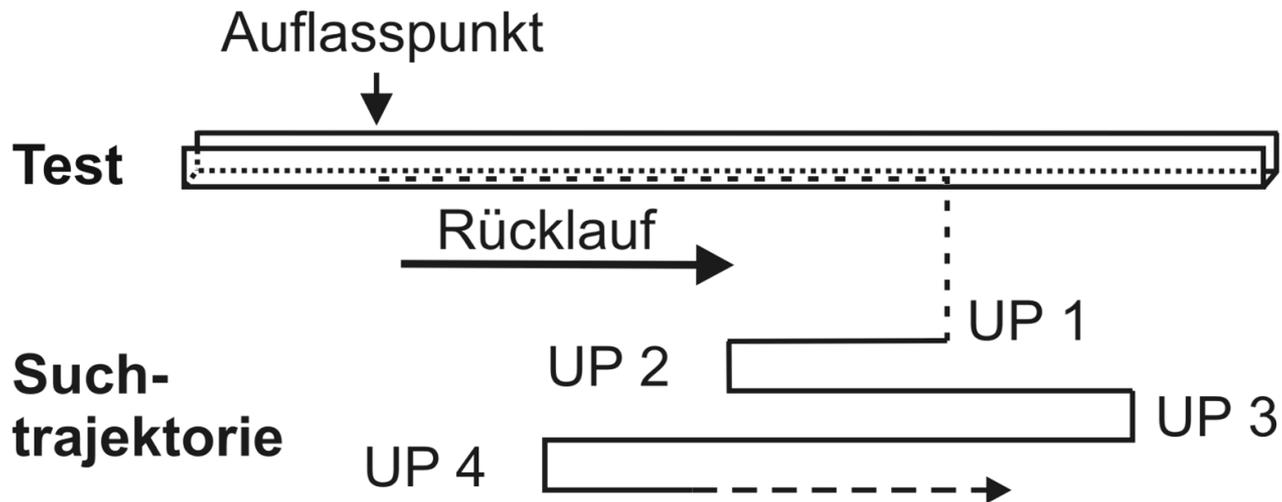
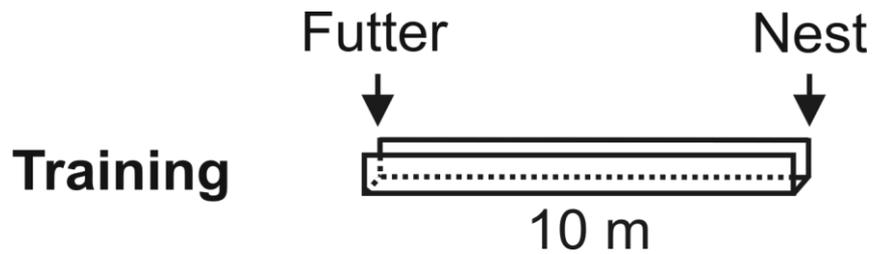
Veränderung der Schrittlängen

- kurze Beine – kurze Schritte
- lange Beine – lange Schritte

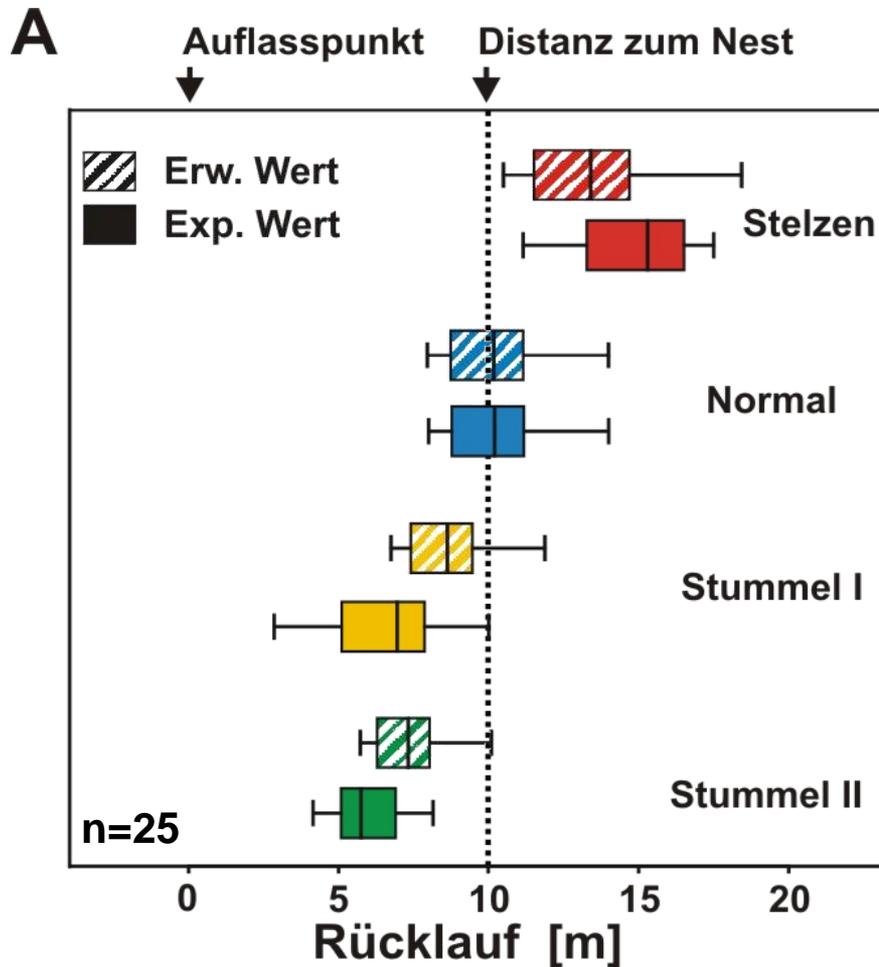
Beziehung zwischen Frequenz und Schrittlänge bleibt erhalten



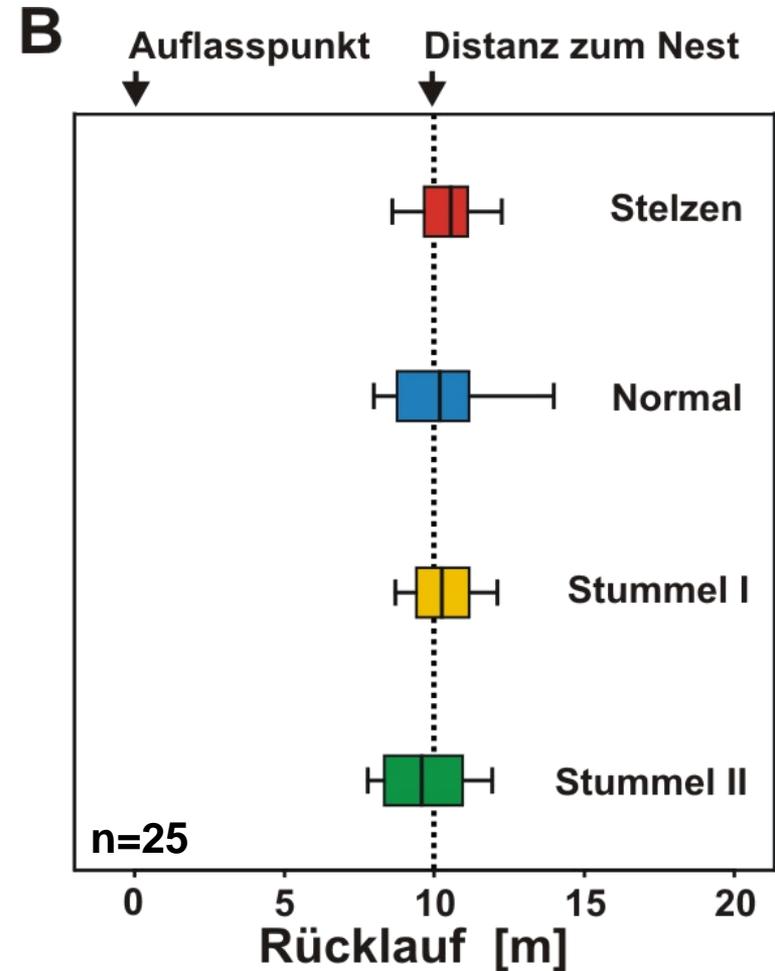
## Odometer



Hinlauf - Rücklauf  
normal manipuliert



Hinlauf - Rücklauf  
manipuliert manipuliert

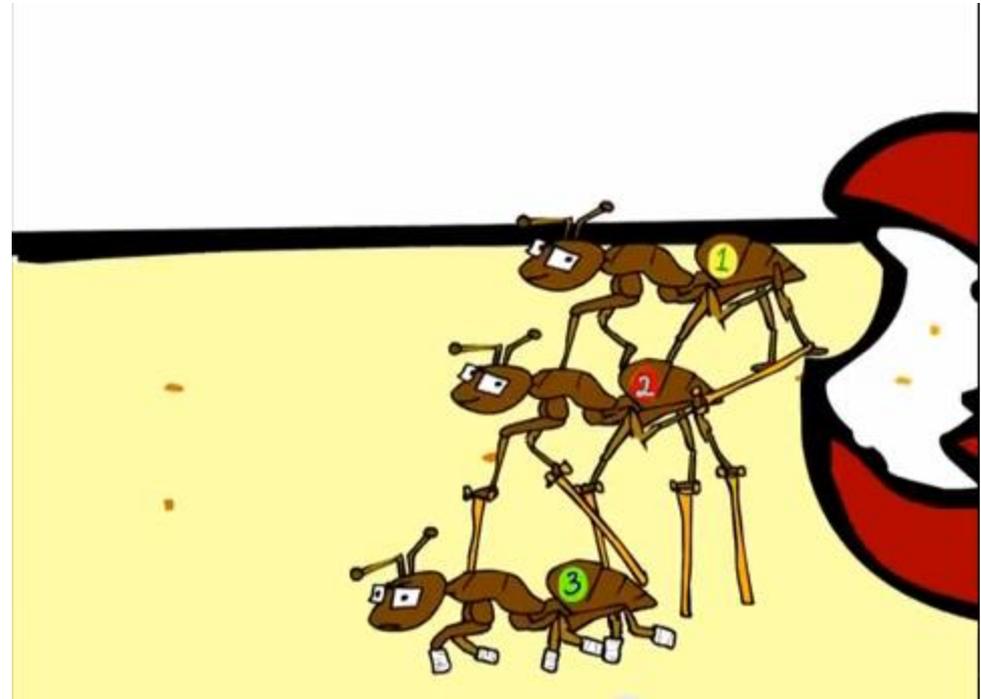


## *Cataglyphis* Wüstenameisen

Wegintegration

Richtung:  
Himmelskompass

Entfernung:  
Schrittintegration



<http://www.youtube.com/watch?v=7DDF8WZFnoU>



## Wie wird die Distanz ermittelt?

### Energieverbrauch ?

Schäfer & Wehner 1993; Wohlgemuth et al. 2002



### Zeitmesser ?

Wohlgemuth et al. 2001; 2002



### Optischer Fluss ?

Ronacher & Wehner 1995; Ronacher et al. 2000

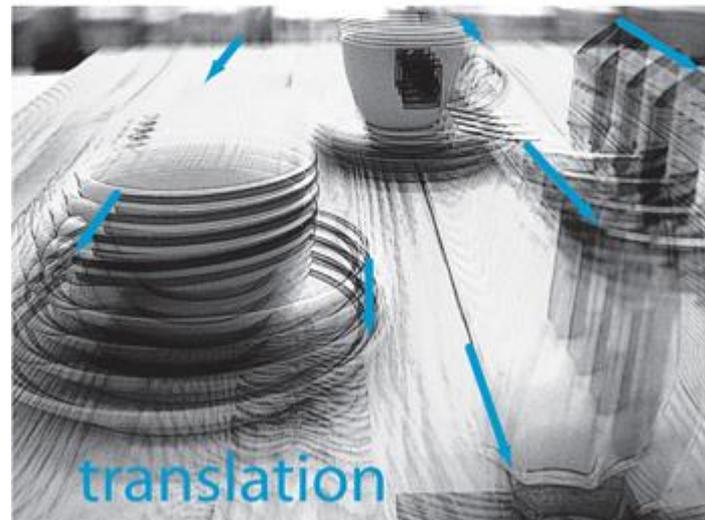
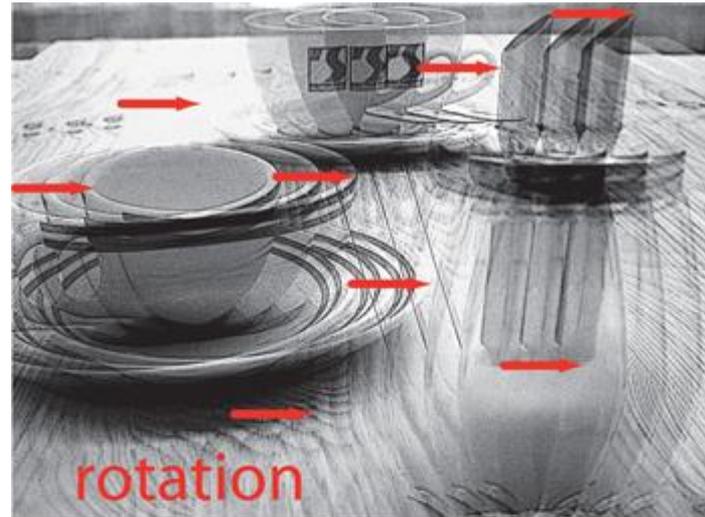


### Schrittintegration !

Wittlinger et al. 2006; 2007



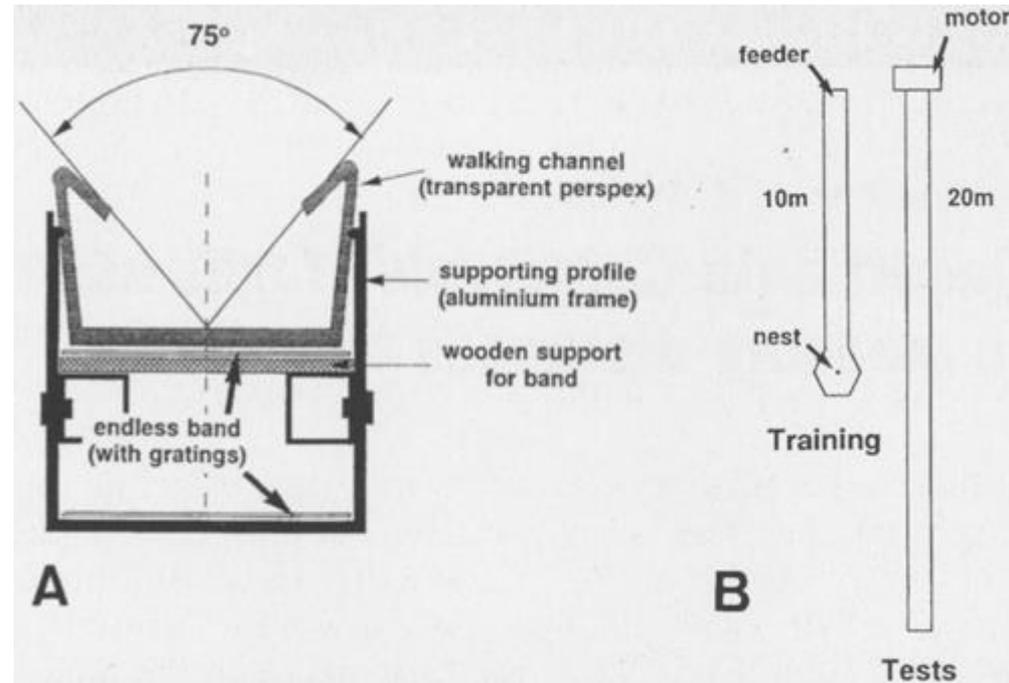
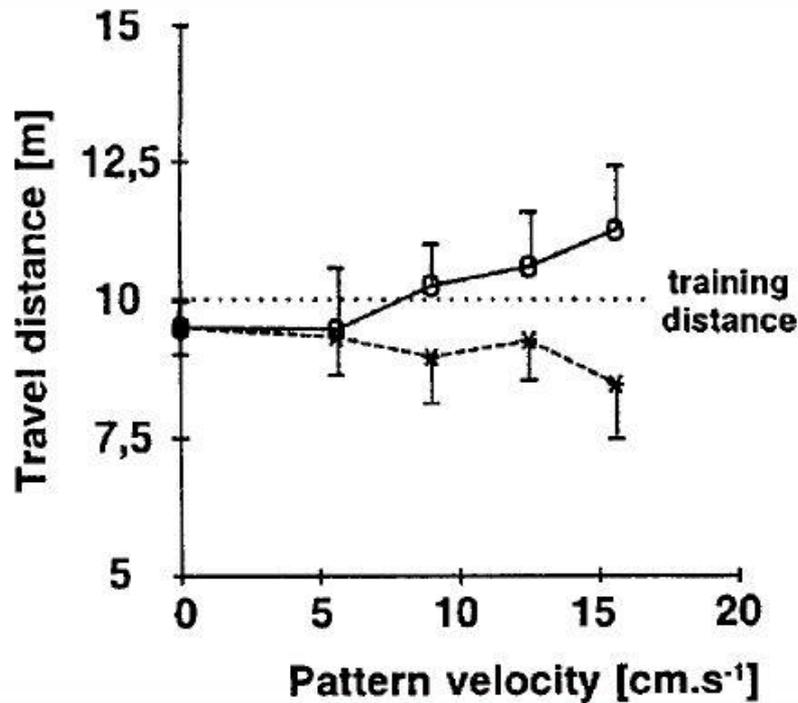
## Was ist optischer Fluss?



ORIGINAL PAPER

B. Ronacher · R. Wehner

# Desert ants *Cataglyphis fortis* use self-induced optic flow to measure distances travelled



## Ameisen laufen und sehen

Verhaltensexperiment gesucht bei dem die beiden Inputs klar voneinander getrennt werden können.

### Blinde Ameisen ???

=> zeigen, dass der Pedometer alleine ausreicht

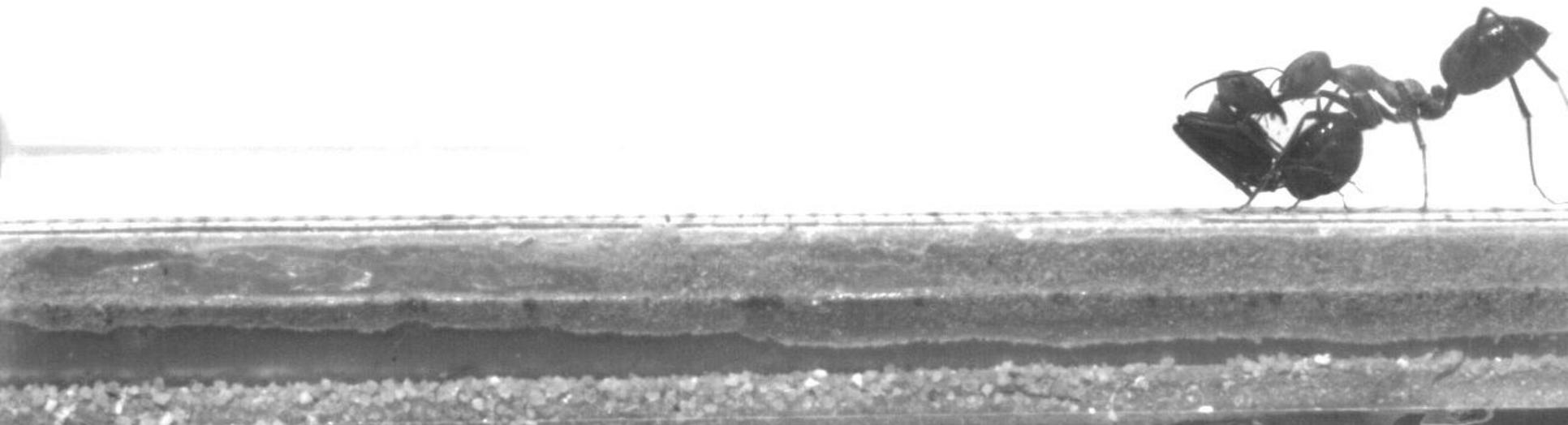


### Nicht-laufende Ameisen ???



## Carrier – Carried Paare

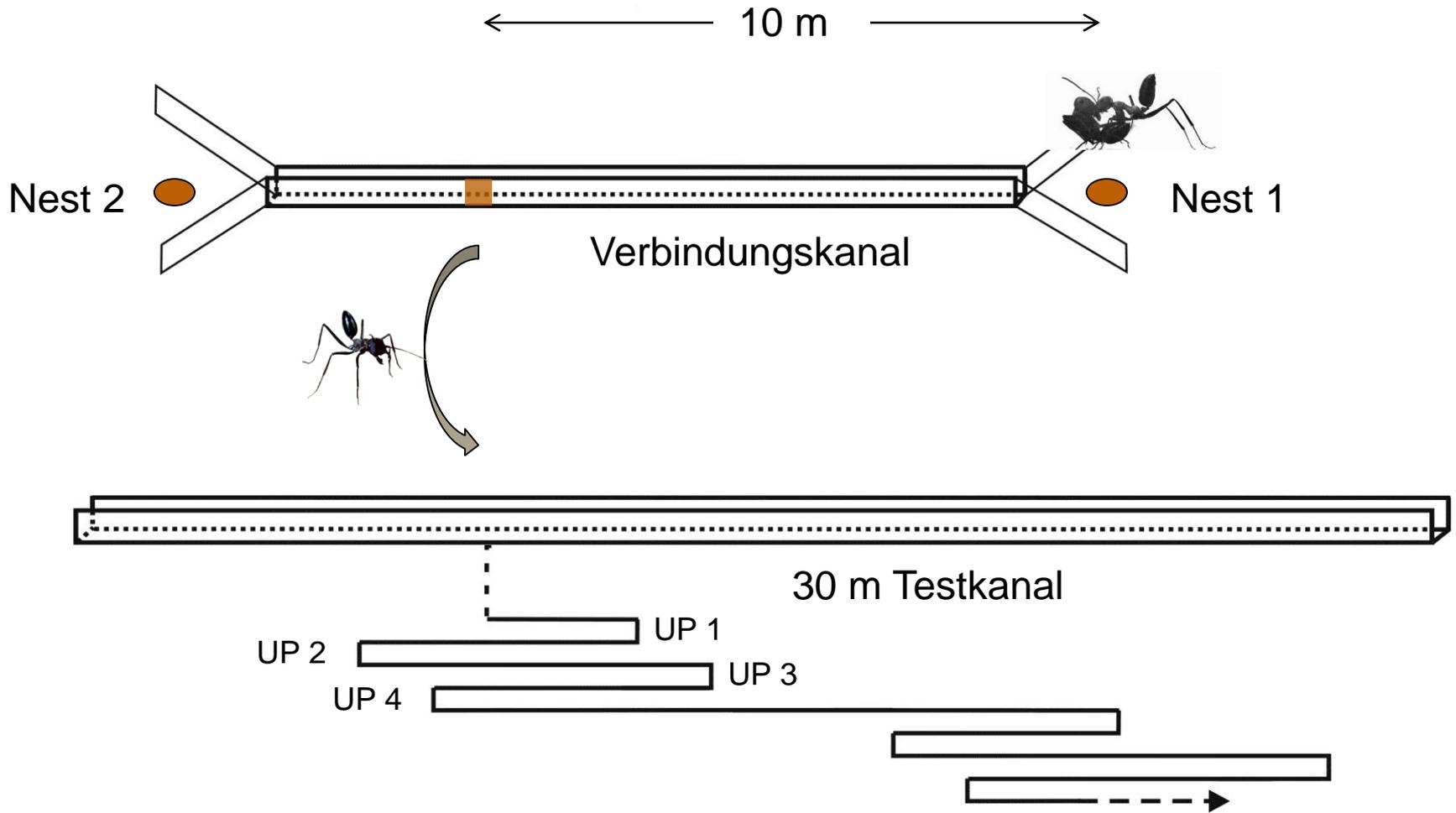
- Trägerin und Getragene Ameise erhalten denselben Betrag an Optischem Fluss
- Nur die Trägerin macht aktiv Lokomotion



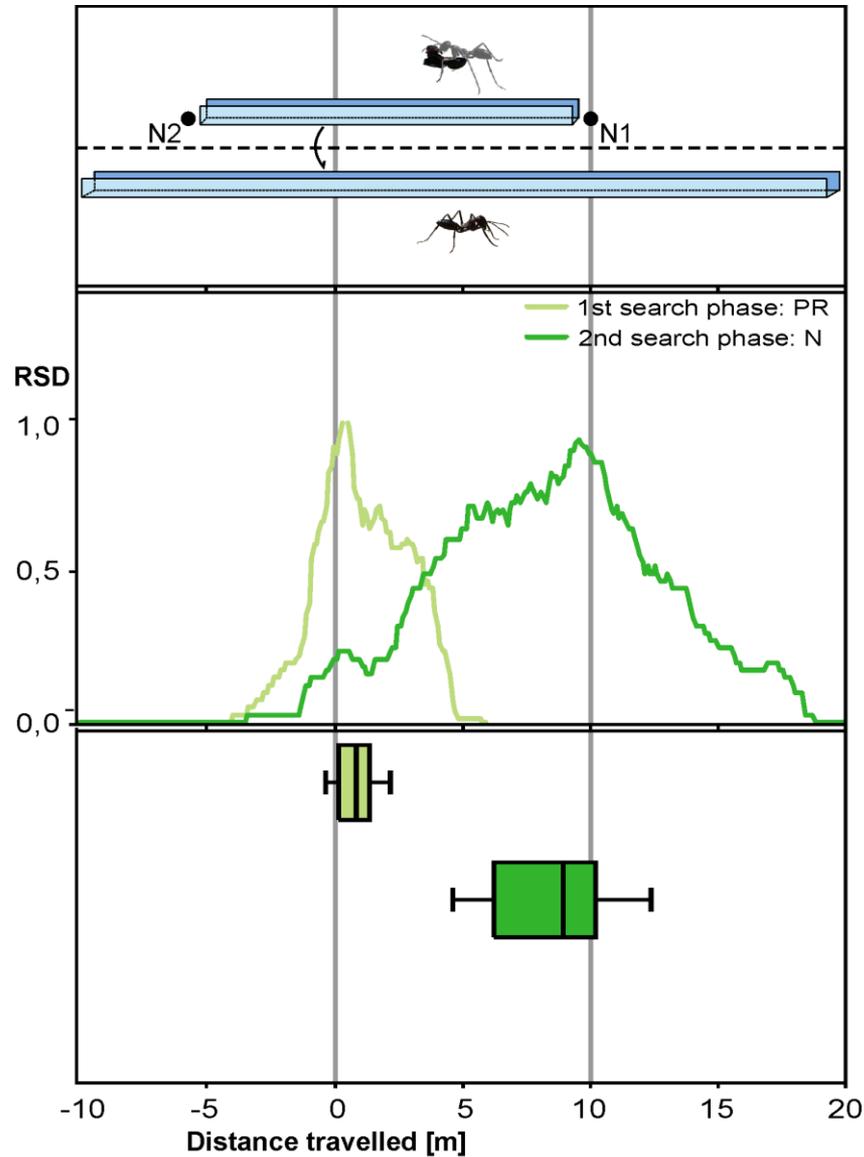


Nest 2 ●

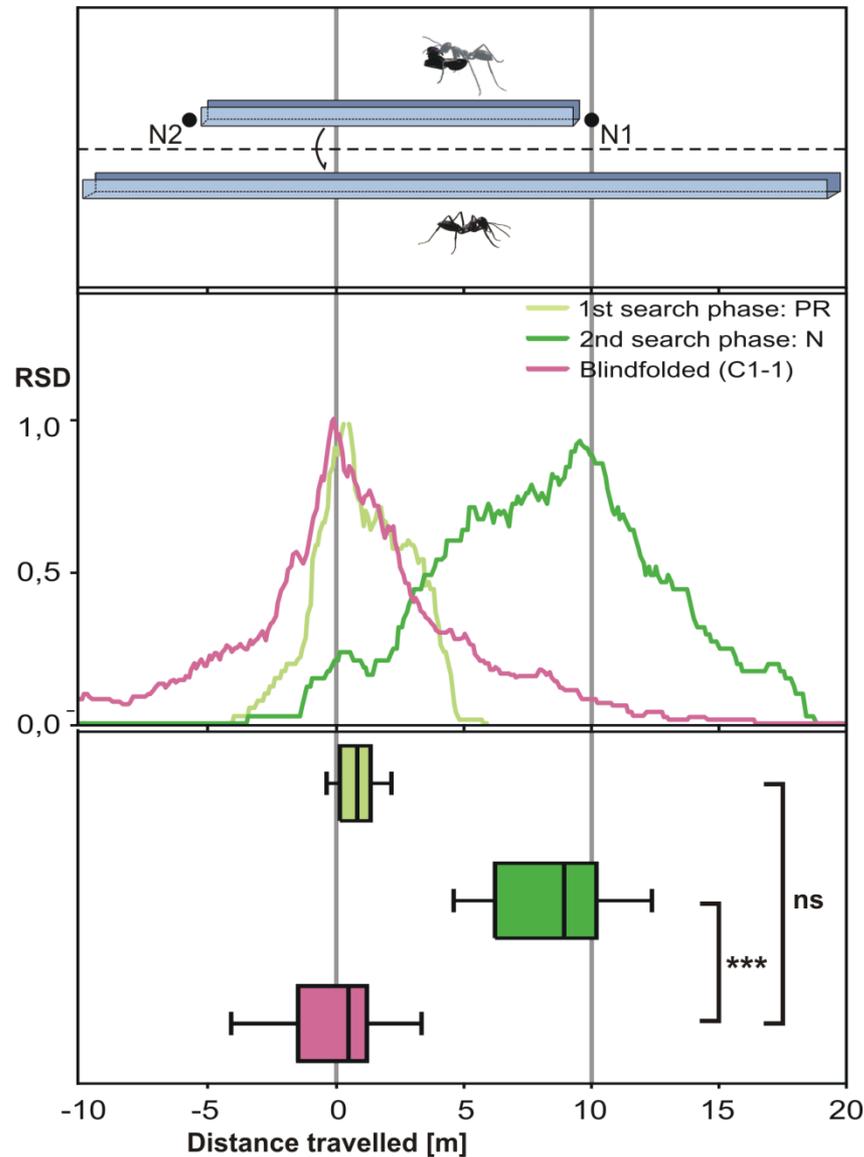
● Nest 1



## Optischer Fluss - Experiment



## Optischer Fluss - Experiment



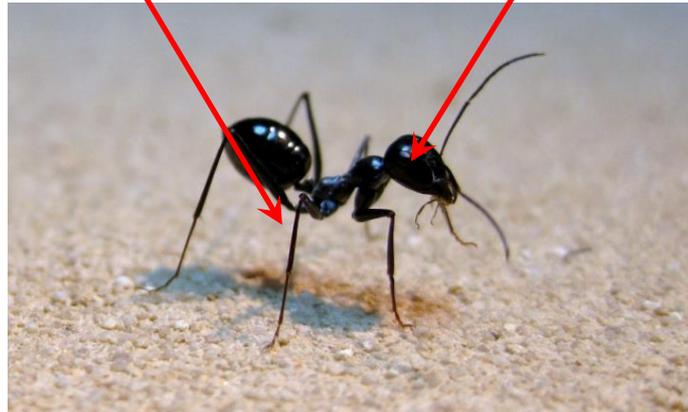
# Odometry in Cataglyphis



step integration

!

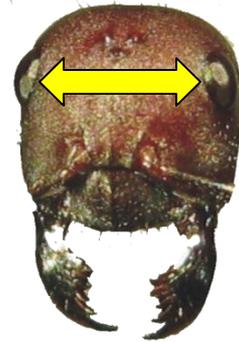
optic flow integration



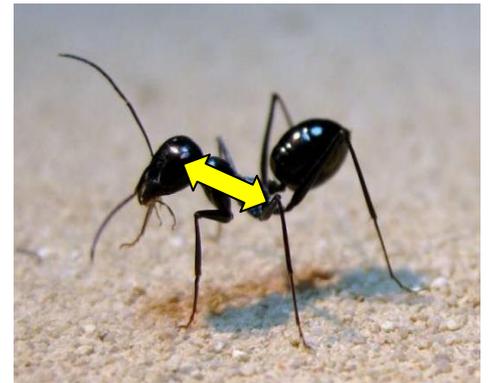
## Questions

Gibt es **Informationstransfer** zwischen:

- **Beiden Augen** (Inter-Ocular Transfer - IOT) ?

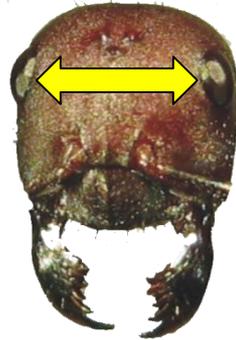


- **Beiden Odometersystemen** (OF-Meter - Pedometer) ?



## Interocular transfer-experiment

- Interocular Transfer (IOT) of OF Information ist möglich



228

LETTERS TO NATURE

NATURE VOL. 315 16 MAY 1985

### Does interocular transfer occur in visual navigation by ants?

Rüdiger Wehner & Martin Müller

Department of Zoology, University of Zurich,  
Winterthurerstrasse 190, CH-8057 Zurich, Switzerland

If an animal that learns to respond to a visual stimulus presented to only one eye can continue to respond accurately when the stimulus is presented to the other eye, it is said to exhibit interocular transfer (IOT). IOT has been studied extensively in many groups of vertebrates<sup>1-11</sup>, but of IOT in an invertebrate (*Oecophylla smaragdina*, an insect, the desert ant *Cataglyphis*) by the pattern of polarized light when it uses landmarks for orientation. In this paper we report on behavioural performance measurements on the strategies adopted by insects and terrestrial cues for navigation.

Insects possess multi-faceted eyes with full panoramic vision. In the long-legged Saharan ant *Oecophylla smaragdina*, which the visual fields of the two eyes cover 93% of the unit

Wehner & Müller, 1985

Polarization Kompass: IOT möglich  
Landmarken: kein IOT

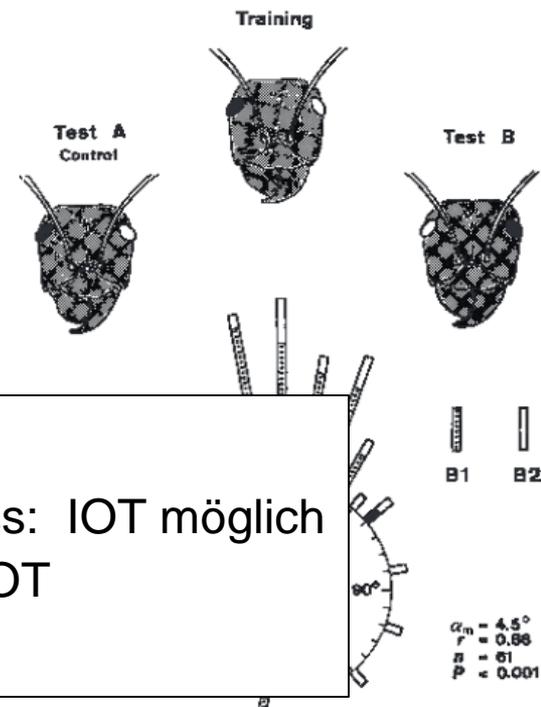
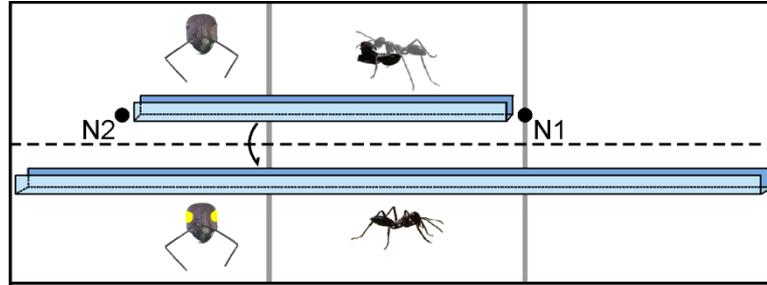
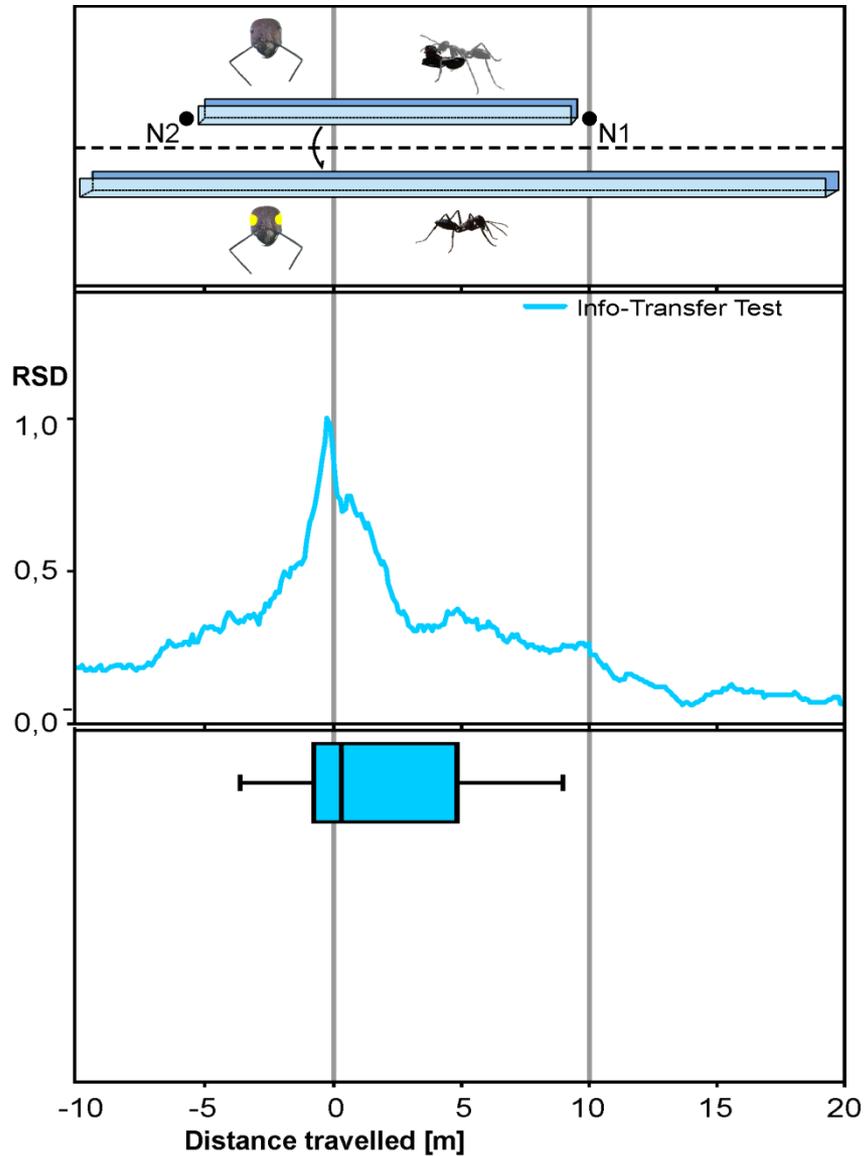


Fig. 1 Ants exhibit interocular transfer of visual information

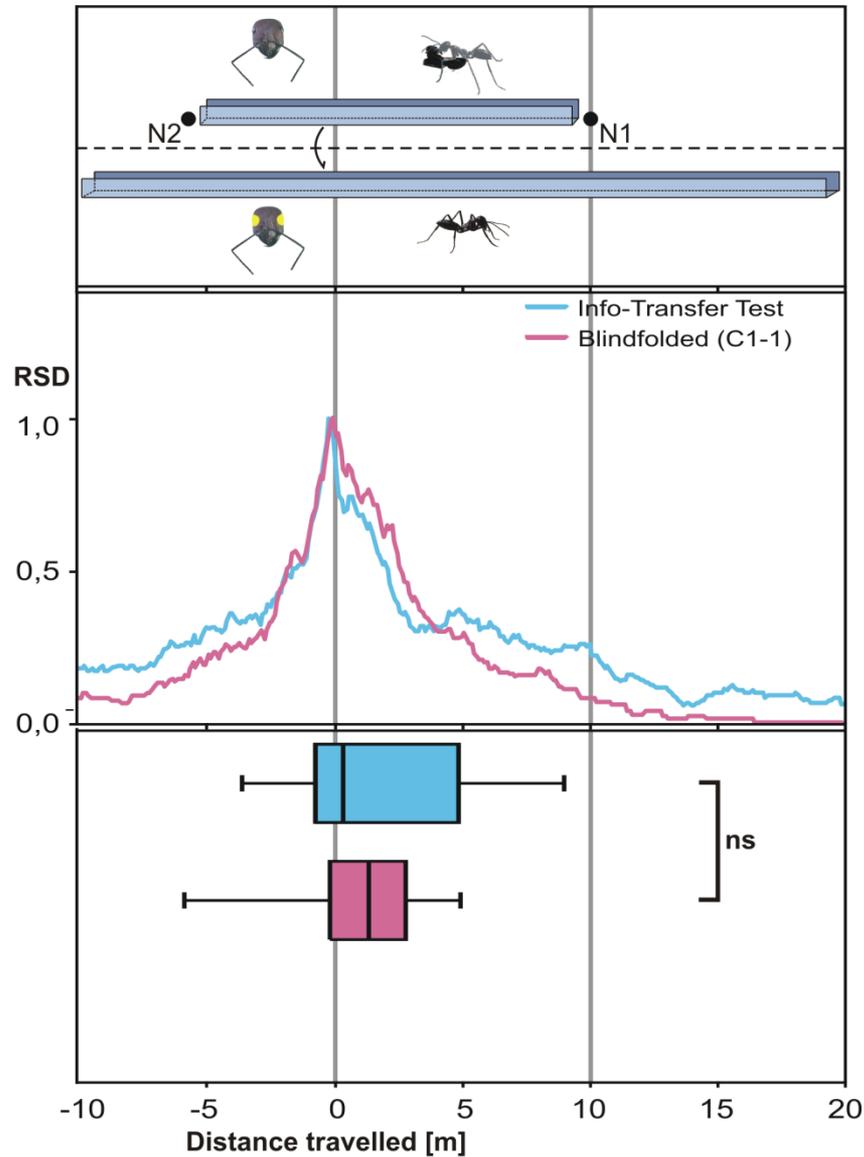
## Odometer Information Transfer - Experiment



# Odometer Information Transfer - Experiment



## Odometer Information Transfer - Experiment



## Odometer Informationstransfer- Experiment

- Kein Informationstransfer zwischen den Odometern

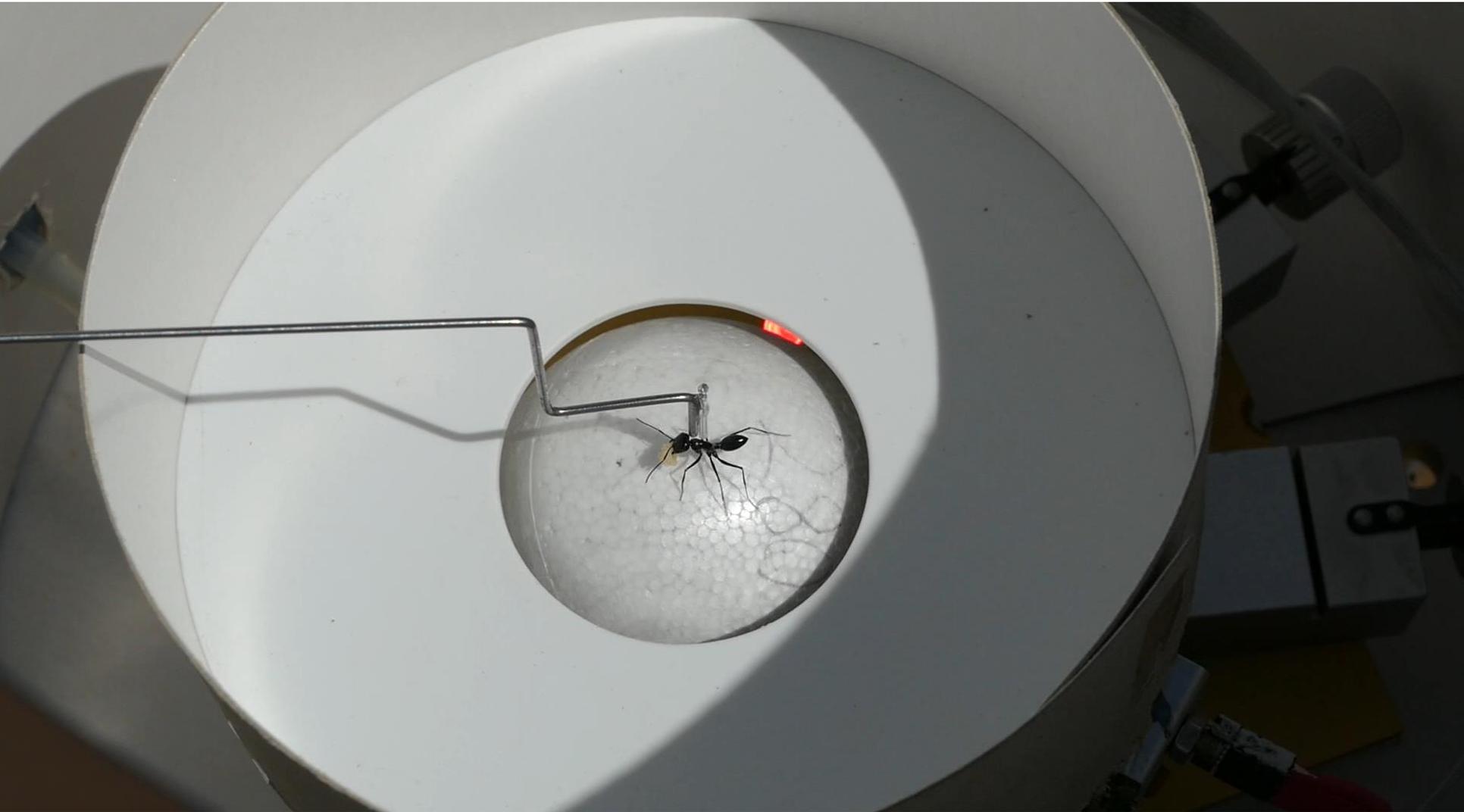


## *Cataglyphis* Odometrie

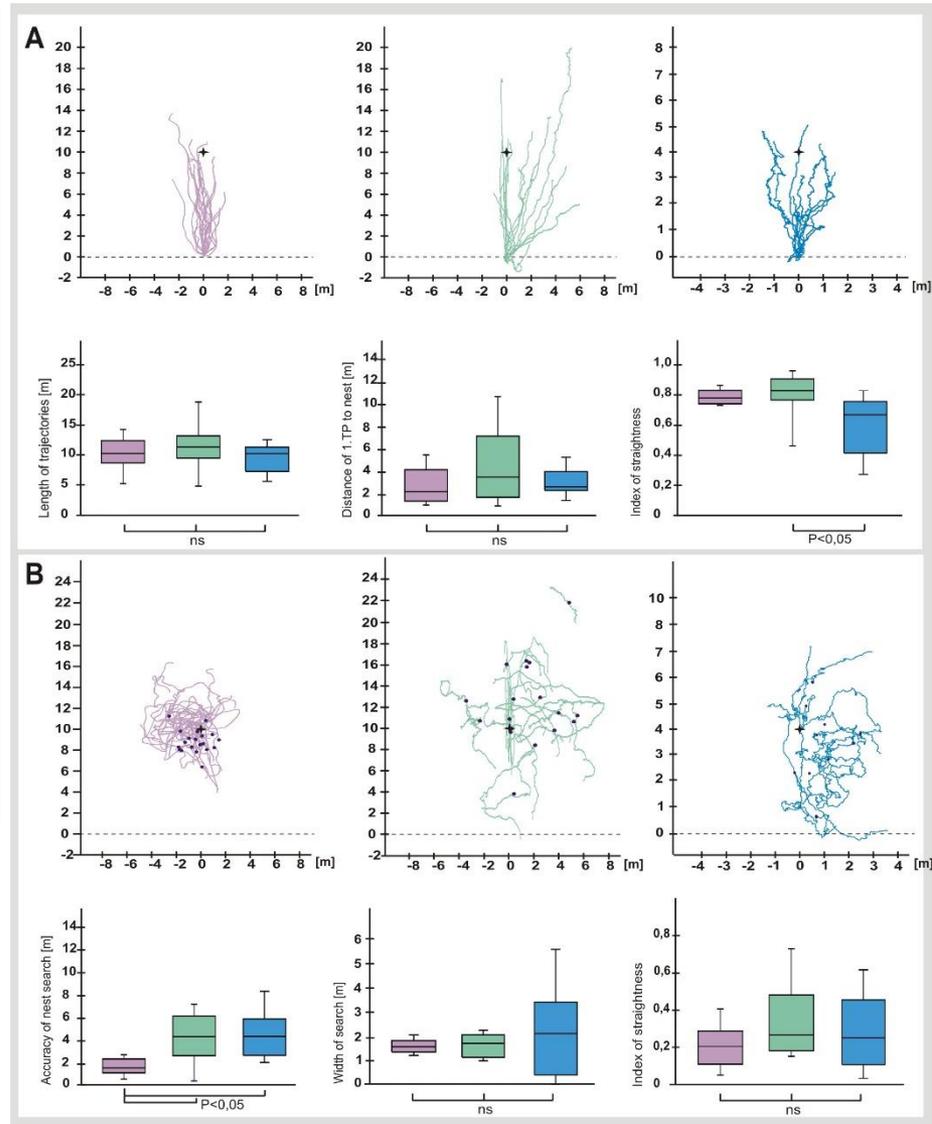
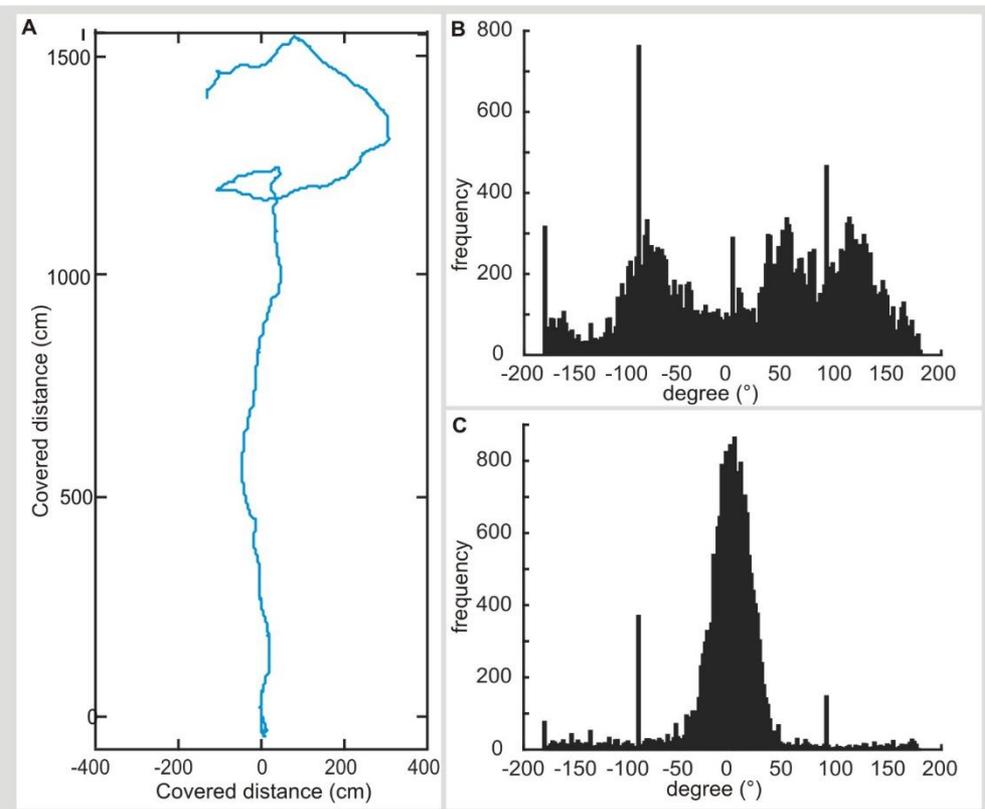
- **Pedometer** – Entfernungsmessung durch **Schrittintegration**
- **Optischer ‘Flussmeter’** – Entfernungsmessung durch **OF-Integration**
  
- **Interokulartransfer (IOT)** von **OF Information**
- Kein **Informationstransfer** zw. **Pedometer** und **OF-Meter**



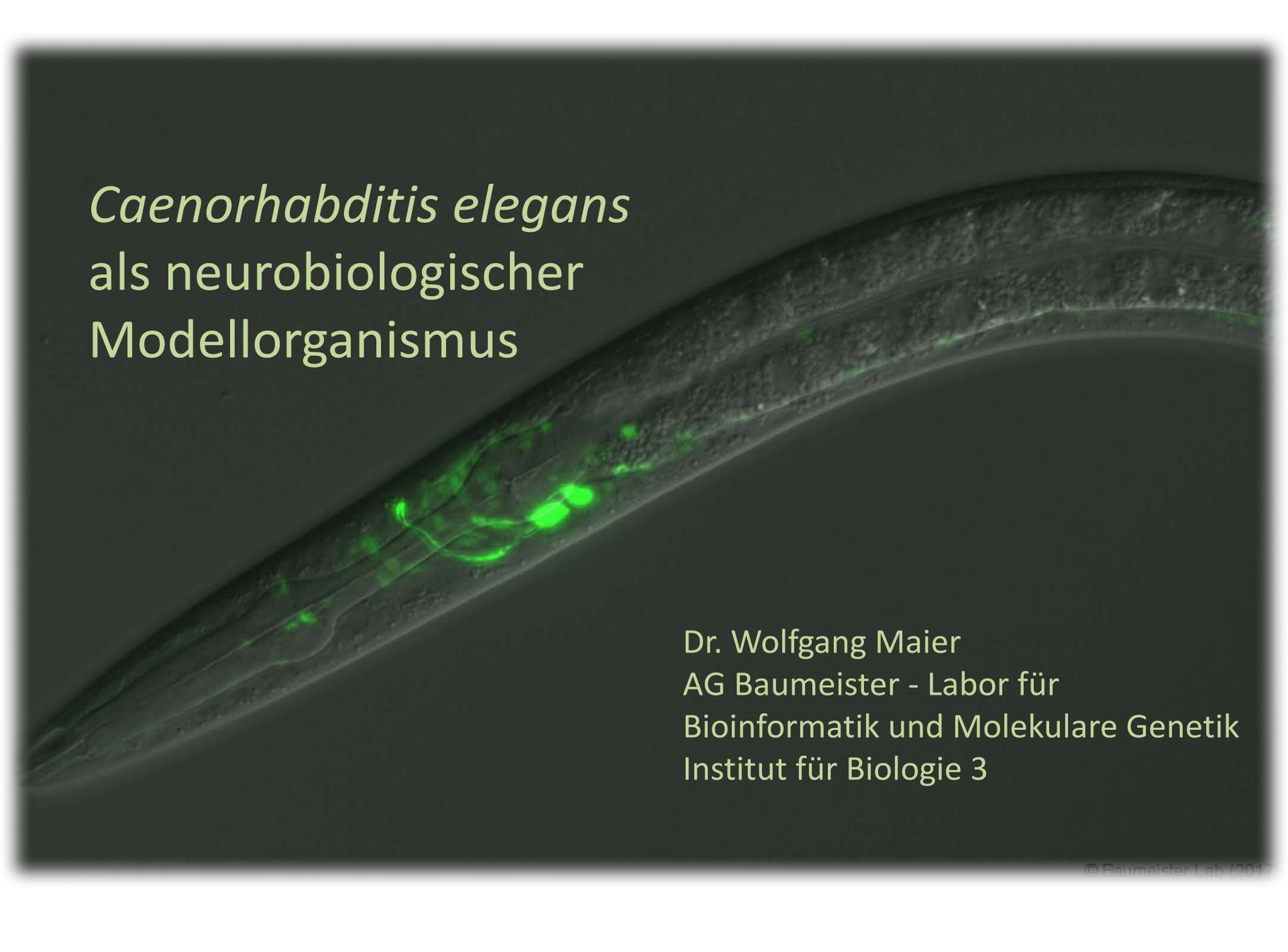




# Laufkugelapparatur - Wegintegration

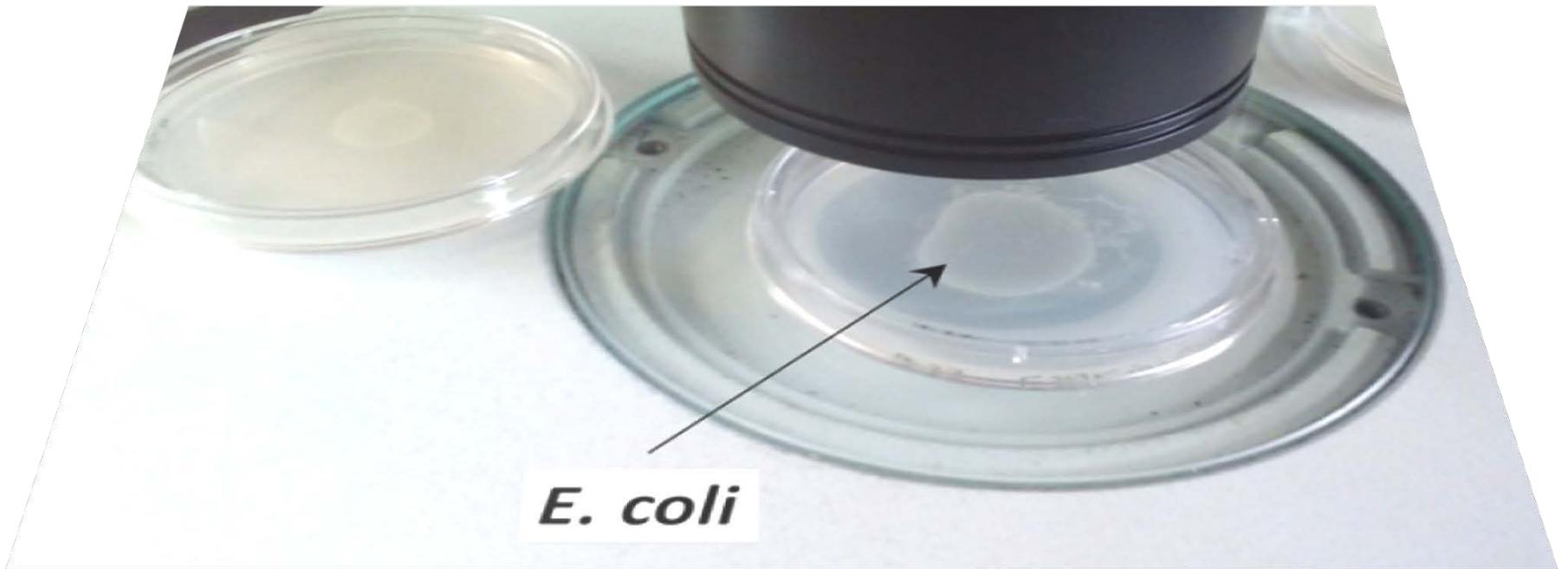
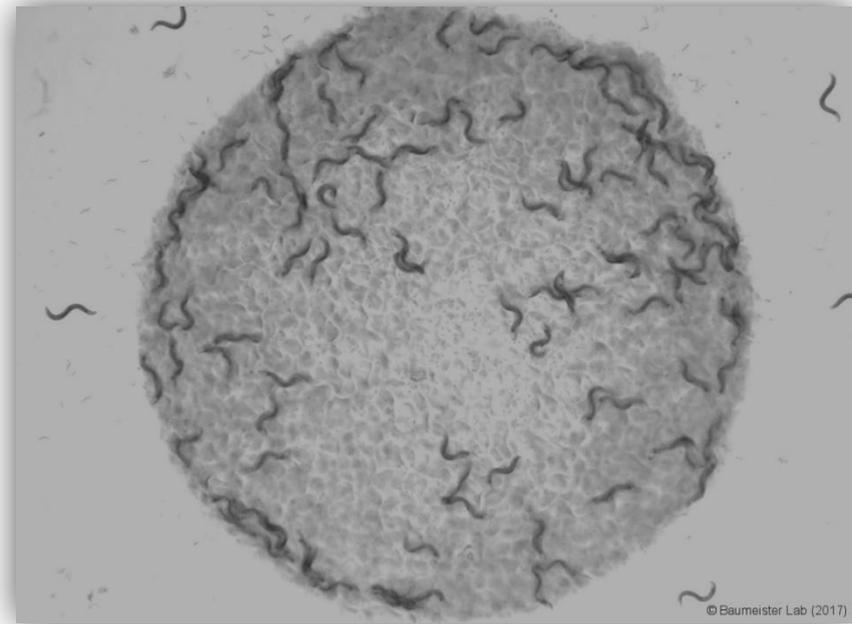




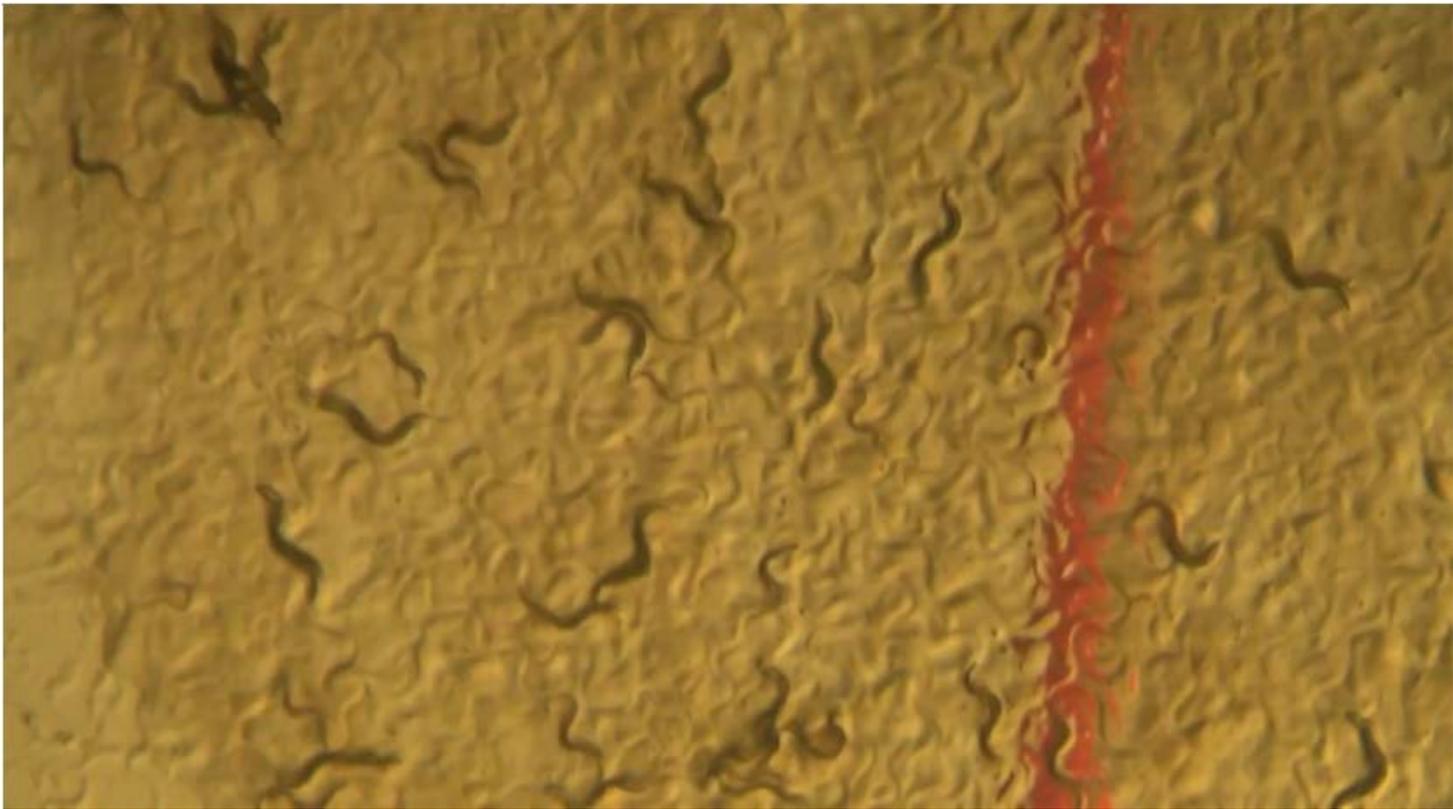


*Caenorhabditis elegans*  
als neurobiologischer  
Modellorganismus

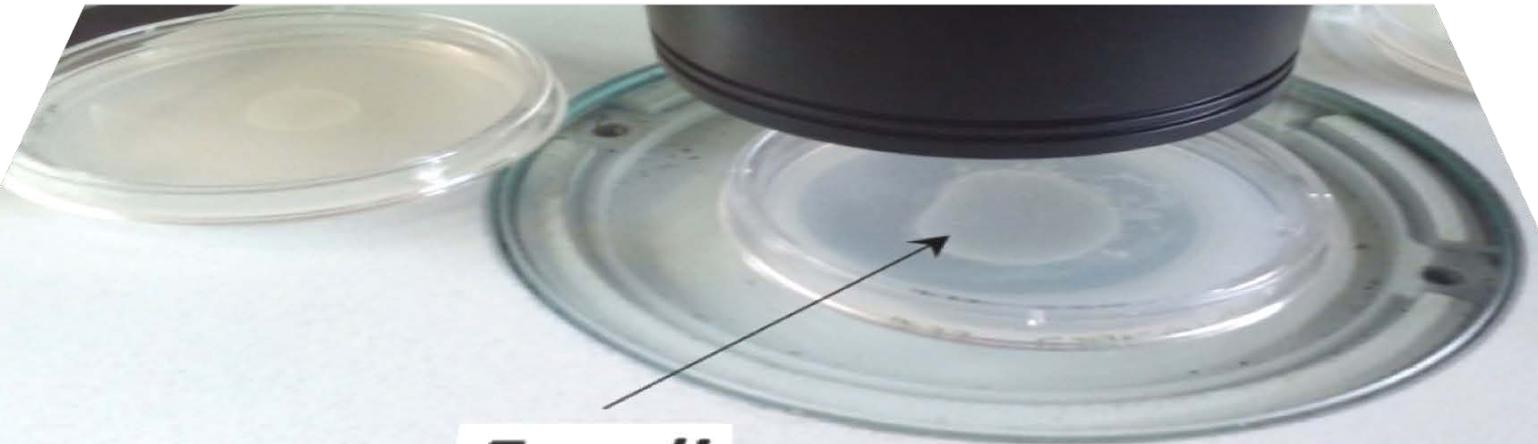
Dr. Wolfgang Maier  
AG Baumeister - Labor für  
Bioinformatik und Molekulare Genetik  
Institut für Biologie 3



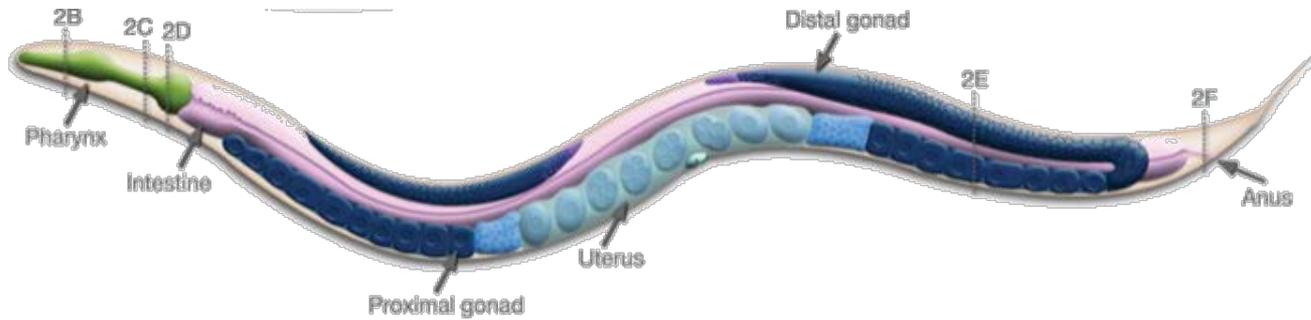
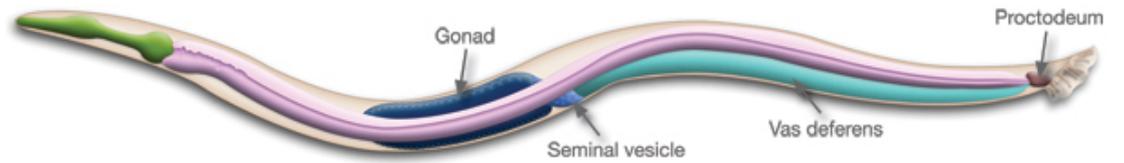
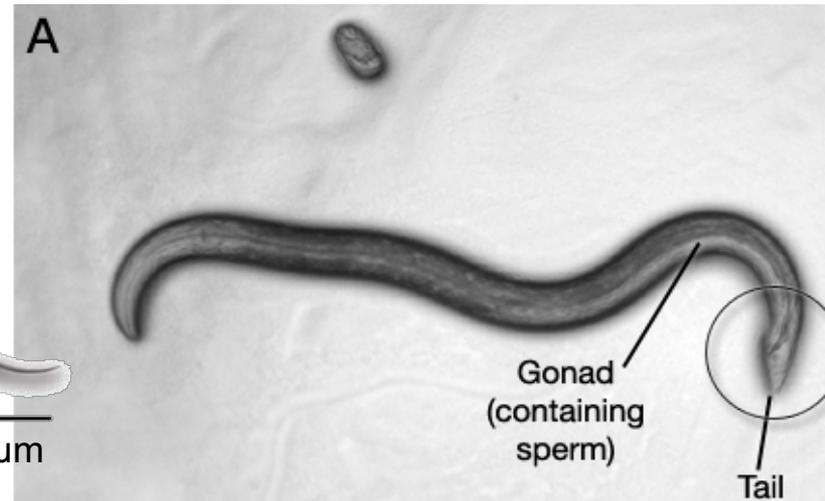
***E. coli***



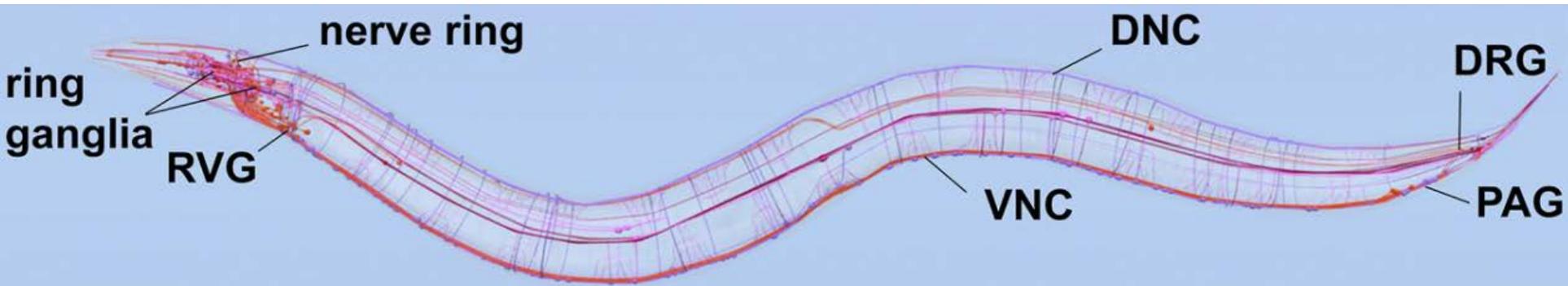
C. elegans Handhabung – Video unter <https://www.youtube.com/watch?v=llklqPULENk&feature=youtu.be>



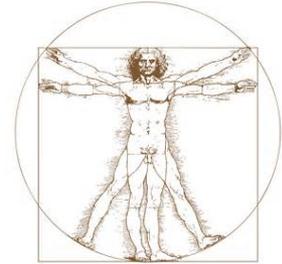
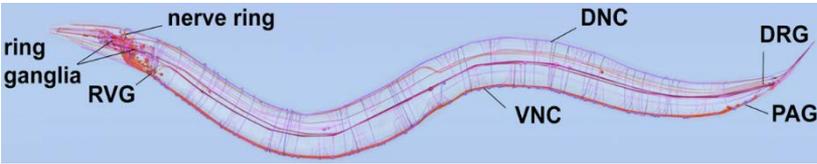
***E. coli***



# Neuroanatomie



# C. elegans - Neuroanatomie



302 Neuronen, 56 Gliazellen

6400 chemische Synapsen

900 Gap junctions

1500 neuromuskuläre Synapsen

Konnektom ~75% identisch

zwischen je 2 Individuen

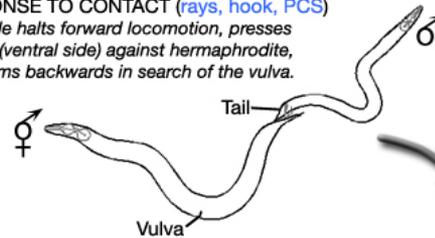
~ 100 000 Neuronen

~ 86 000 000 000 Neuronen

?? Synapsen ~ 100 000 000 000 000 Synapsen

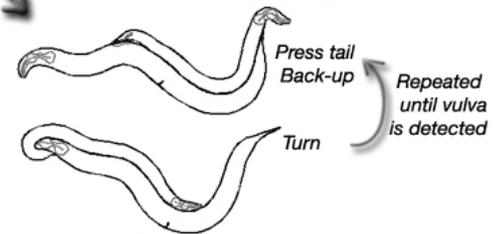
RESPONSE TO CONTACT (rays, hook, PCS)

Male halts forward locomotion, presses tail (ventral side) against hermaphrodite, swims backwards in search of the vulva.



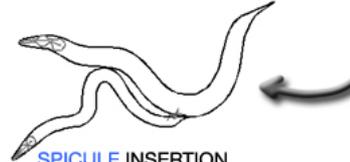
TURNING (rays)

If the male reaches the end without detecting the vulva, a tight turn is executed and searching continues along the other side.



VULVAL LOCATION

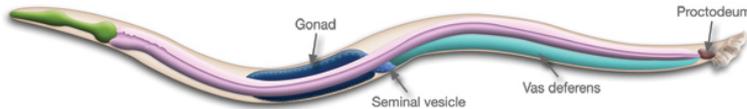
If the male detects the vulva (hook, PCS), he commences a slow search of the area, prodding for the slit with his spicules.



SPICULE INSERTION  
SPERM TRANSFER

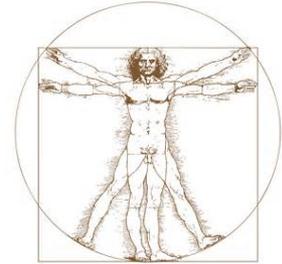
The male inserts spicules fully into the vulva, locking himself to the hermaphrodite and ejaculates

Tail sensory structures (blue) required for this step.



383 Neuronen, 92 Gliazellen

# *C. elegans* - Neuroanatomie



302 Neuronen, 56 Gliazellen

6400 chemische Synapsen

900 Gap junctions

1500 neuromuskuläre Synapsen

Konnektom ~75% identisch  
zwischen je 2 Individuen

~ 100 000 Neuronen

~ 86 000 000 000 Neuronen

?? Synapsen ~ 100 000 000 000 000 Synapsen



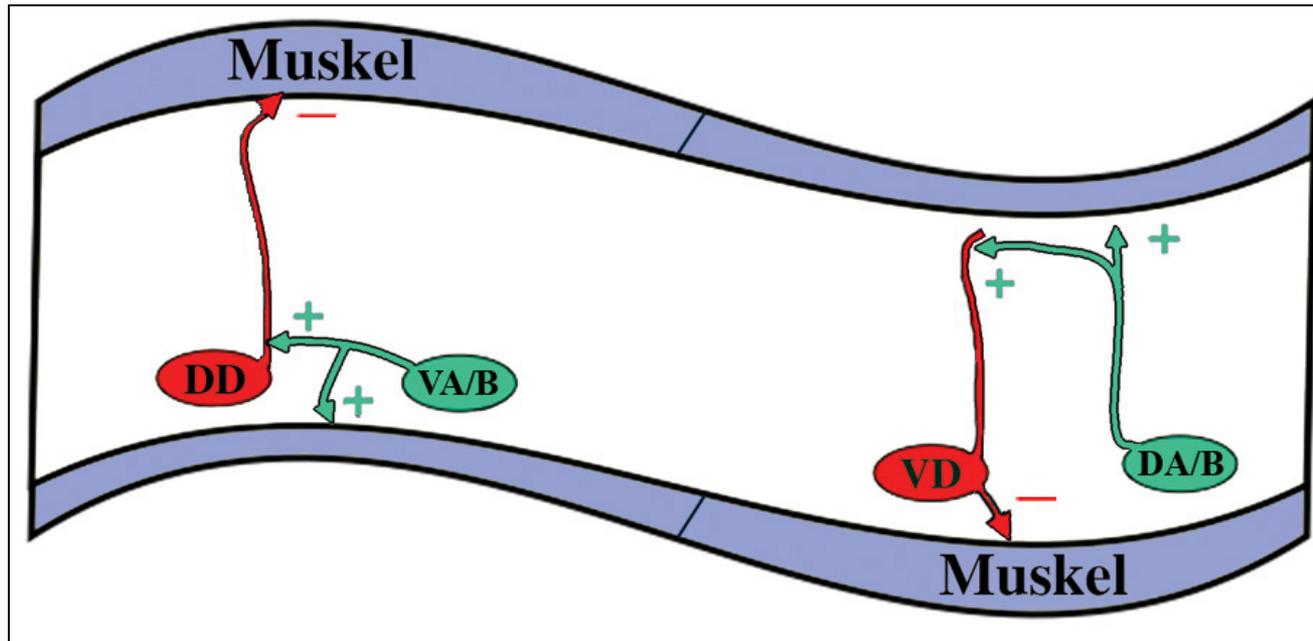
## Vision der 1970er Jahre: Computermodell des Nervensystems

→ „The Mind of a Worm“ (White et al., 1986)

Karte des gesamten Nervensystems inklusive aller Synapsen

→ aber: große Schwierigkeiten bei der **funktionellen** Vermessung

# Grunds Schaltkreis der Lokomotion

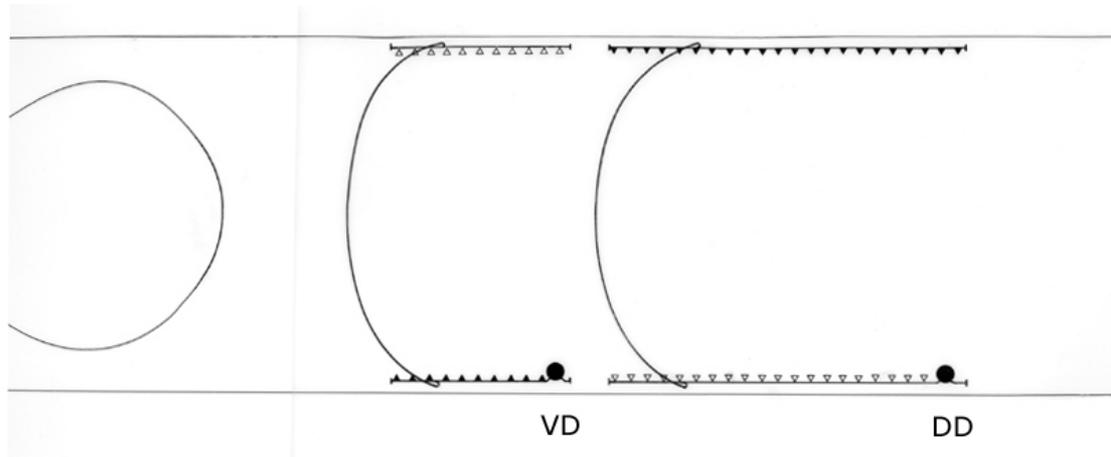
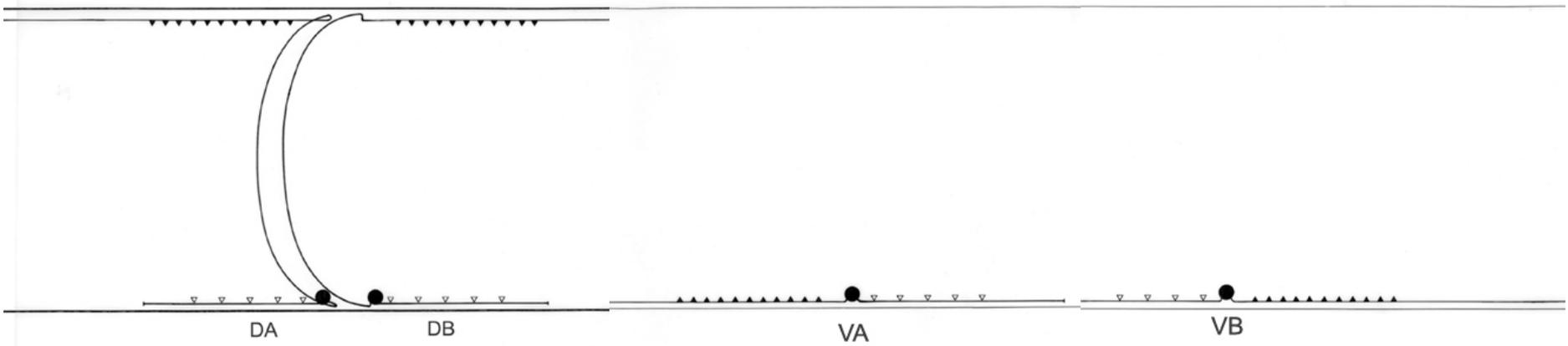
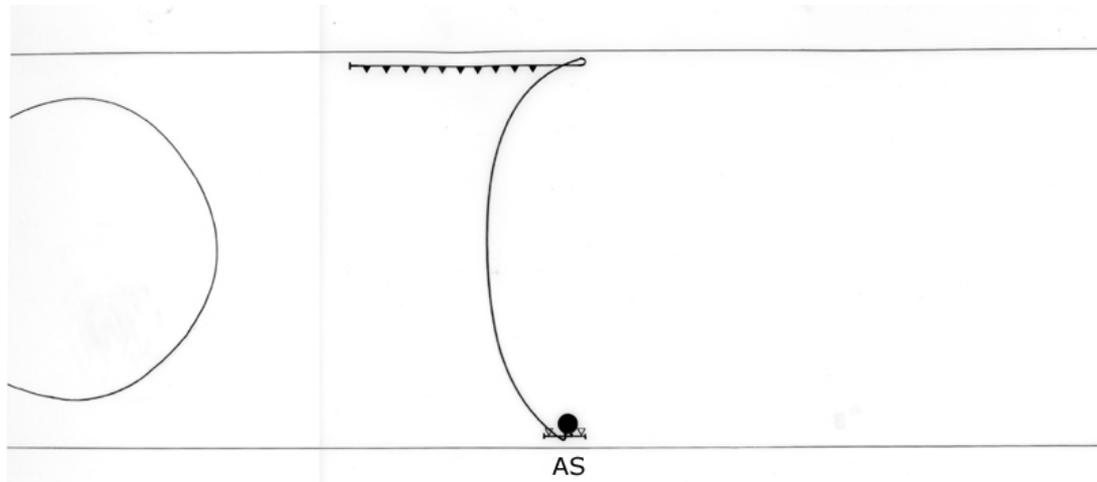


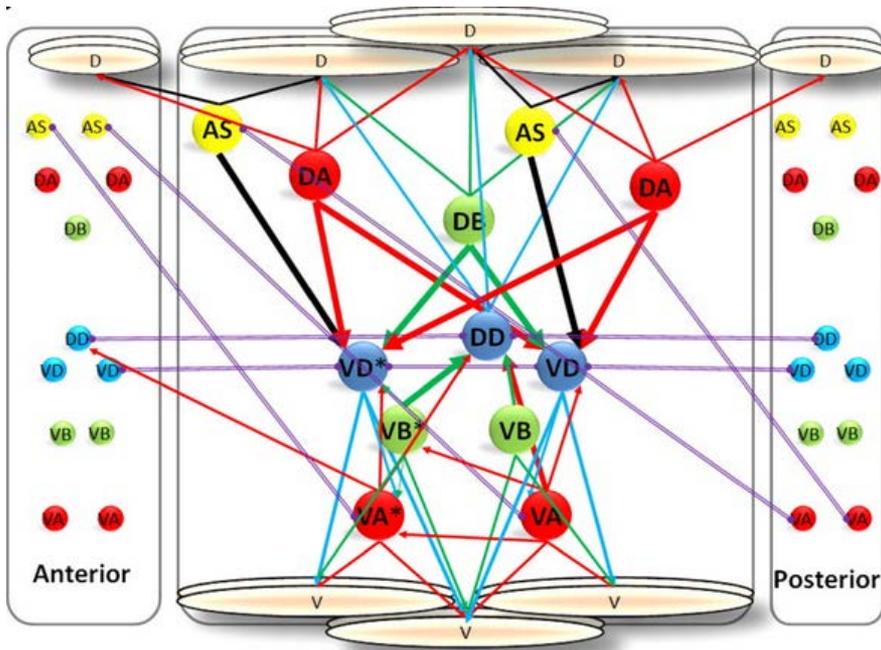
● = GABAergic

● = cholinergic

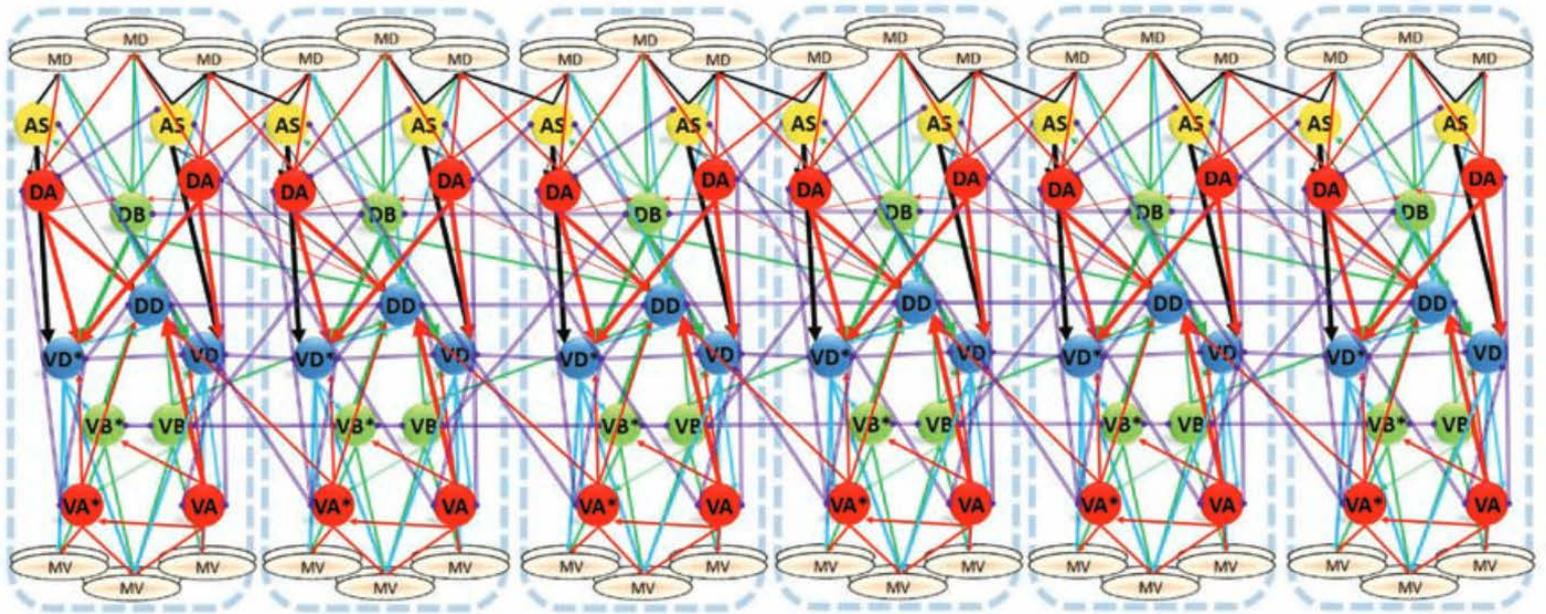
Reziproke Inhibition

# Grundschaltkreis der Lokomotion

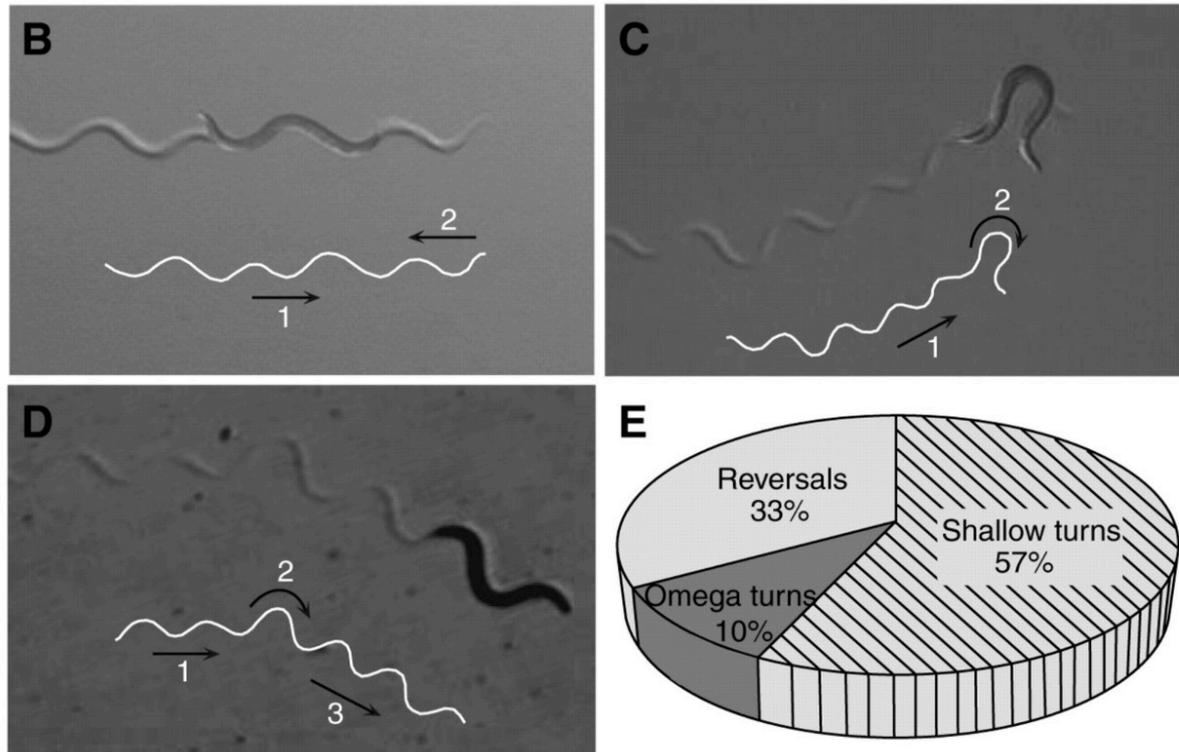




# Grundschatkreis der Lokomotion

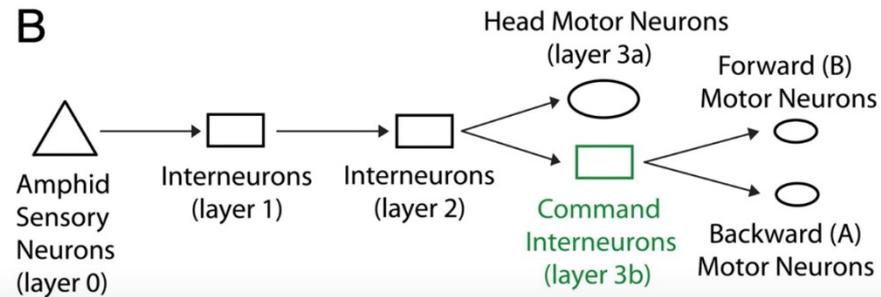
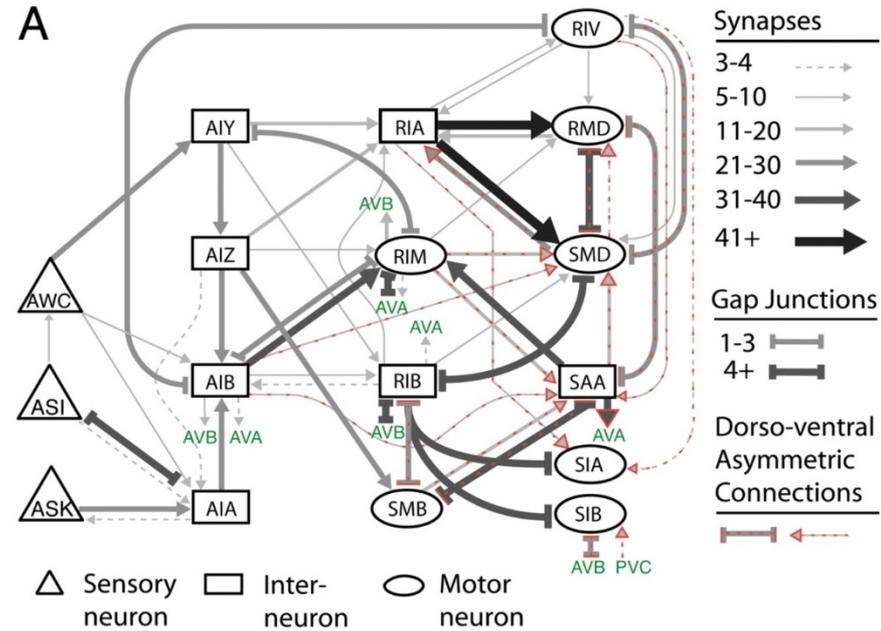
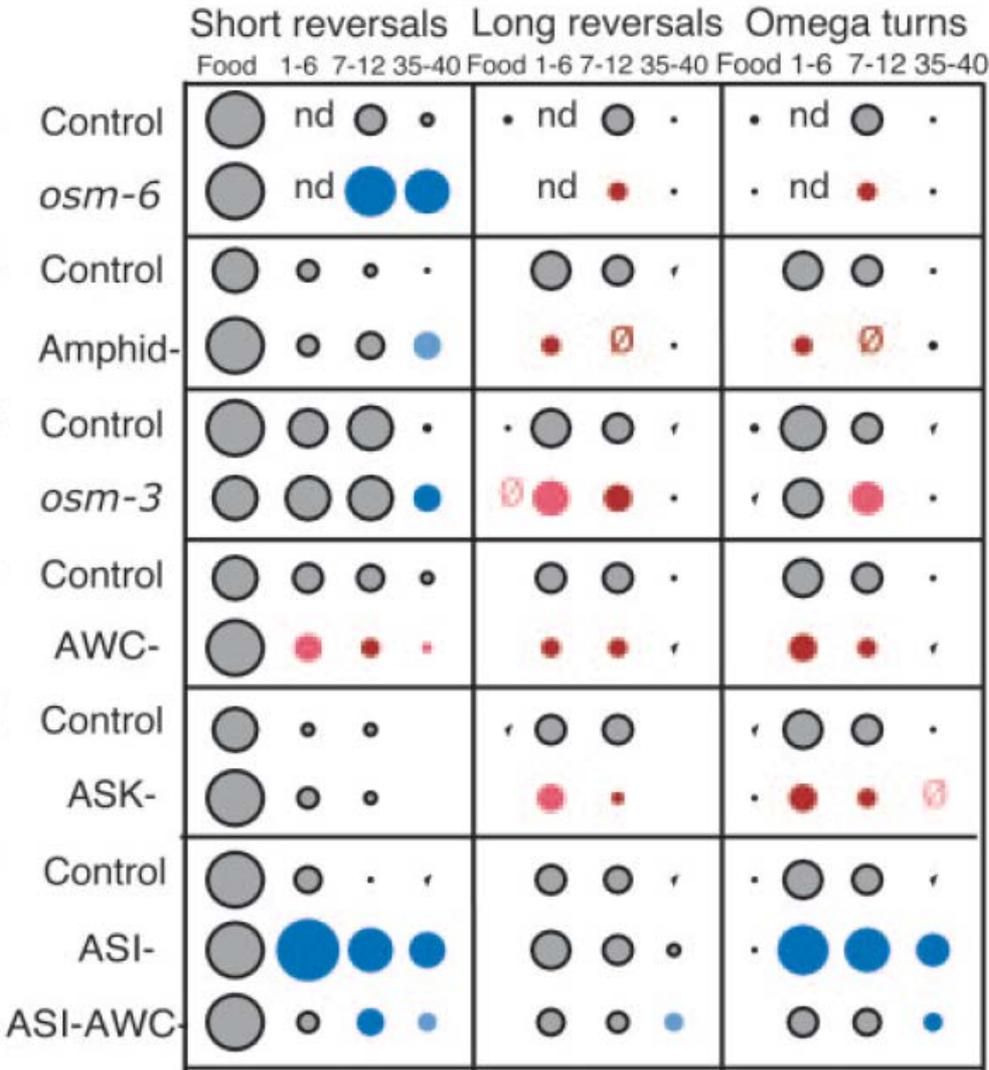


# Schaltkreis „echter“ Lokomotion



(Kim et al., 2011)

# Schaltkreis „echter“ Lokomotion



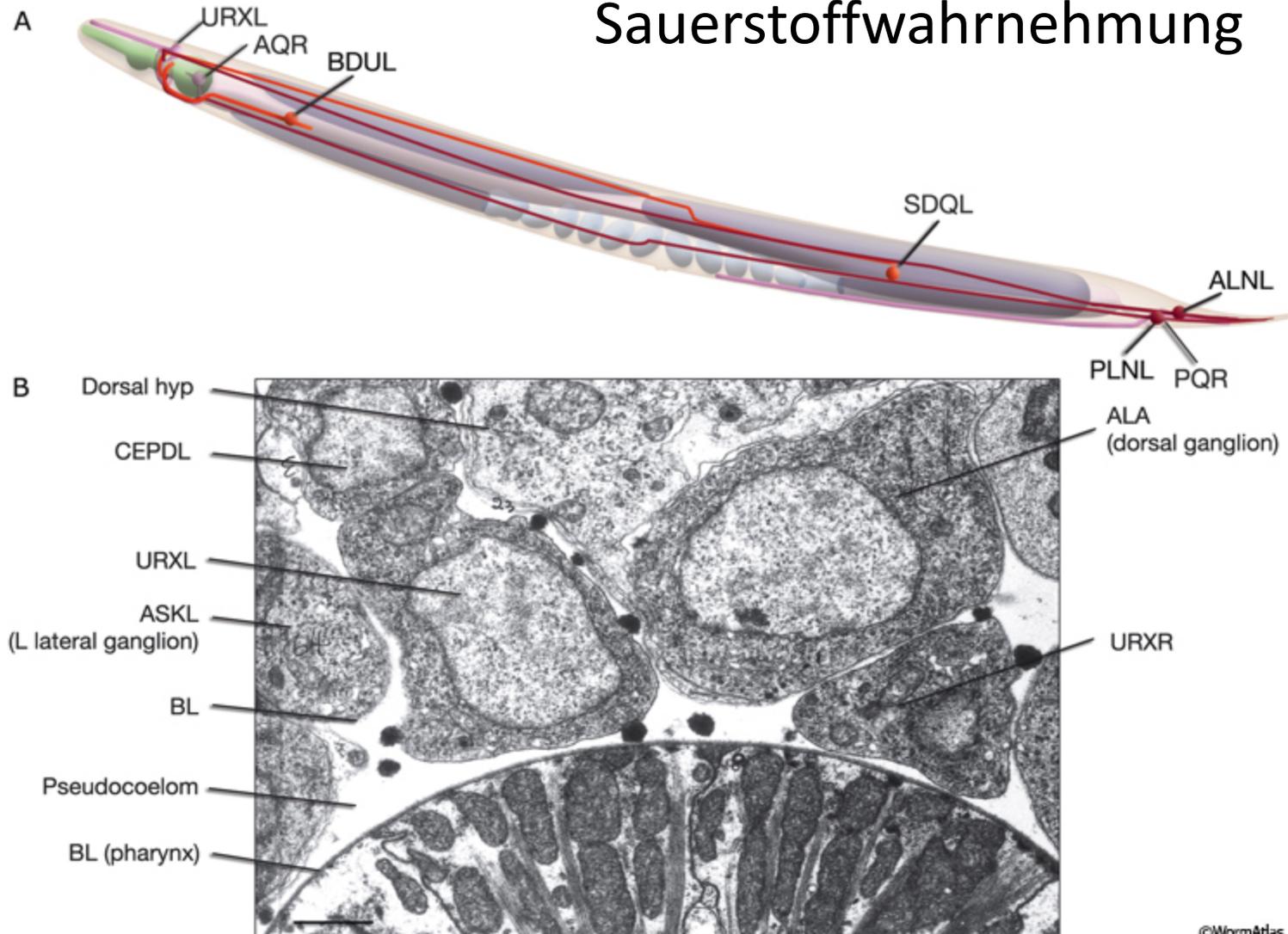
(Gray et al. 2005)

# Sensorischer Input verändert Verhalten

Welche Umweltreize  
verarbeitet ein Wurm überhaupt?

# Sensorischer Input verändert Verhalten

## Sauerstoffwahrnehmung



# Sensorischer Input verändert Verhalten

Oberflächenbeschaffenheit  
(auch Biofilme)

Temperaturgradienten

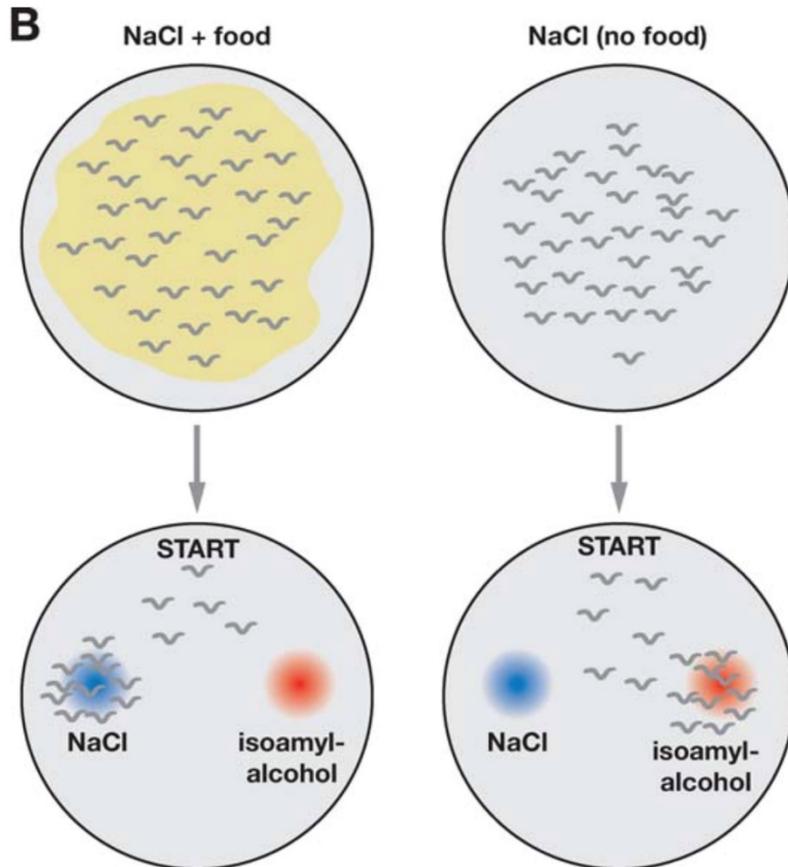
O<sub>2</sub>  
CO<sub>2</sub>  
H<sub>2</sub>S

elektromagnetische Felder

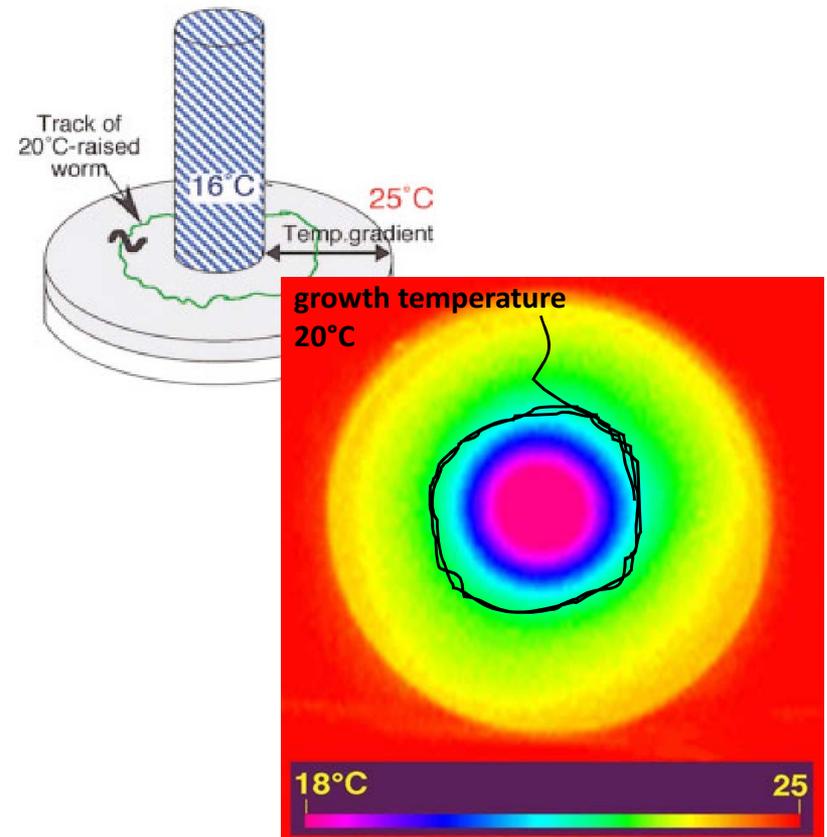
Pheromone

# Lernen ändert Verhalten auch im Wurm

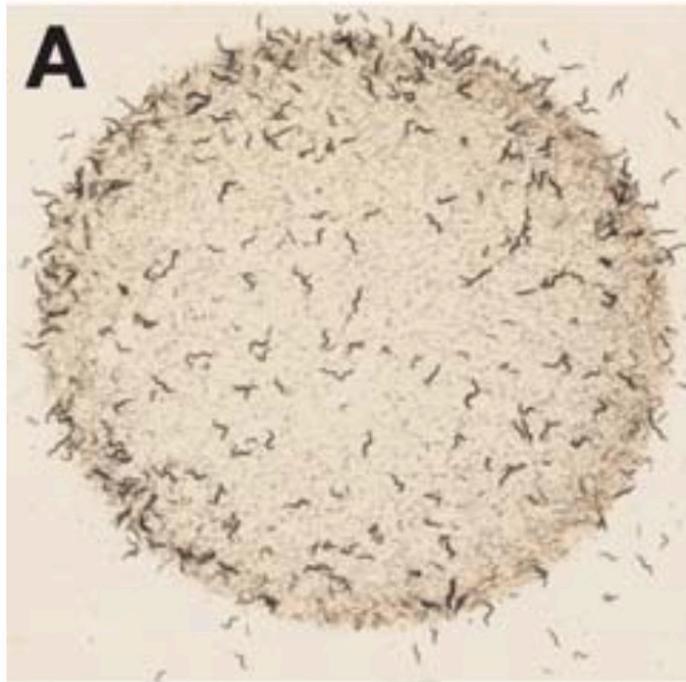
## Chemotaxis



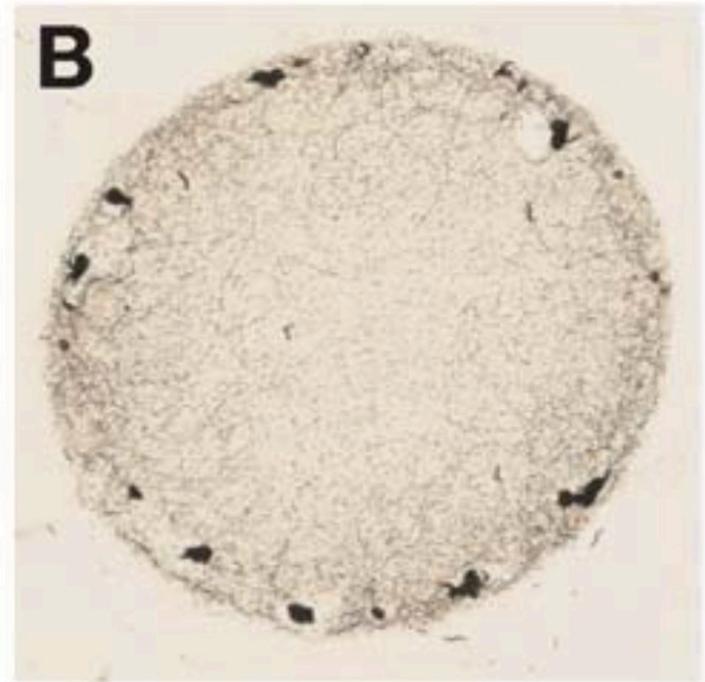
## Thermotaxis



# Neuropeptide – Modulation von Verhaltensweisen



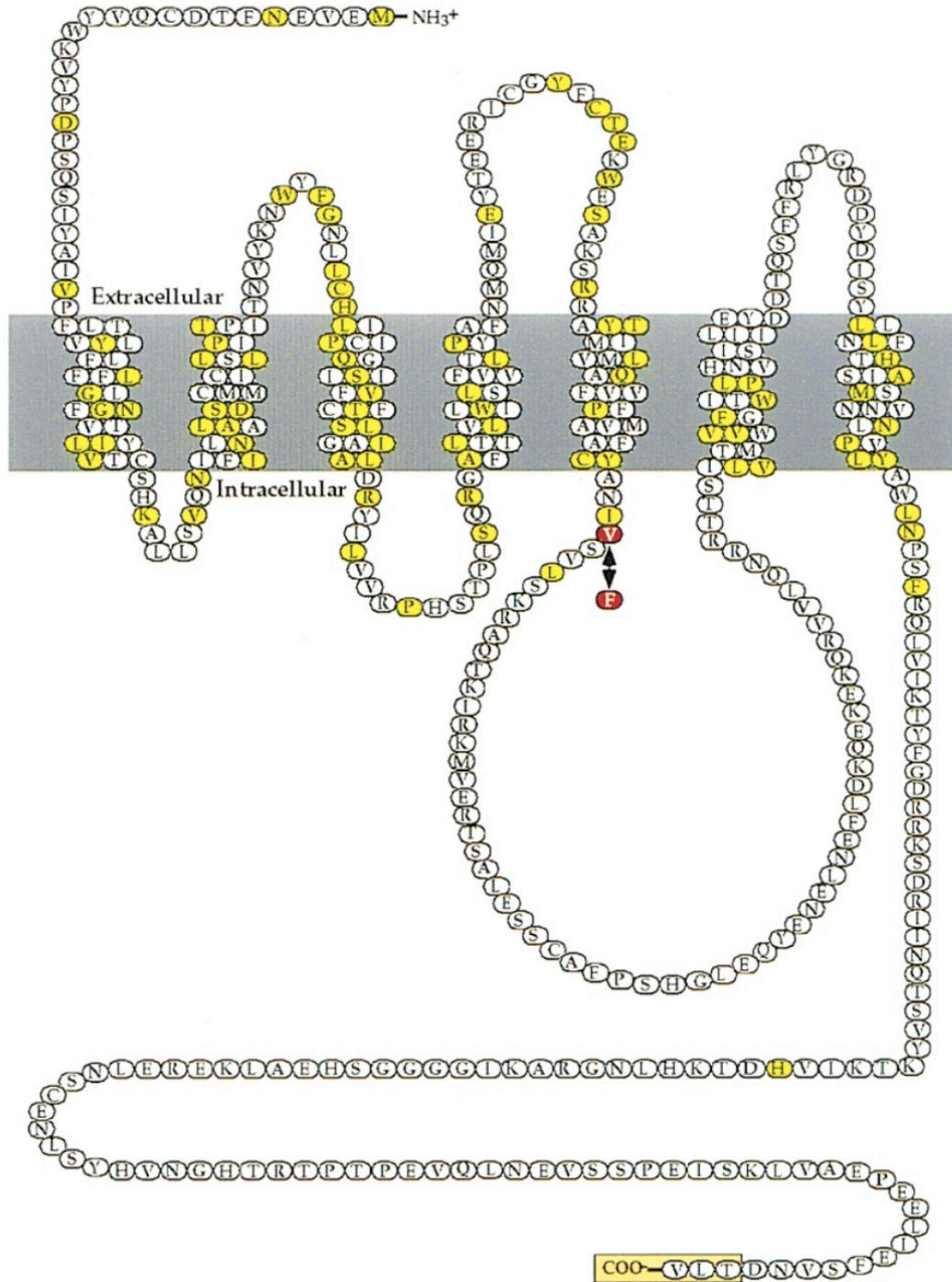
solitary



social

feeding

(de Bono & Bargmann, 1998)



## Neuropeptidrezeptor-1 (NPR-1)

molekulare Determinante des  
Freßverhaltens

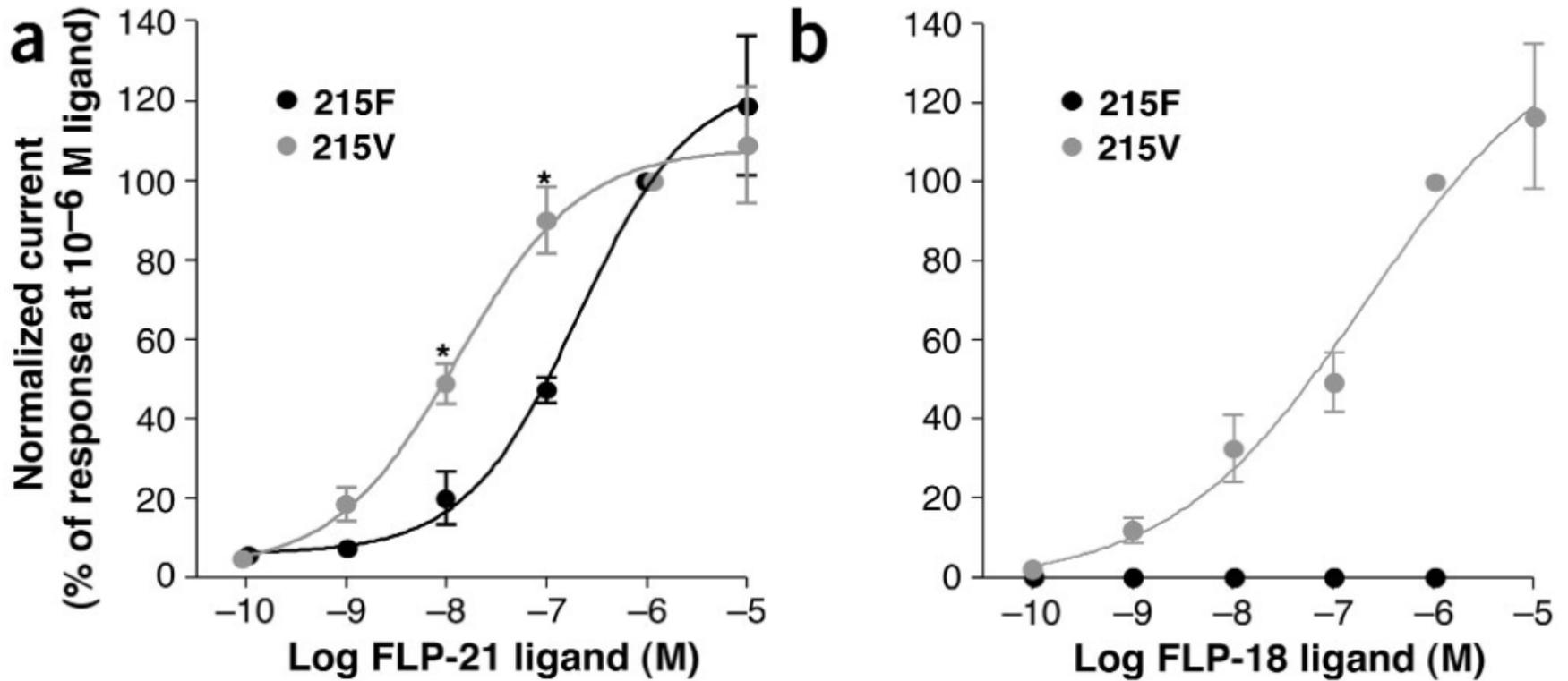
Würmer mit **Valin** an Position 215 des  
7-Transmembrandomänen-Proteins  
sind **“solitary feeder”**, solche mit  
**Phenylalanin** sind **“social feeder”**

“normale” Laborwürmer tragen die  
Valin-Variante und sind deshalb  
Einzelgänger

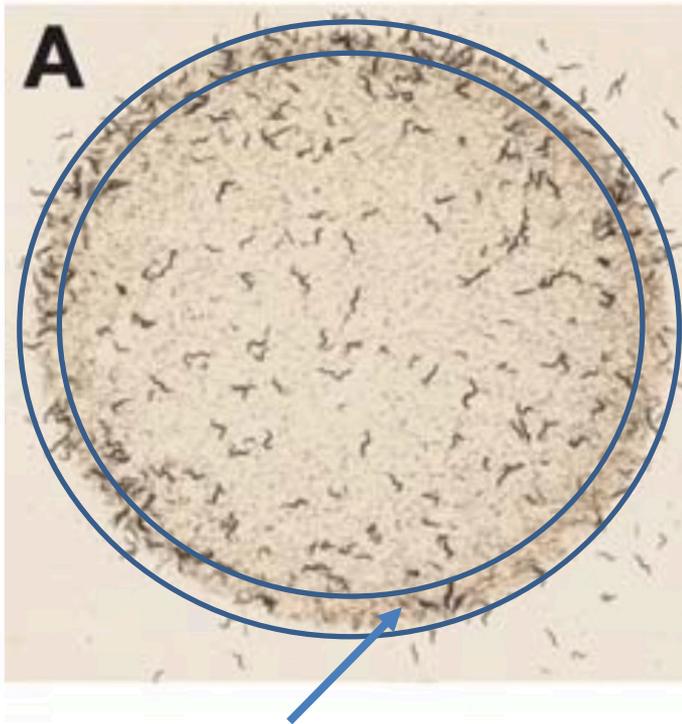
NPR-1 ist der molekulare Rezeptor für  
die Neuropeptide FLP-18 und FLP-21

(de Bono & Bargmann, 1998)

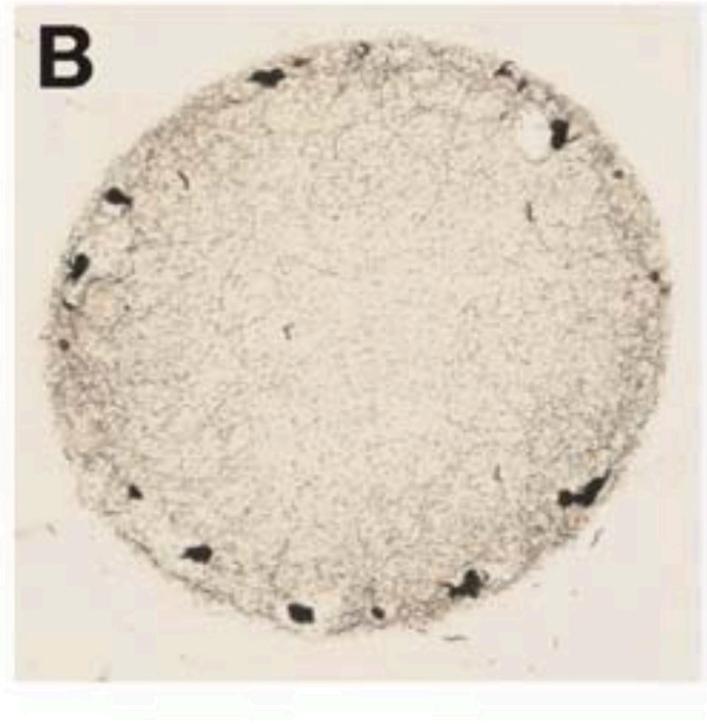
Die Valin-Variante von NPR-1 antwortet stärker auf FLP-21 und FLP-18



## Gemeinschaftssinn in Würmern?

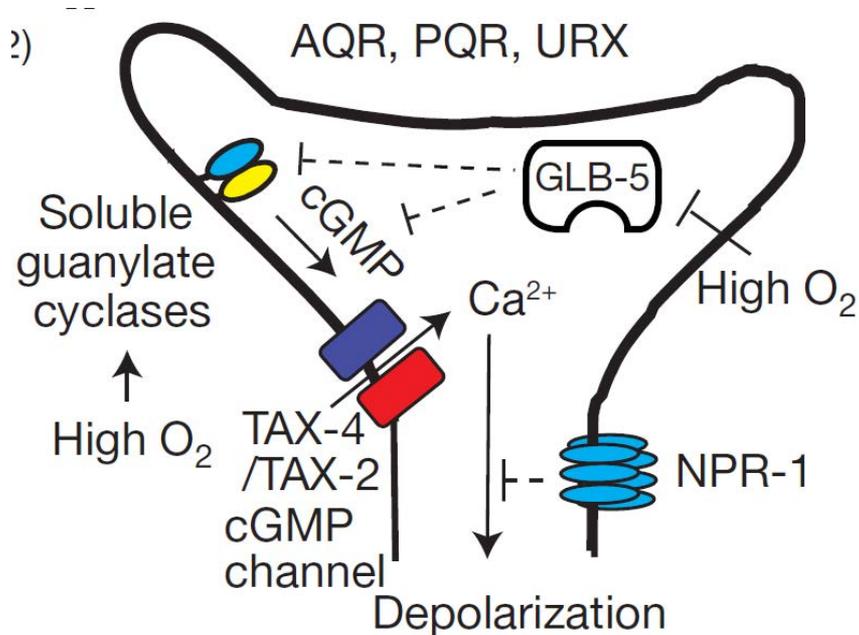


etwas dickere Bakteriensicht am Rasenrand -> mehr Stoffwechsel -> weniger O<sub>2</sub>

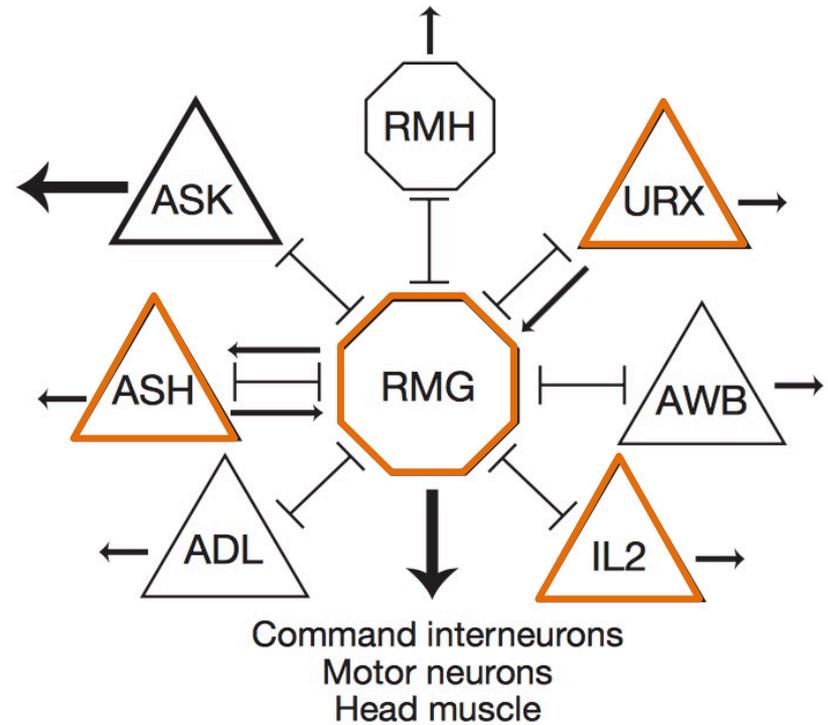


Würmer mit O<sub>2</sub>-Aversion sammeln sich in den Randbereichen -> Selbstverstärkung des Effekts durch Wurmmetabolismus

# NPR-1 moduliert einen Schaltkreis zur O<sub>2</sub>-Vermeidung



(Persson et al., 2009)

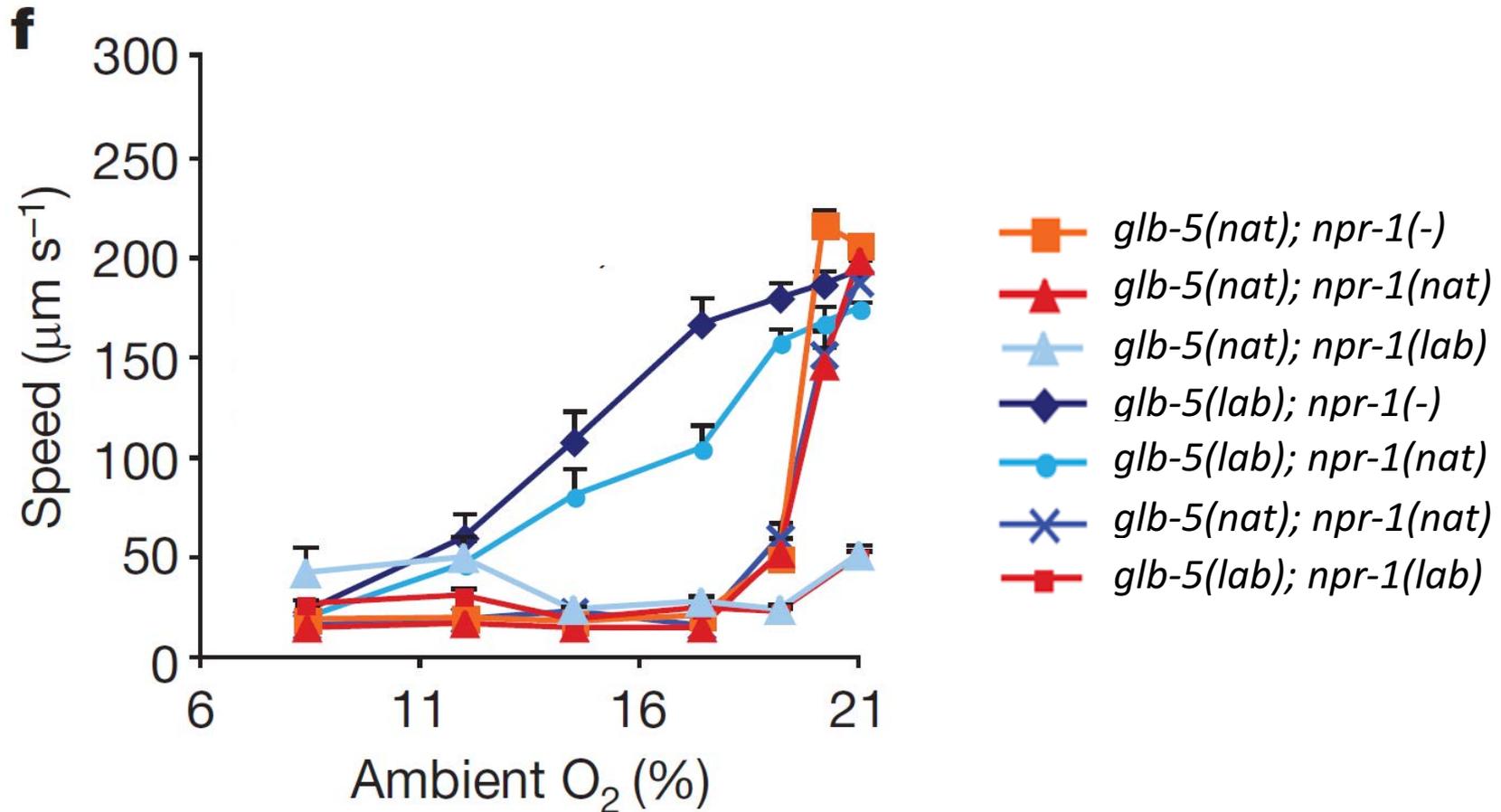


- |—| Gap junction
- Chemical synapse
- △ Sensory neuron
- Inter/motor neuron

## Expression von NPR-1

(Macosko et al., 2009; Choi et al., 2013)

# Anpassung eines komplexen Verhaltens durch nur zwei Punktmutationen

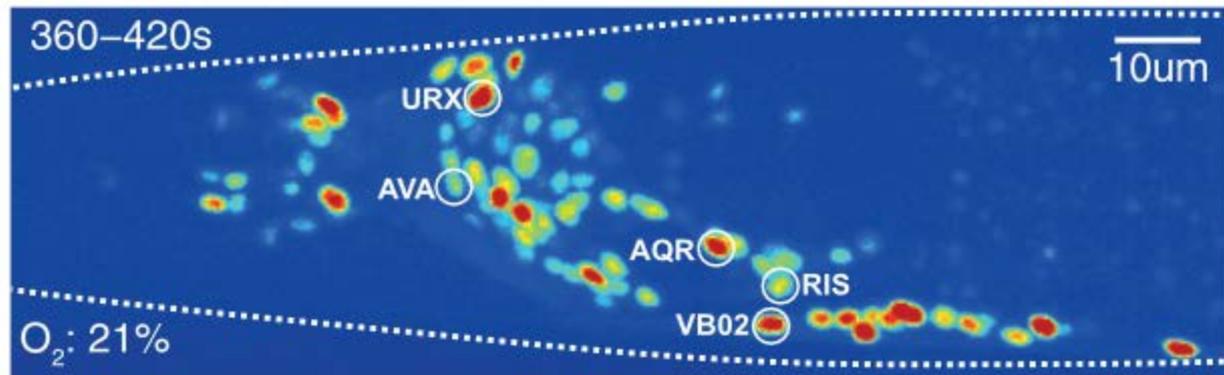
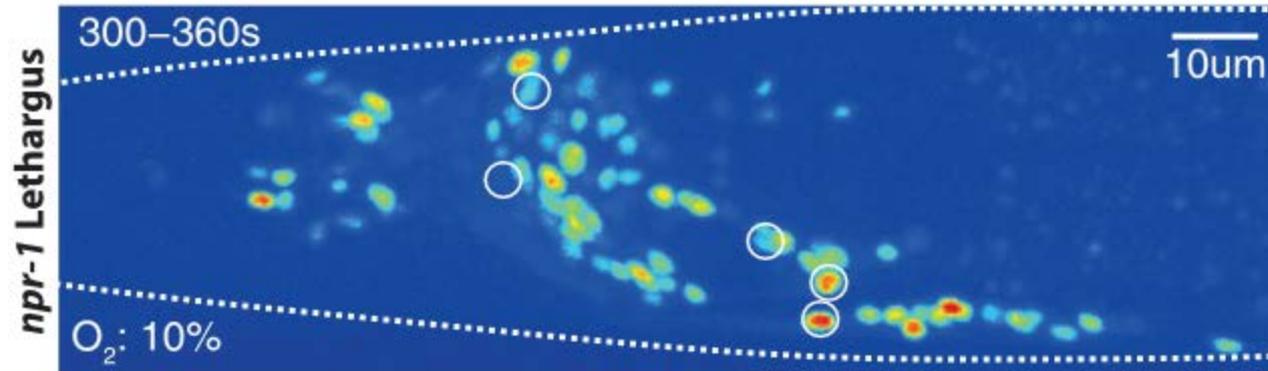


(Persson et al., 2009)

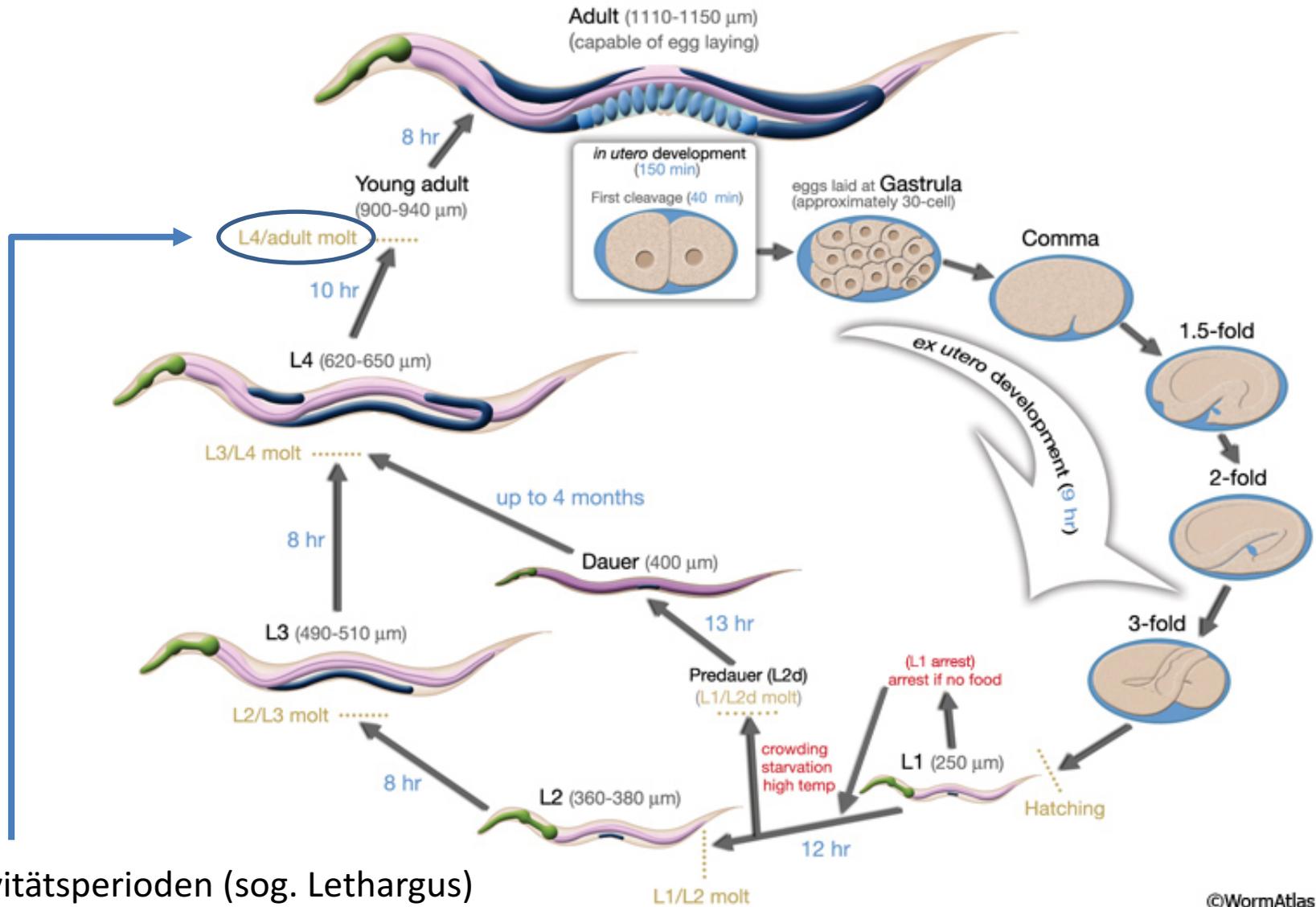
# Moderne Bildgebungsverfahren

Live-Beobachtung von Aktivierungsmustern  
im Wurm-Nervensystem

# Grundlagen des “Schlafs” bei Würmern



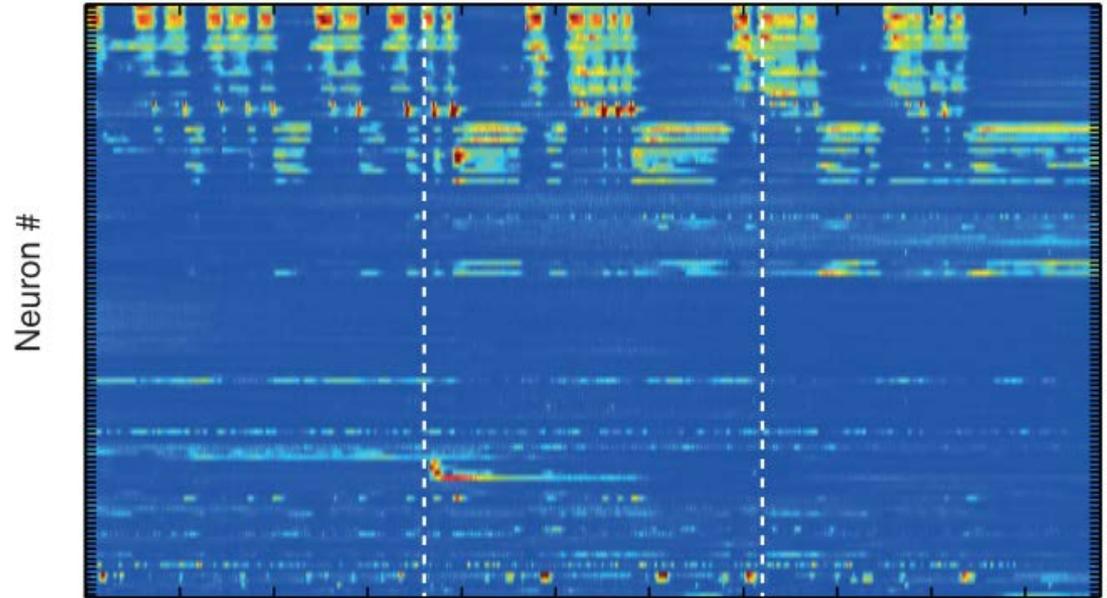
(Nichols et al., 2017)



Inaktivitätsperioden (sog. Lethargus) während der Häutung vom 4. Larvenstadium (L4) zum jungen adulten Tier dienen als „Schlaf“-Modell

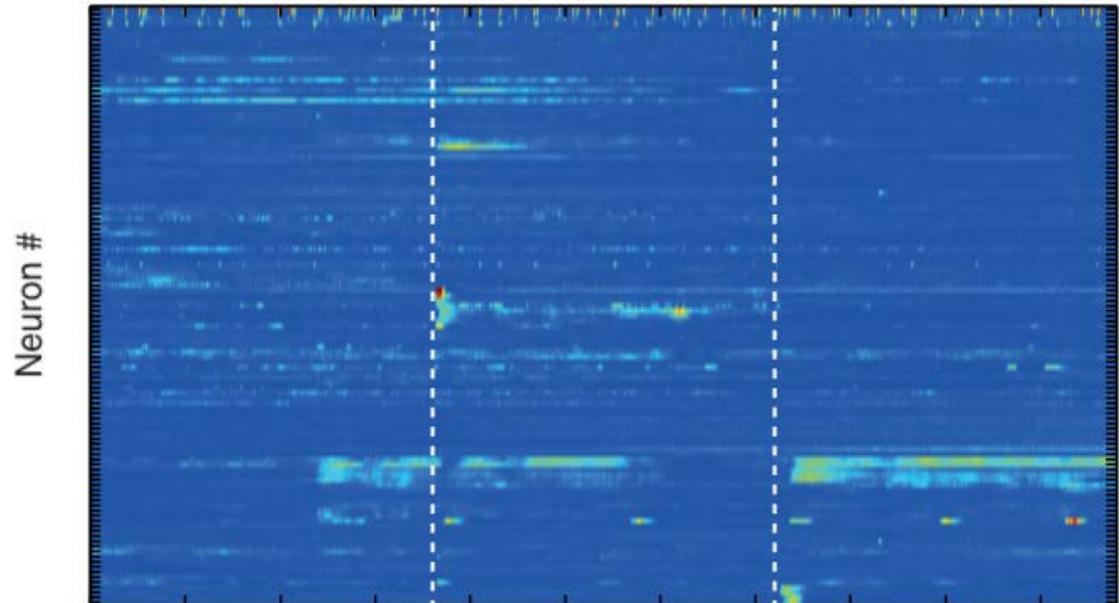
aktiver Wurm

normales L4-Aktivitätsmuster



ruhender Wurm

Aktivitätsmuster während des Lethargus-Zustands

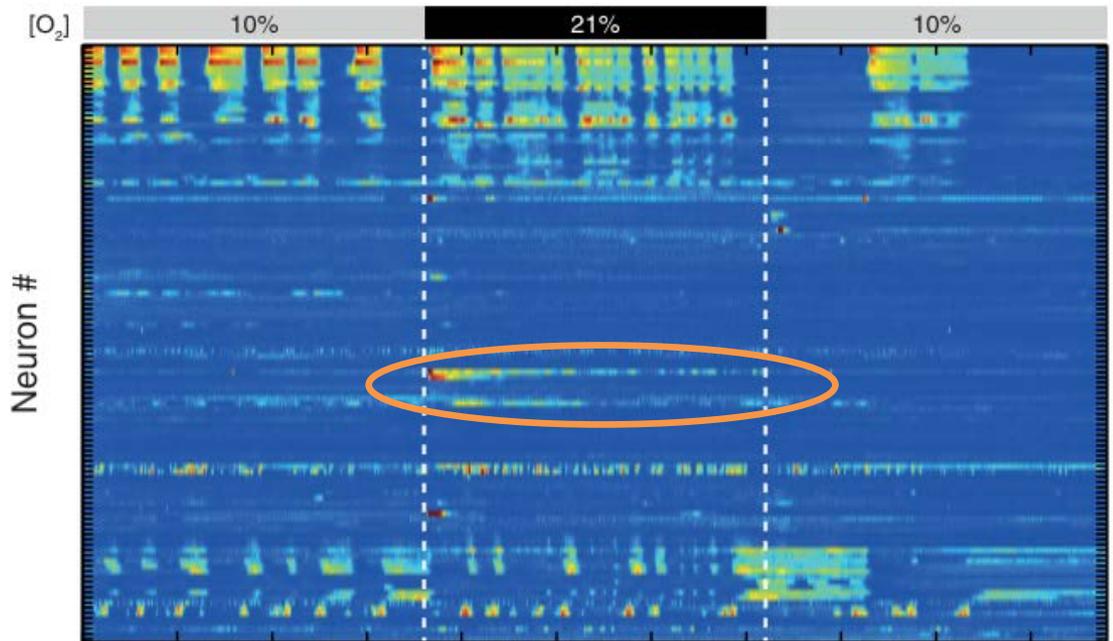


O<sub>2</sub>-empfindliche social feeder Stämme  
lassen sich durch Erhöhung der Sauerstoffkonzentration aufwecken

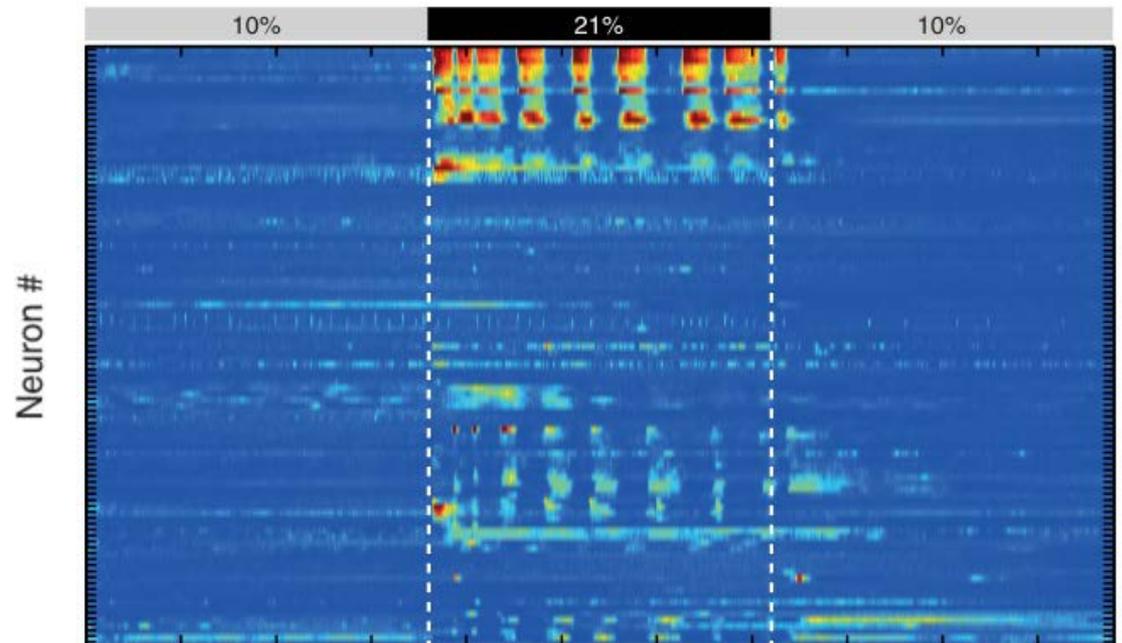
-

direkte Beobachtung eines erwachenden Nervensystems!

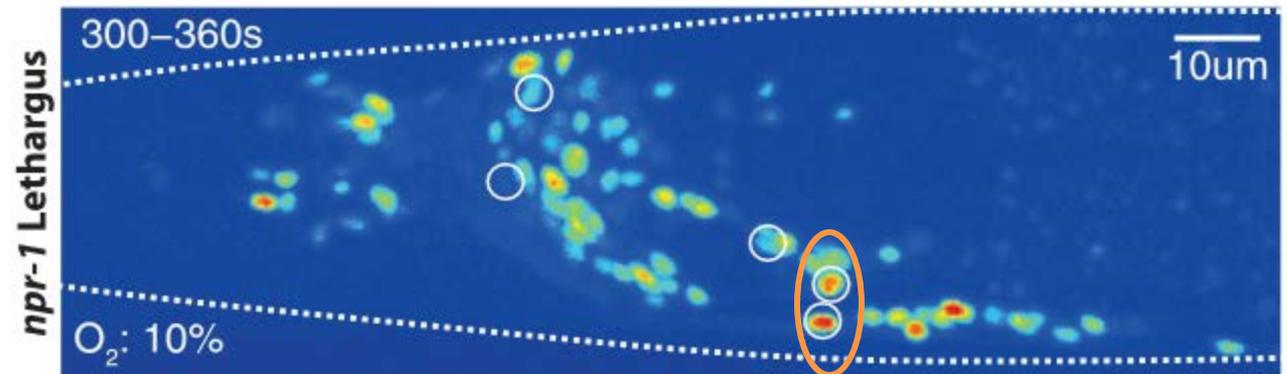
Im wachen L4-Tier verursacht eine Änderung der  $O_2$ -Konzentration nur lokale Änderungen in der Nervenzellaktivierung (v.a. in primär sauerstoffwahrnehmenden Neuronen).



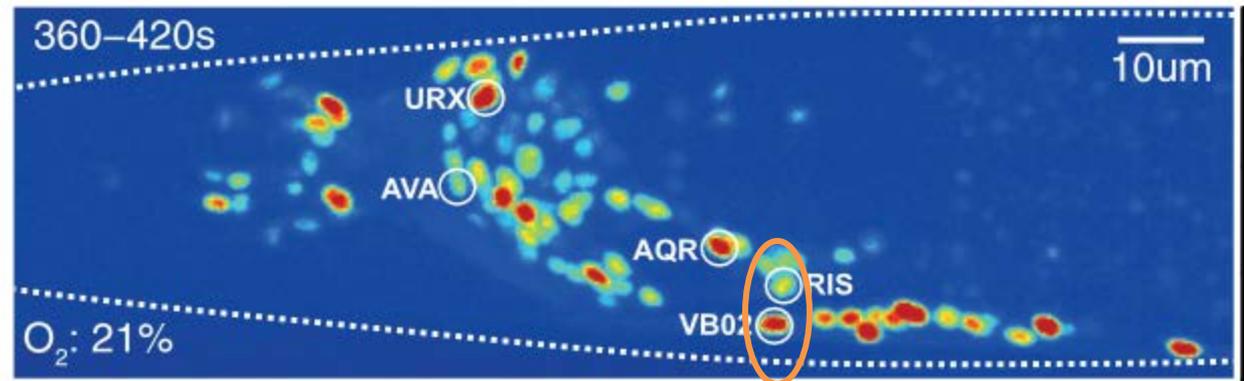
$O_2$ -vermitteltes Aufwachen und Wiedereintreten in den Letharguszustand sind mit weitreichenden Änderungen verbunden, deren genaue zeitliche Abfolge aktuell analysiert wird.



ruhend



nach dem Aufwachen



(Nichols et al., 2017)

VB02: ein nicht-schlafendes Motorneuron  
RIS: ein v.a. im Schlaf aktives Interneuron

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