



Searching In Random Environments

Jean-Baptiste Masson

Physics of Biological Systems, Institut Pasteur, CNRS UMR 3525, Paris, France

Janelia Research Campus, HHMI, Ashburn, USA.

Laboratoire Physico-Chimie, Institut Curie, CNRS UMR168, Paris France.

Harvard Seminar, 23rd September 2015

Searching

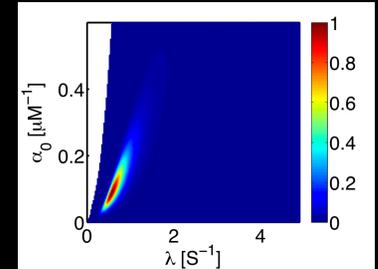
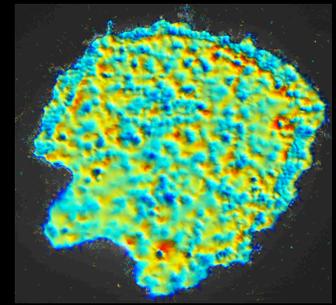
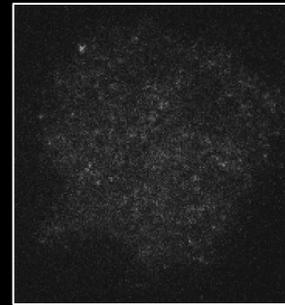
- *Scale*: nm, μm , mm, m, 10^{th} m, km.
- *Cue (if any) propagation*: Diffusion, ballistic, turbulence.
- *Statistics of the environment*: homogeneous, heterogeneous, disappearing probability.
- *Searcher motion dynamics*: velocity, run-tumble, crawl-headcast, fly-walk etc.
- *Computation capacities of the searcher*: Biochemistry, few neurons, numerous neurons.
- *Representation of the environment*: Space perception, statistics of environment, other searchers.

Outline

- Biomolecules Random Walks

Large knowledge, Models
Strategies and Bayesian Inference

- Bacteria (*E. coli*), *C. elegans*,
Neutrophils



- Larva

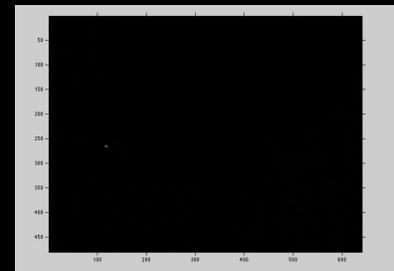


- Robots

Heterogeneity, Intermittency, turbulence
Less knowledge (growing)



- Insects



M. El-Beheiry *et al*, *Nature Methods* 12, 594-595 (2015)
JBM *et al*, *PNAS* 109, No 5, p1802-1807, (2012)
M. Sarris *et al*, *Current Biology*, 22, p2375-2382, (2012)

E. Korobkova *et al*, *Nature* 428:574-578. (2004)
H. Park *et al*, *Nature* 468(7325): 819-23, (2010).
L. Luo *et al*, *Neuron* 82:1115-1128 (2014)

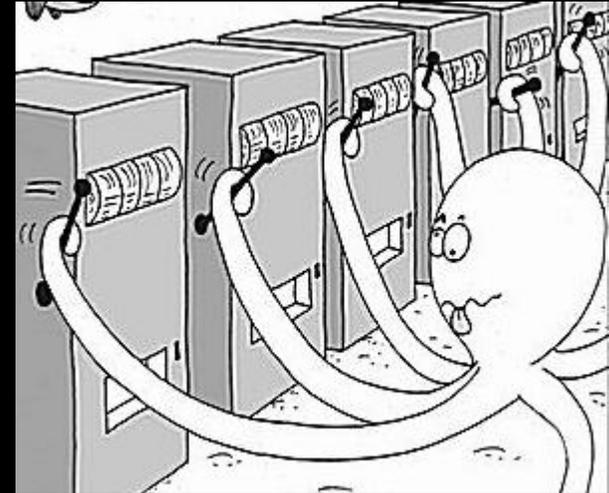
Exploration/Exploitation

- Searching is an information game
- Source sends noisy message that the searcher attempts to decode
- for all searchers there is a balance in decision making
 - **Explore** the environment to acquire more information
 - **Exploit** accumulated information to make decision

2-Armed Bandit: explore-exploit Games

- Multi-Armed Bandit Game

- N “Bandit” machines with unknown paying probabilities, p_i
- Operator sequentially plays bandit to find the best one
- Goal: efficient strategies to have the smallest regret

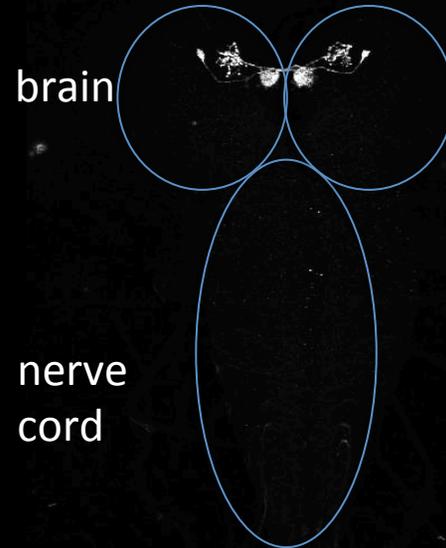
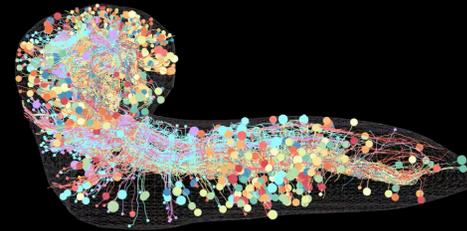
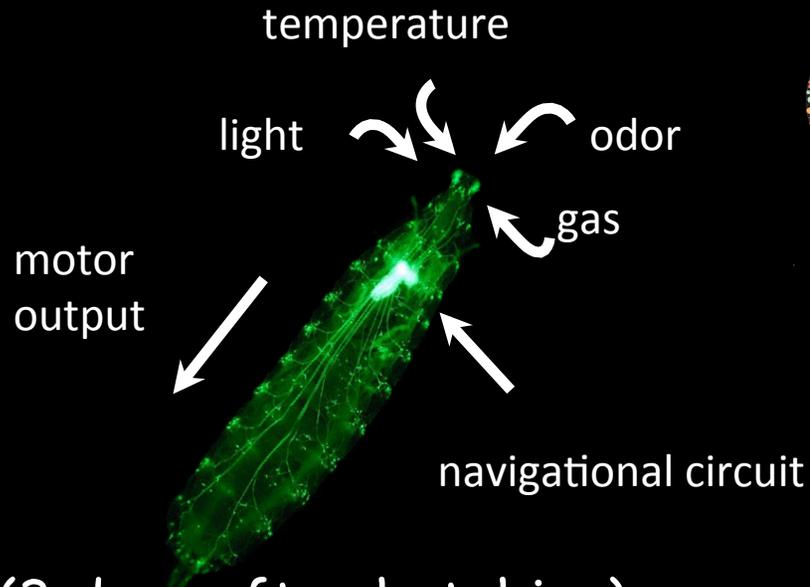


- Explore/Exploit
- Playing the same machine increase information on the machine
- Playing another machine : it might a better one
- Hard decision Making: Pain/Threat (Low level) ppk

J.C. Gittins, J. Roy. Stat. Society Series B, 148-177, (1979)

T. Ohyama *et al*, *Nature* **520**, 633–639 (2015)

Drosophila Larval



- 3 instar (3 days after hatching)
- 2-5mm
- Start development on their food
- No Food: immediately start to search
- 10000 neurons
- Genetic targeting of individual neurons
- Optogenetic Stimulation of identified neuron/s with chrimson

Albert Cardona



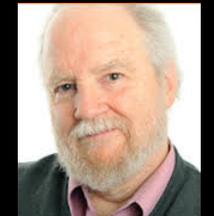
Stephan Saalfeld



Marta Zlatic



James Truman



T. Ohyama *et al*, *Nature* **520**, 633–639 (2015)

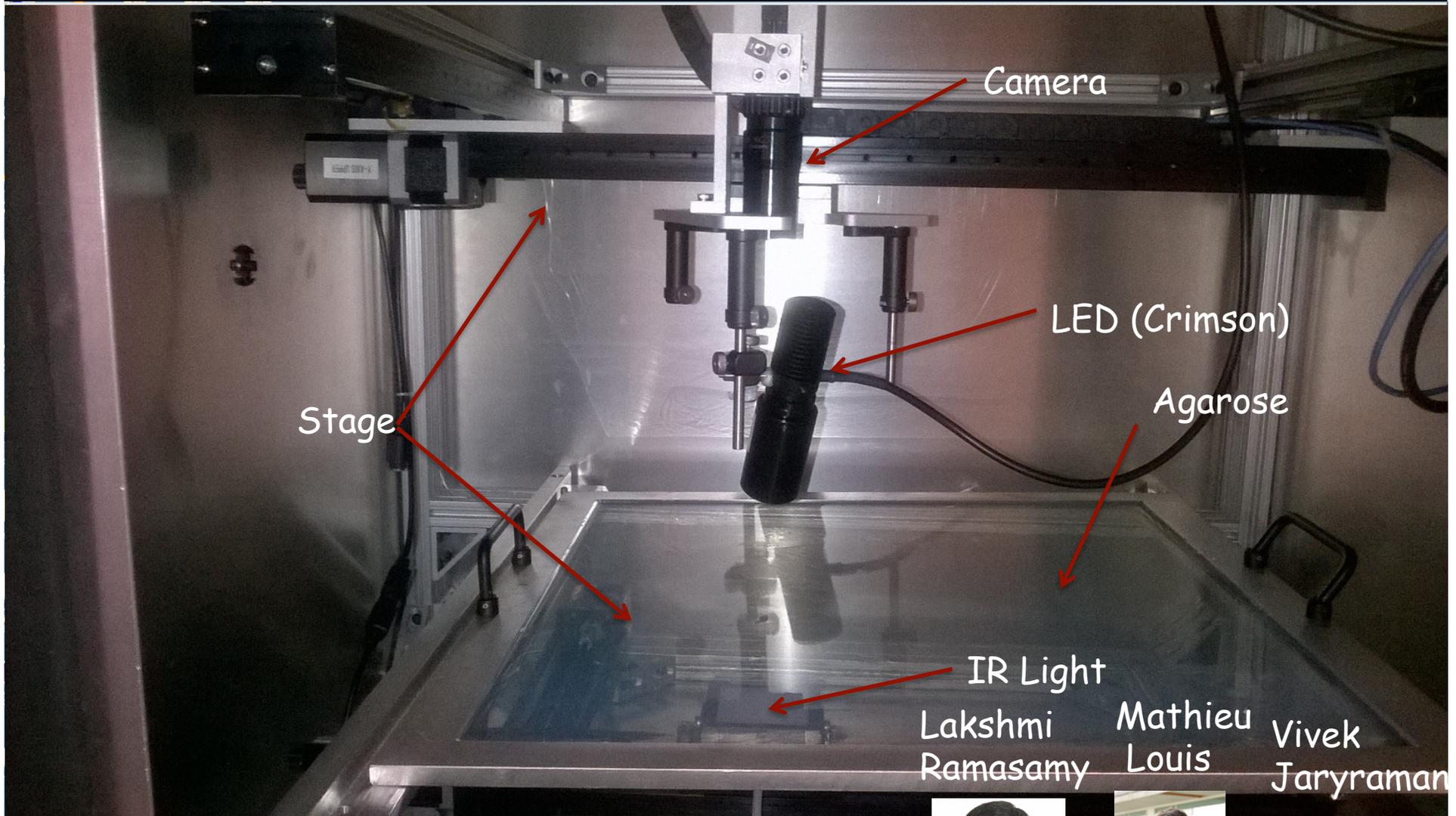
B.D. Pfeiffer *et al*, *PNAS* vol. 105 no. 28, p 9715–9720 (2008)

Playing the Bandit Game

- We need a close-loop system:
 - Assessing behaviour live
 - Stimuli depending on behaviour
- Increasing attempt to quantify Behaviour from video
- Large number of features extracted + Data Tagging
- JAABA based on GentleBoost
- The larva is complex
 - Large variance in images.
 - Deformable object, multiscale dynamics.
- Limited number of features
- Features are accessible up until time t
- Image analysis with OpenCV
- 15ms data acquisition and basic processing
- 5ms features + classification

M. Kabra et al, Nature Methods 10, 64-67, (2013)
F. De Chaumont et al, Nature Methods 9, 410-417 (2012)
G.J. Stephens et al, Plos Comp Biol, 4(4): e1000028 (2008)
G.J. Stephens et al, PNAS (USA) 108, 7286-7289 (2011).

Setup



Lakshmi Mathieu Vivek
Ramasamy Louis Jaryraman

• C++, Qt and OpenCV

A. Schulze *et al*, eLife 2015;4:e06694



Eric
Trautman



Features

- Angle

$$\theta = a \cos(\vec{u} \cdot \vec{v})$$

- Nematic spline

$$S = \frac{1}{N-1} \left(3 \sum_{i=1}^{N-1} \vec{u}_i \cdot \vec{w}_i - \frac{1}{2} \right)$$

- Reduced eigenvalues

$$\tilde{\lambda} = \frac{\lambda_1 - \lambda_2}{\lambda_1 + \lambda_2} = \sqrt{1 - \frac{4(\langle x^2 \rangle \langle y^2 \rangle - \langle xy \rangle^2)}{(\langle x^2 \rangle + \langle y^2 \rangle)^2}}$$

- Agitation velocity

$$\langle \|\vec{V}\| \rangle = \frac{1}{3} (\|\vec{V}_{neck}\| + \|\vec{V}_{top_neck}\| + \|\vec{V}_{down_neck}\|)$$

- Asymmetry factor

$$As = \vec{u} \cdot \vec{v}$$

- Damped distance

$$d = \sum_{i=0}^t \gamma^i d_{t-i} \quad d_{t-i} = \|\vec{r}_{neck}^{t-i} - \vec{r}_{neck}^{t-i-1}\|$$

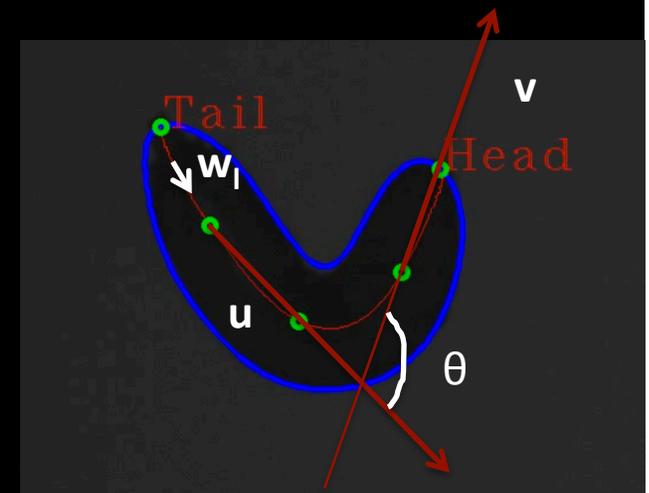
- Negative velocity

$$\vec{V}_{neg} = \vec{V}_{neck} \cdot \vec{u}$$

- Squared Smoothed delayed derivatives

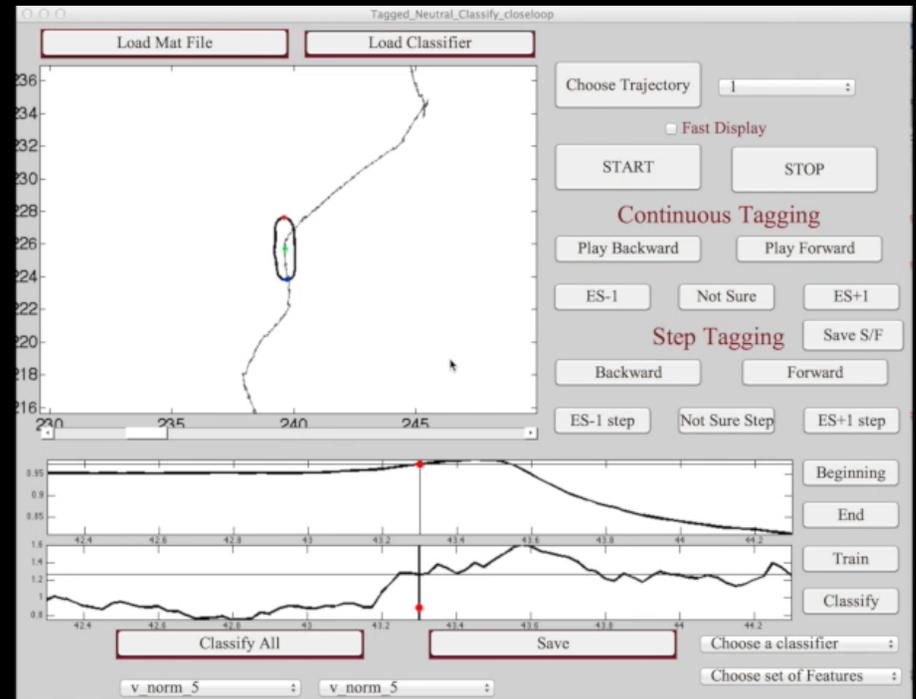
$$F'(t) = \left\| \int_{-\infty}^t K(t-s) F(s) ds \right\|^2$$

$$K(t) = e^{-\lambda t} (1 - \lambda t)$$



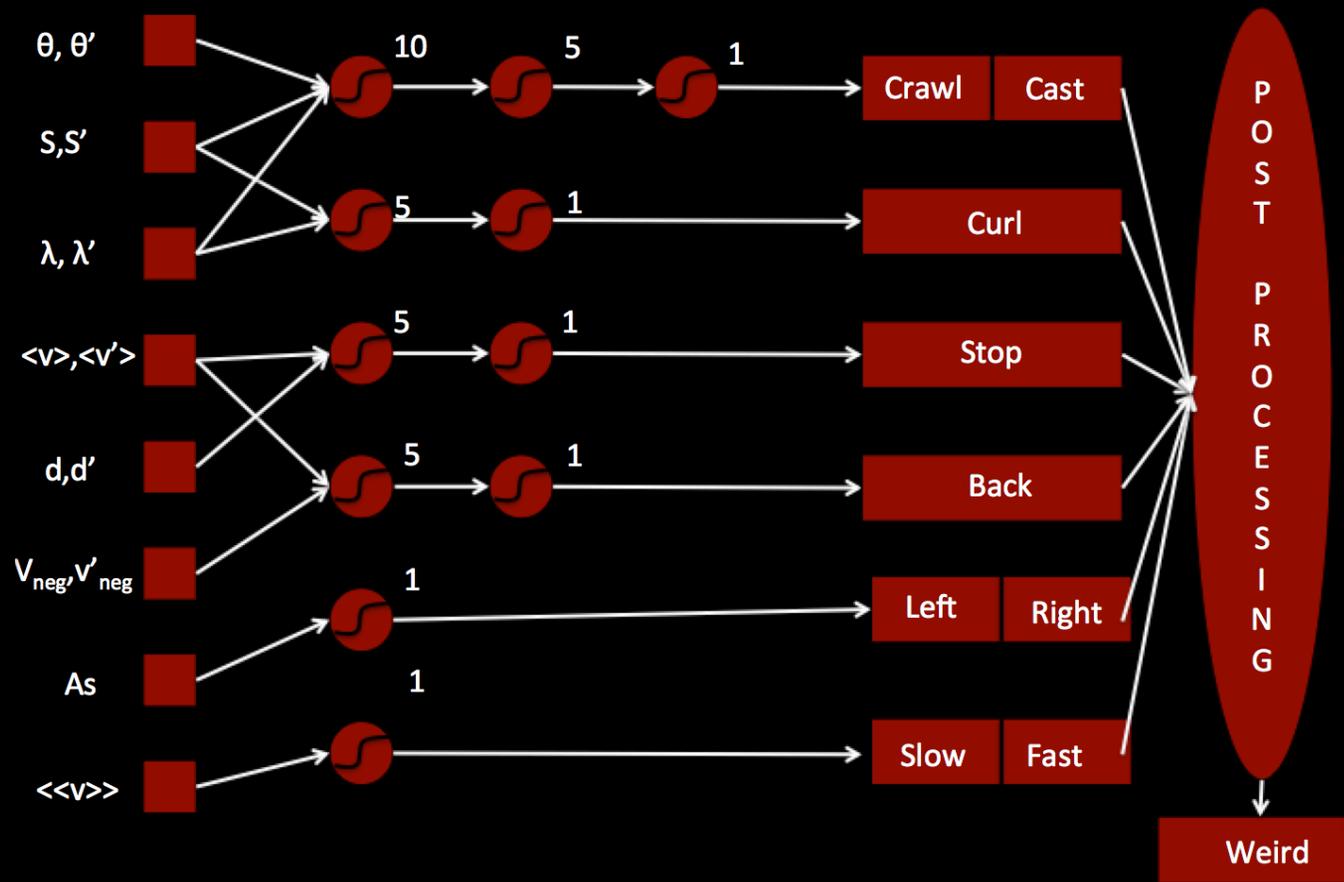
Custom tagging software

- Matlab Gui
- Replay experimental data
- Evaluate features at all time
- Trajectory + specific points
- $\{+1;0;-1\}$ tagging
- Issue with Ground-Truth-ing
 - No easy agreement on some behaviour
 - Tagging extreme state
 - 2-3 larvae tagging
- Save features + states

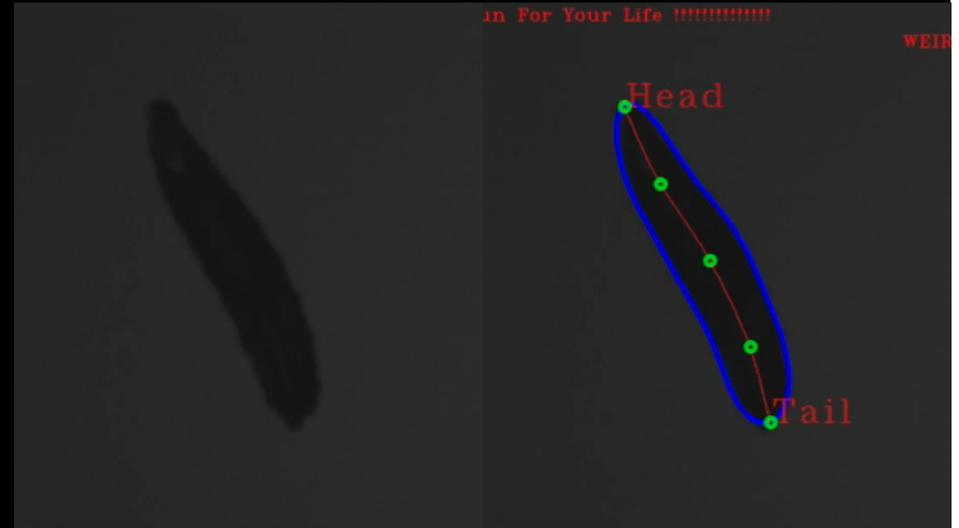


Classifying

- Simple Neural Network
- Pre-structure architecture
- Small data set
- New Version: Random Forest



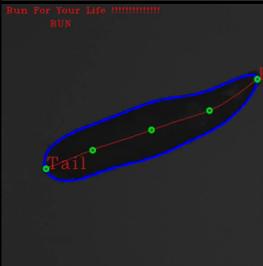
Live Behaviour



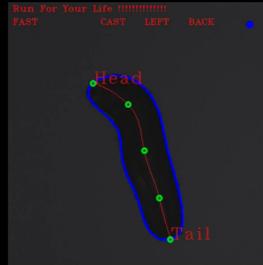
- 40-50 Hz recording
- Live behaviour assessment
- No fast oscillations between Behaviour
- 2 larvae tagging
- Save videos
- Save features + contour in text files
- 5min-5hours recording

Behaviour

Crawl



Cast



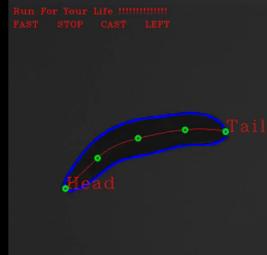
Back



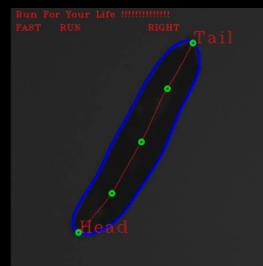
Curl



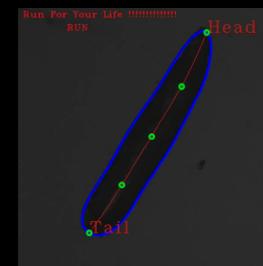
Stop



Roll

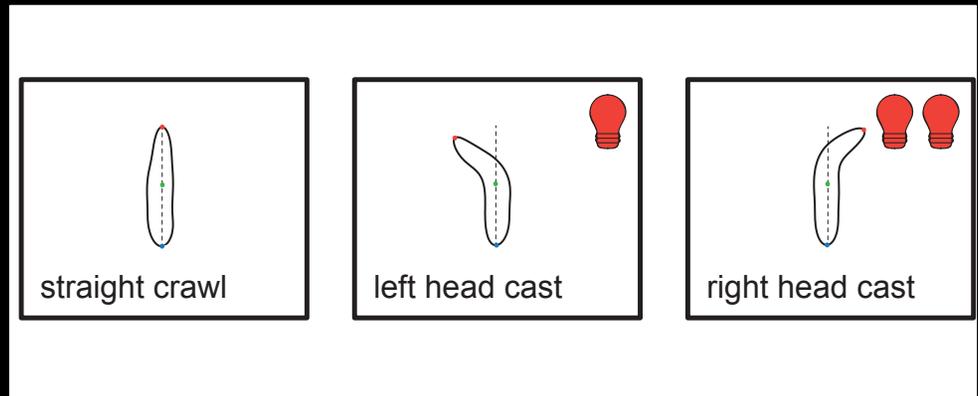


Escape

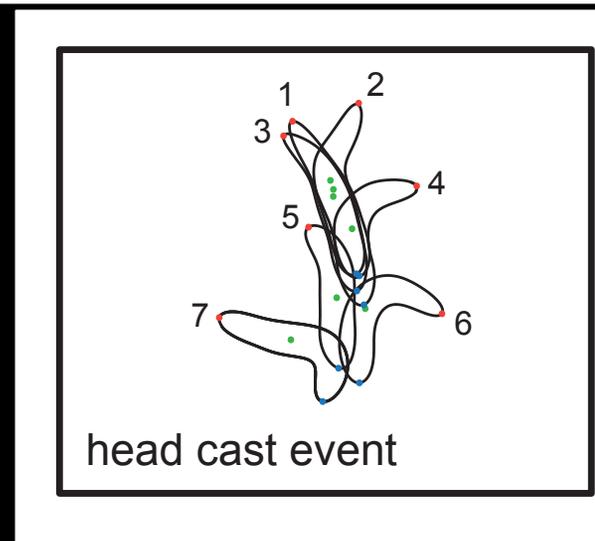
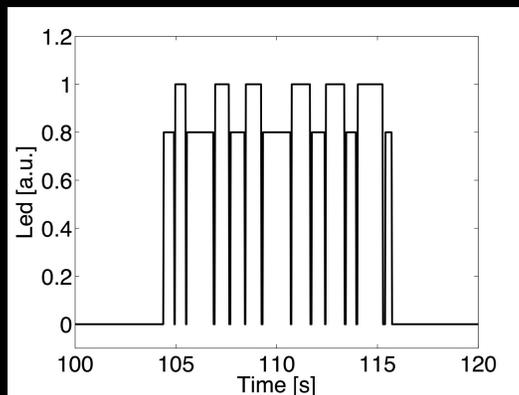


Larva Playing The Bandit Game

- 2-Armed Bandit
 - The Game starts when the larva starts Head-Casting
 - Each Side Is associated to a stimulus
 - The Game is finished when the Larva choses a side and crawl
-
- 2 Games
 - Game 1: $S_0=0$, $S_1=50\%$ - $S_2=100\%$
 - Game 2: $S_0=100$, $S_1=25\%$ - $S_2=75\%$

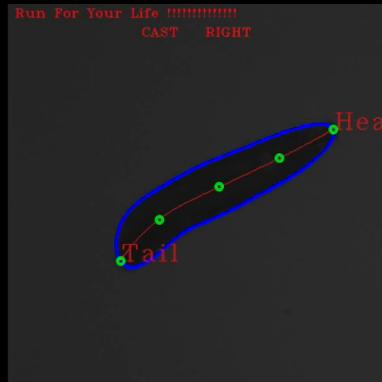


Example Stimuli Game 1

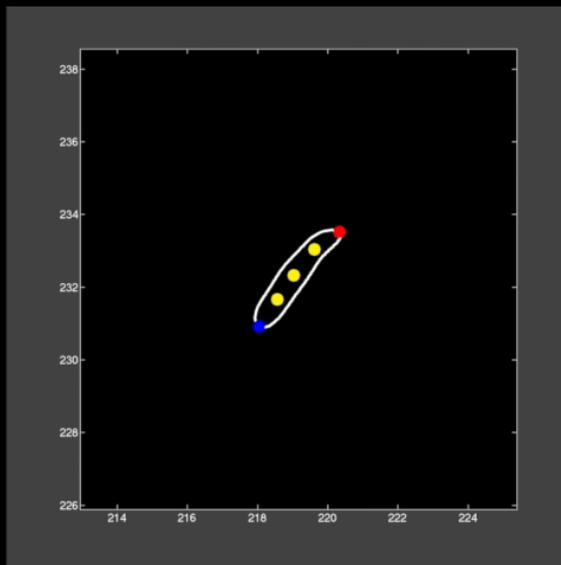


Larva Playing the Game

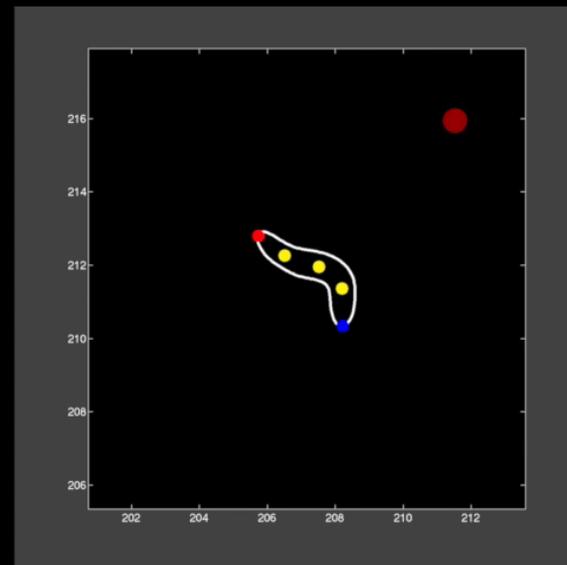
HeadCast



Game 1



Game 2

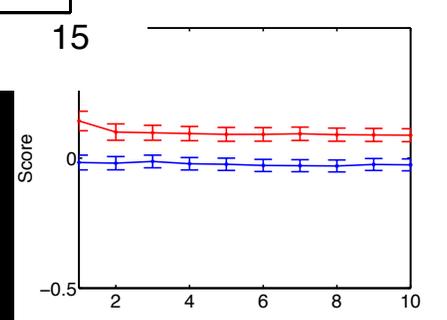
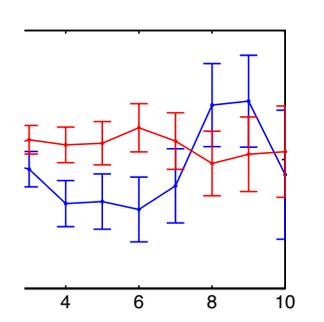
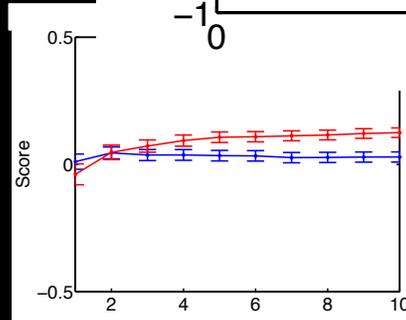
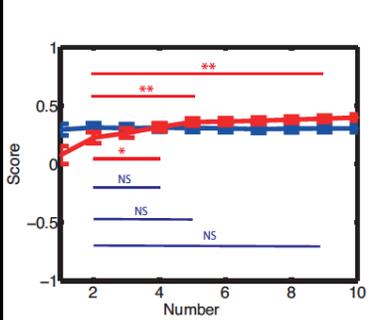
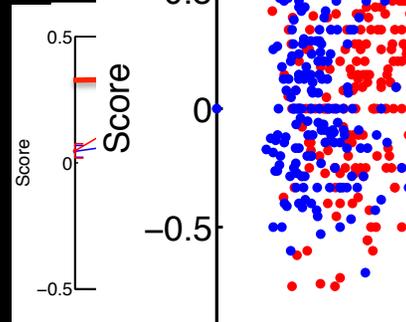
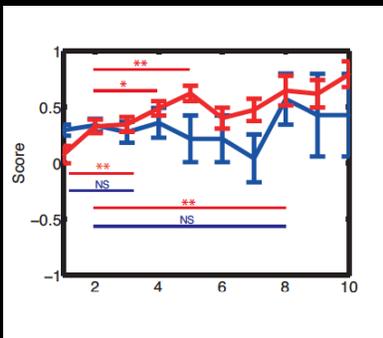
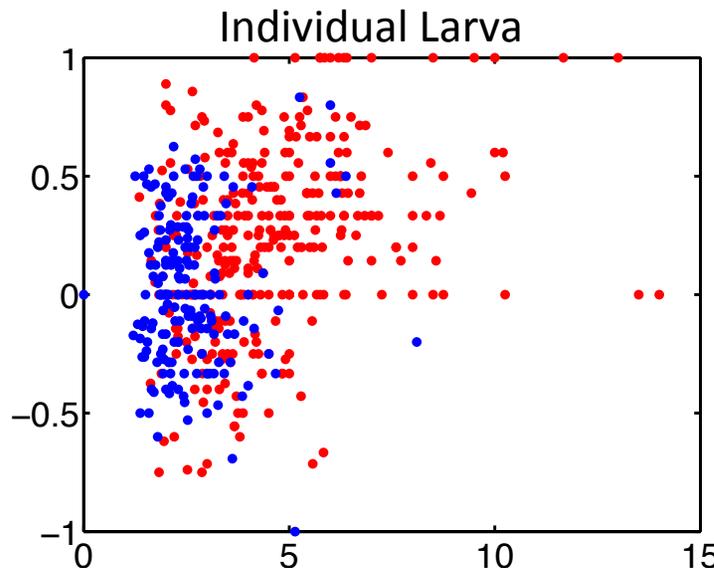
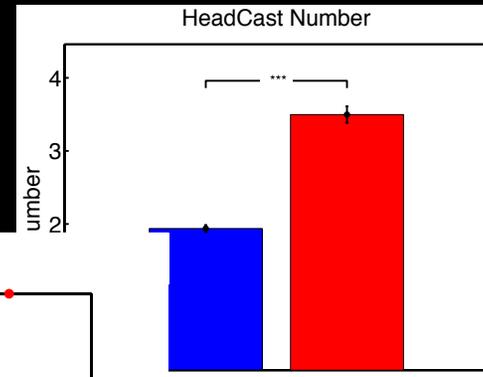
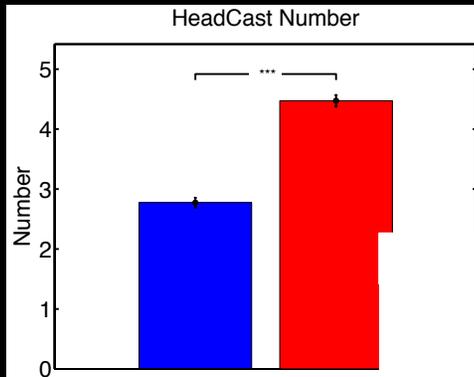


Exploring to make good decision vs ϵ -greedy

Game 1
(5500 games)

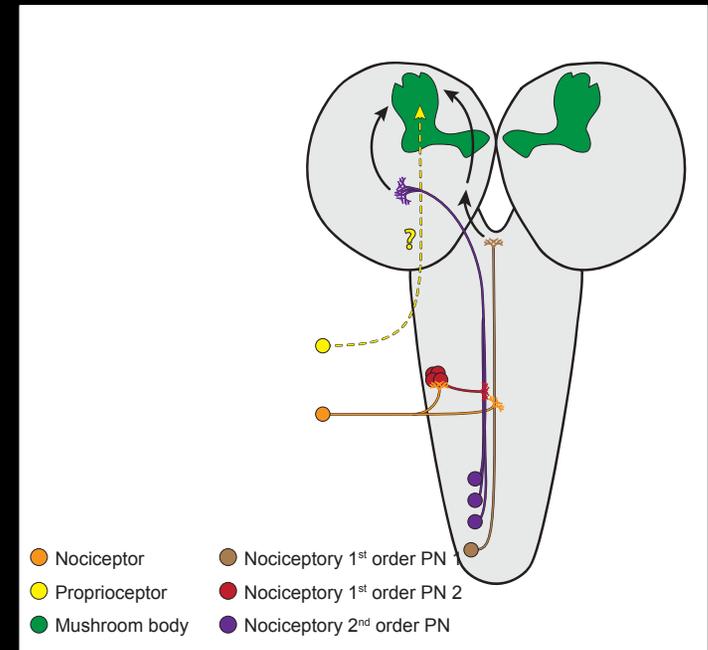
ppk
attp2

Game 2
(3000 games)

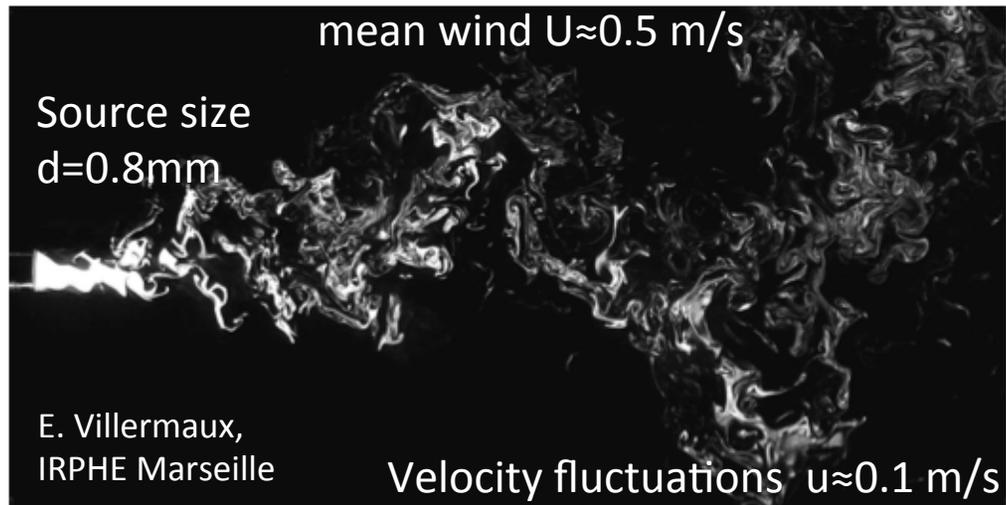


Larva playing the Bandit Game

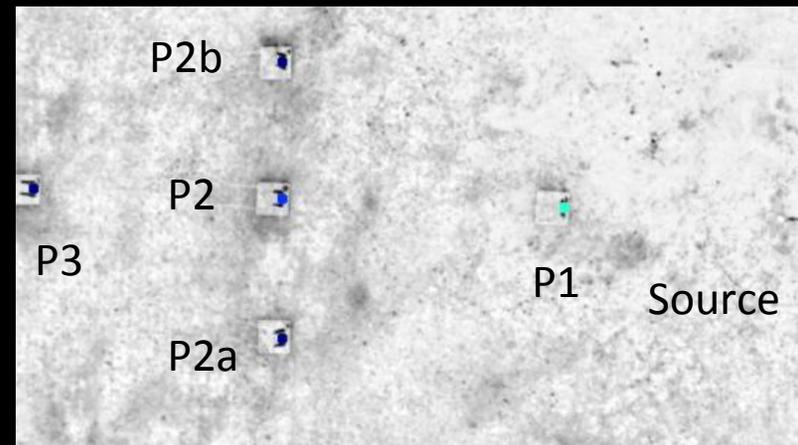
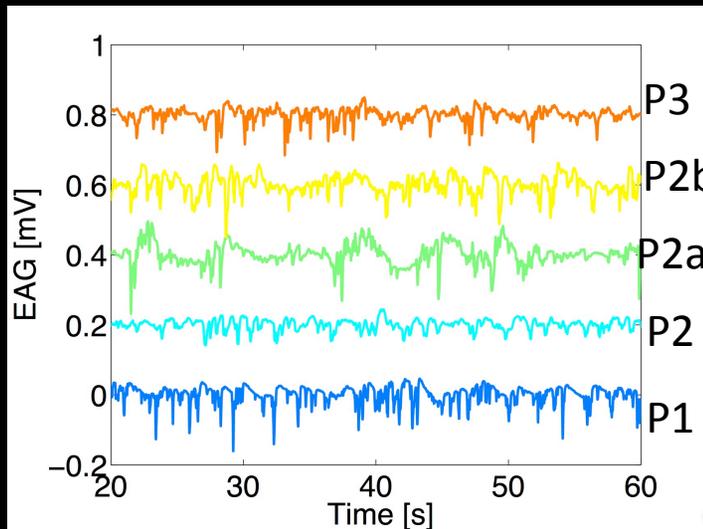
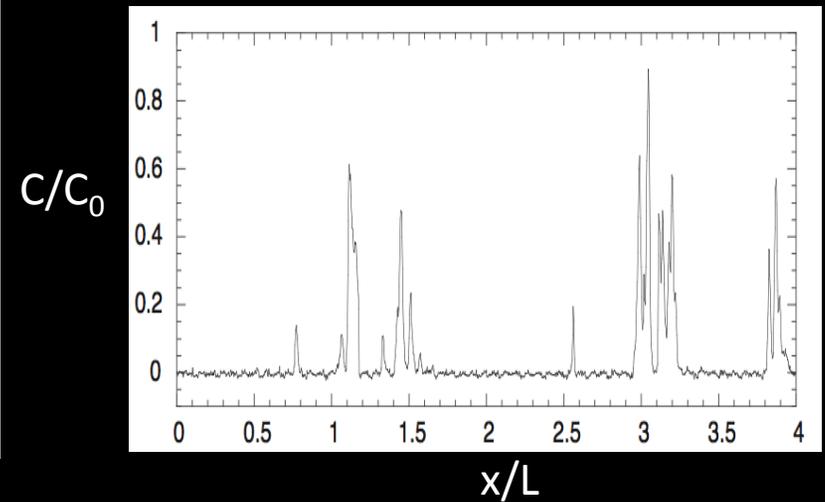
- The Bandit Game as a probe of exploration/exploitation dynamics
- Larva modulates the number of HeadCasts
- Explorers outperforms exploiters
- Strategy Switch between games
- Neural substrate for the strategy
- Strategies depend on the nature of the stimuli:
Nociceptive, Olfactory, Thermal.



Turbulence



turbulent velocity correlation length $L = 8$ cm



Consequences

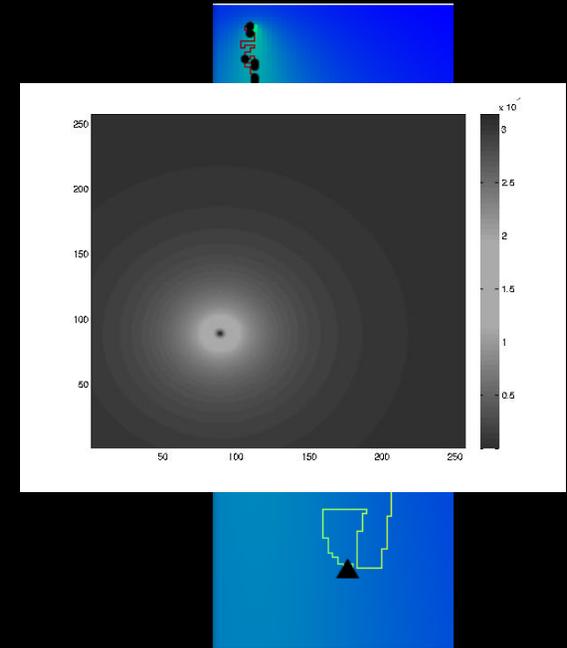
- No Global Gradients
- Intermittent Signal
- Local Gradients don't point towards the source
- Local detections give very limited information on the source (Position, Emission Rate, Multiple Sources)
- Information Theory
 - R.S. Sutton & A.G. Barto, MIT Press, Cambridge (1998)
 - R.E. Bellman, Princeton University Press (1957)
 - K.L. Leyton-Brown & Y. Shoham, Syn. Lect. Art. Int. Mach. Learn. (2008)
 - D. Mackay, Cambridge Univ Press (2003)

Deciphering the Noisy Message sent by the source

- Detections (and no detections) are messages sent by the source
- $R(r | r_0)$ hit rate at the position r when the source is at r_0
- After H detections

$$P_t(r_0) = \frac{e^{-\int_0^t R(r(s)|r_0)ds} \prod_{h=1}^H R(r(t_h) | r_0)}{\int dz e^{-\int_0^t R(r(s)|z)ds} \prod_{h=1}^H R(r(t_h) | z)}$$

- Maximizing Likelihood : Lost Searchers
- Information Based Decisions: Infotaxis



$$\langle \Delta S \rangle (r \rightarrow r_j) = P_t(r_j)[0 - S] + (1 - P_t(r_j))[\rho_0 \Delta S_0 + \rho_1 \Delta S_1 + \dots]$$

Insect Space Perception

- Probability Map building requires space perception and odometry error corrections.
- How to integrate external cues?
- Definition of cognitive maps and space perception?
- Various Orientation/navigation Strategies depending on insects
- Integrating space perception in search strategies

R. Wehner, Birkhauser, Basel (1987)

P.K. Visscher *et al*, Ecology 63:1790-1801 (1982)

A.T. Bennet, J. Exp. Biol. 199, p219-224 (1996)

M. Colett *et al*, Nature 394:269-272 (1998)

J. Jefferey, Oxford Univ Press (2003)

M. Mizumani *et al*, J. Comp. Neurol. 402, 501-537, (1998)

R. Wehner *et al*, Annu. Rev. Neurosci. (1990)

T.A. Ofstad *et al*, Nature 474(7350):204:207

J. Murlis *et al*, Annu Rev Entomol 37:505-532 (1992)

A. Mafra-Neto *et al* Nature 369:142-144 (1994)

J.S. Kennedy *et al*, Physiol Entomol 27:58-66 (1983)

N.J. Vickers *et al*, Nature 410(6827):466-470 (2001)

N.J. Vickers *et al*, Biol Bull 198(2):203-212 (2000)

M.A. Willis *et al*, Exp Biol 214, 4121-4132 (2011)

F. Van Breugel, Cur. Biol , 25, 2123-2129 (2015)

Free Energy Based Search Strategy

- Limited Space Perception

$$P_t^M(\vec{r}_0 | \Theta_t) = \frac{e^{-\frac{\|\vec{r}_0 - \vec{r}_G\|^2}{\lambda_G^2}} \left(1 - \frac{1}{N_M} \sum_{j=N_t - N_M + 1}^{N_t} e^{-\frac{\|\vec{r}_0 - \vec{r}_j\|^2}{\lambda_u^2}} \right)}{Z_t}$$

$$\vec{r}_G = \sum_{i=1}^G \gamma^{G-i} \vec{r}(t_i) / \sum_{i=1}^G \gamma^{G-i}$$

Detections term

No Detections term

- Decision process

$$F_t(\Theta_t) = \underbrace{W_t(\Theta_t)}_{\text{Work}} + \underbrace{TS_t(\Theta_t)}_{\text{Entropy}} = \underbrace{\int \int d\vec{r}_0 P_t^M(\vec{r}_0 | \Theta_t)}_A - \underbrace{T \int \int d\vec{r}_0 P_t^M(\vec{r}_0 | \Theta_t) \log P_t^M(\vec{r}_0 | \Theta_t)}_{\text{Max Likelihood}} + \underbrace{\int \int d\vec{r}_0 P_t^M(\vec{r}_0 | \Theta_t) \log P_t^M(\vec{r}_0 | \Theta_t)}_{\text{Exploration/exploitation}}$$

Work

Entropy

Max Likelihood

Exploration/exploitation

$$\Delta F_t(\vec{r}_t \rightarrow \vec{r}_{t+dt} | \Theta_t) = \underbrace{P_t^M(\vec{r}_{t+dt}) [1 - F_t]}_{\text{Discovery}} + \underbrace{(1 - P_t^M(\vec{r}_{t+dt})) \sum_{i=0}^1 \rho_i(\vec{r}_{t+dt}) \Delta F_t^i}_{\text{Nothing}}$$

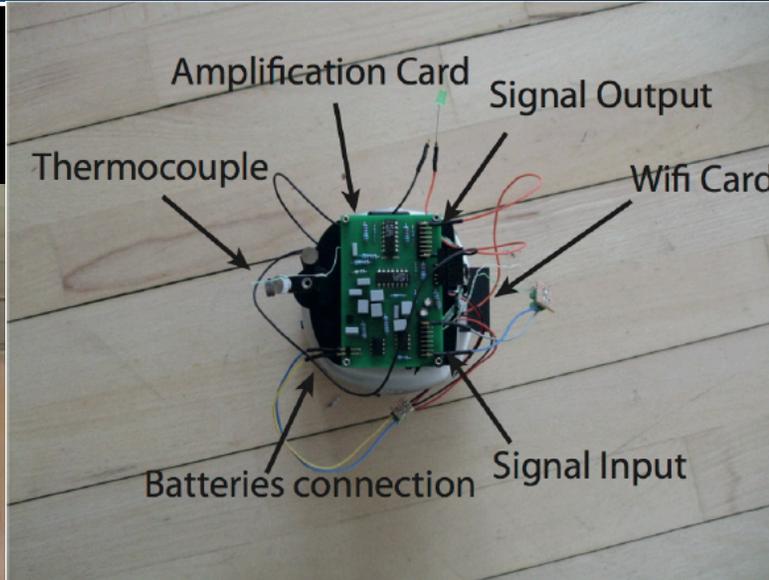
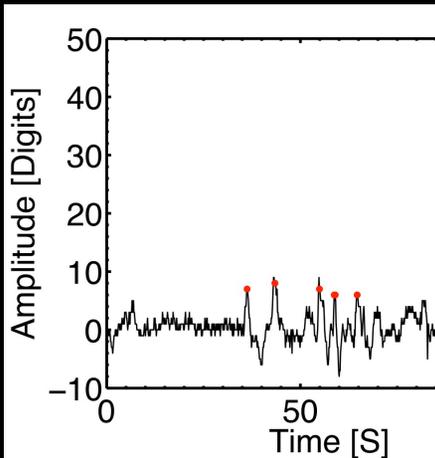
Discovery

Nothing

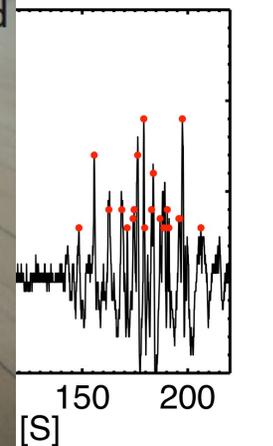
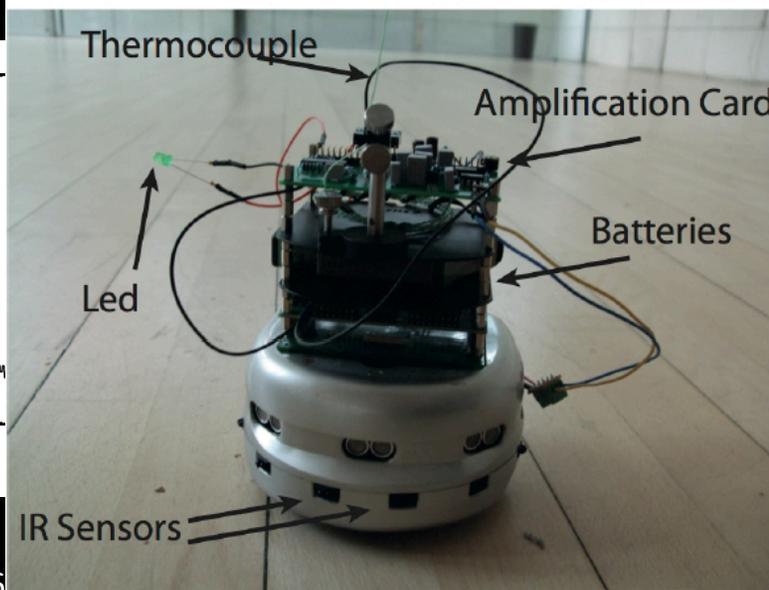
- Tradeoff between exploration and exploitation : Control with T

Experimental Searches

Windless



Information



Swarm of Robots

$$\Delta F_t^s(\vec{r}_t^s \rightarrow \vec{r}_{t+dt}^s | \Theta_t) = P_t^M(\vec{r}_{t+dt}^s | \Theta_t) [1 - F_t] \\ + (1 - P_t^M(\vec{r}_{t+dt}^s | \Theta_t)) [\rho_0 \Delta F_t^{s,0} + \rho_1 \Delta F_t^{s,1}]$$

$$\Theta_t = \{\Theta_t^1, \Theta_t^2, \dots, \Theta_t^s, \dots\}$$



Searching in the Turbulent Realm

- Space Perception not required
- Error accumulation
- Short memory
- Greedy Decision
- Sharing incomplete and noisy Information

Rhyncophorus Ferrugineus (Rhynco)

- Advantage
 - Complex Behaviour
 - Large and small scale searches
 - Flying (5m.s^{-1}) Walking ($1\text{-}5\text{cm.s}^{-1}$) search strategies
 - No predators (in some ways)
 - Eat Palm Trees (No more Palm Trees)
- Disadvantage
 - Very Limited knowledge
 - Realistic environments (light, sky, landscape)
 - Small pieces of knowledge on neuro-biology
 - No Dictionary of Behaviour

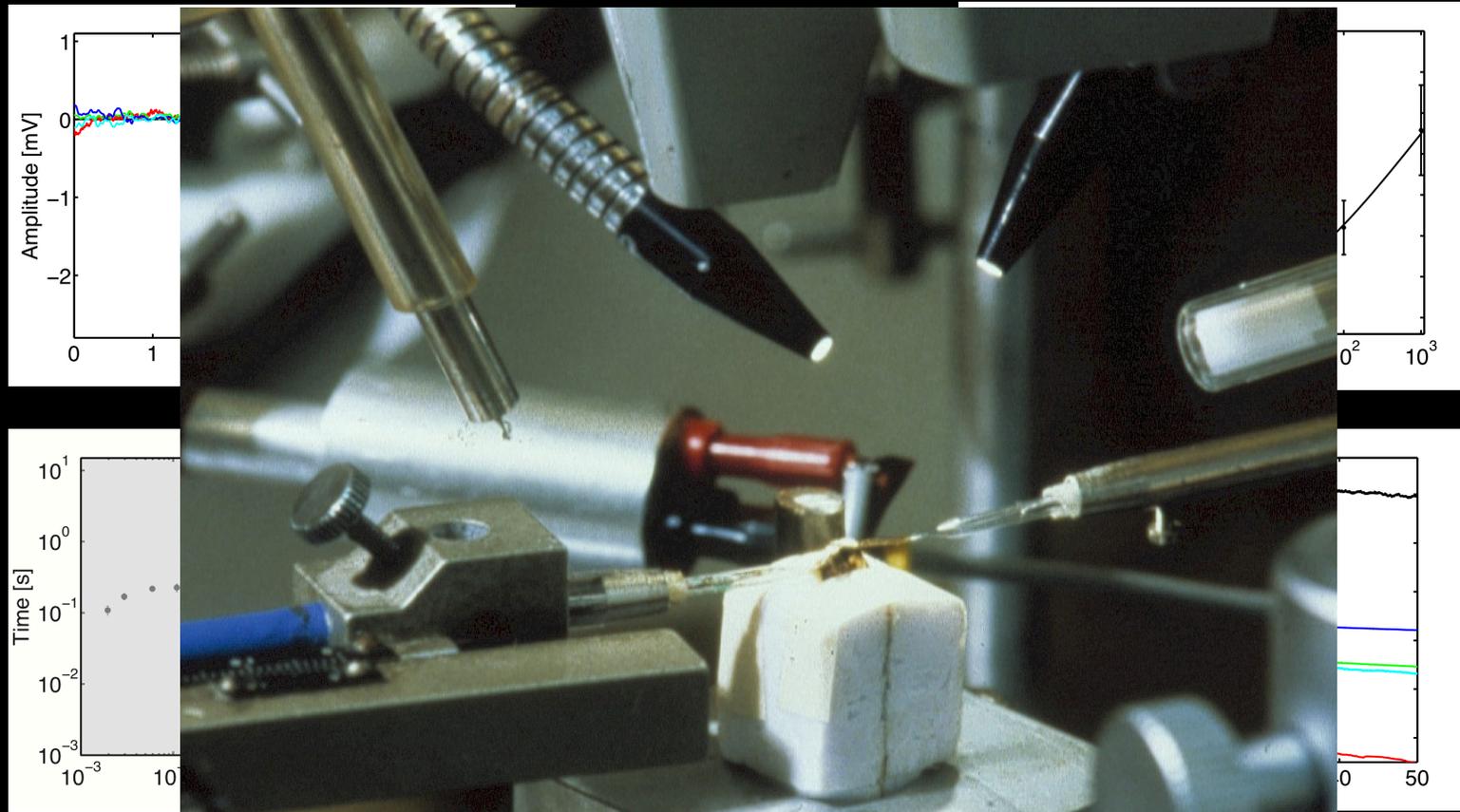


Experimental Searches

- Infer detections from behaviour is too difficult
- 2 Elements
 - Insect trajectories
 - Olfactory signal along the decision path

Antenna as “Sensors”

- Insects' Antenna highly efficient detectors
- Simple ElectroAntennoGram measures *cis-7-dodecenyl acetate*



K.-E Kaissling *et al*, *Naturwissenschaften* 55:395, (1968).

Vivkers

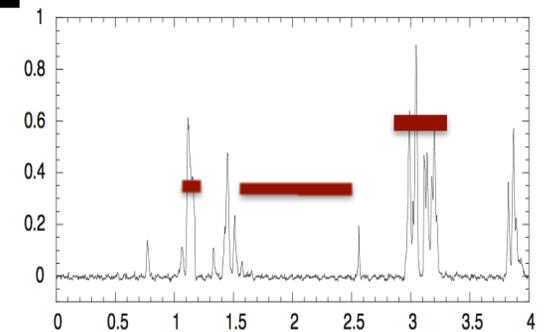
G. Falkovich *et al*, *Rev. Mod. Phys.* 73:913-975 (2001)

Exploiting Turbulence properties and Antenna Selectivity

- Few Scaling and order of magnitudes

$$p(t) \propto \frac{1}{\tau} \left(\frac{\tau}{t} \right)^{\frac{3}{2}} f(\tau) \quad \text{Whiffs/Blank duration} \quad \text{Whiff Clumps}$$

$$\kappa \propto 10^{-7} - 10^{-8} \text{ m}^2 \cdot \text{s}^{-1} \quad Pe = \frac{UL}{\kappa} \quad N(T_w) \propto \sqrt{T_w/\tau}$$



- **Turbulence maintains blends in the plumes**
- Pheromones are specific to insect species
- Add Pheromone detected by another antenna to the odor mix.

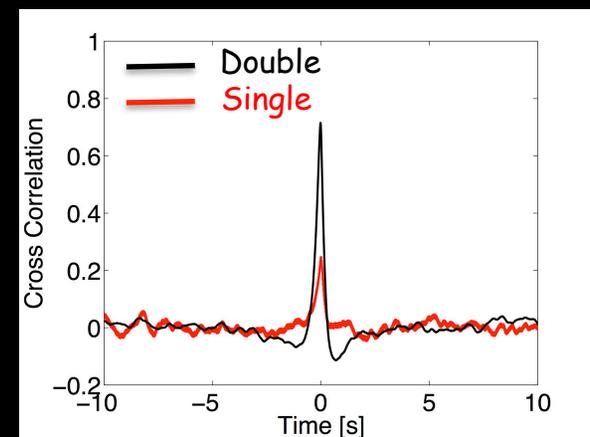
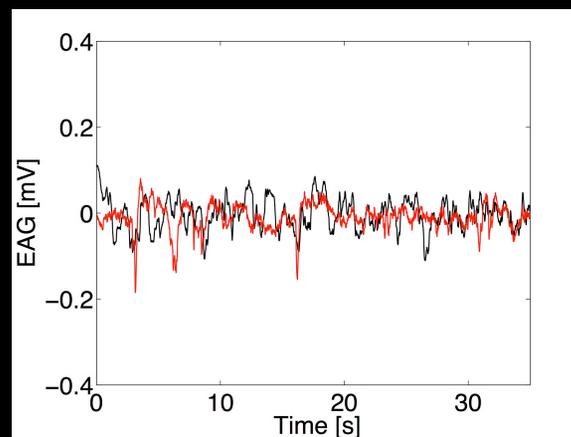
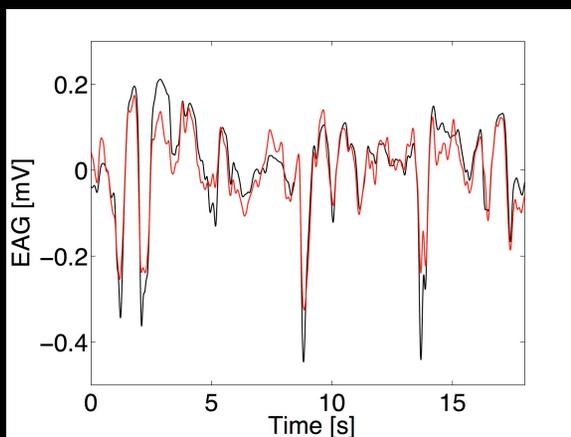
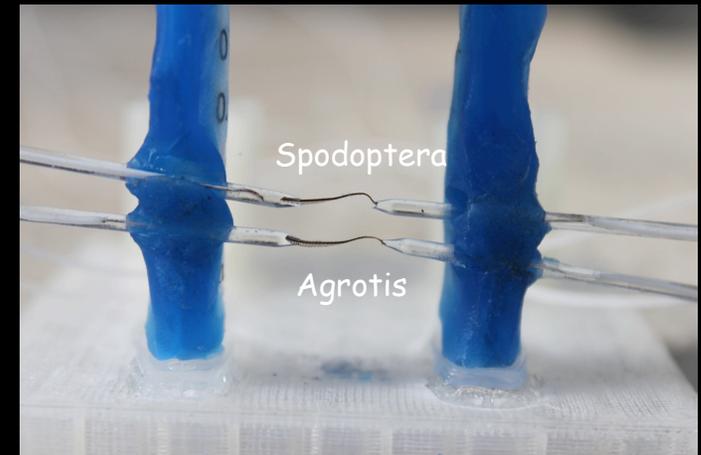
M. Kree *et al*, Phys. Fluids 25:091103 (2013)

A. Celani *et al*, Phys. Rev. X 4, 041015 (2014)

G. Falkovich *et al*, Rev. Mod. Phys. 73:913-975 (2001)

Mixture Plume Detection

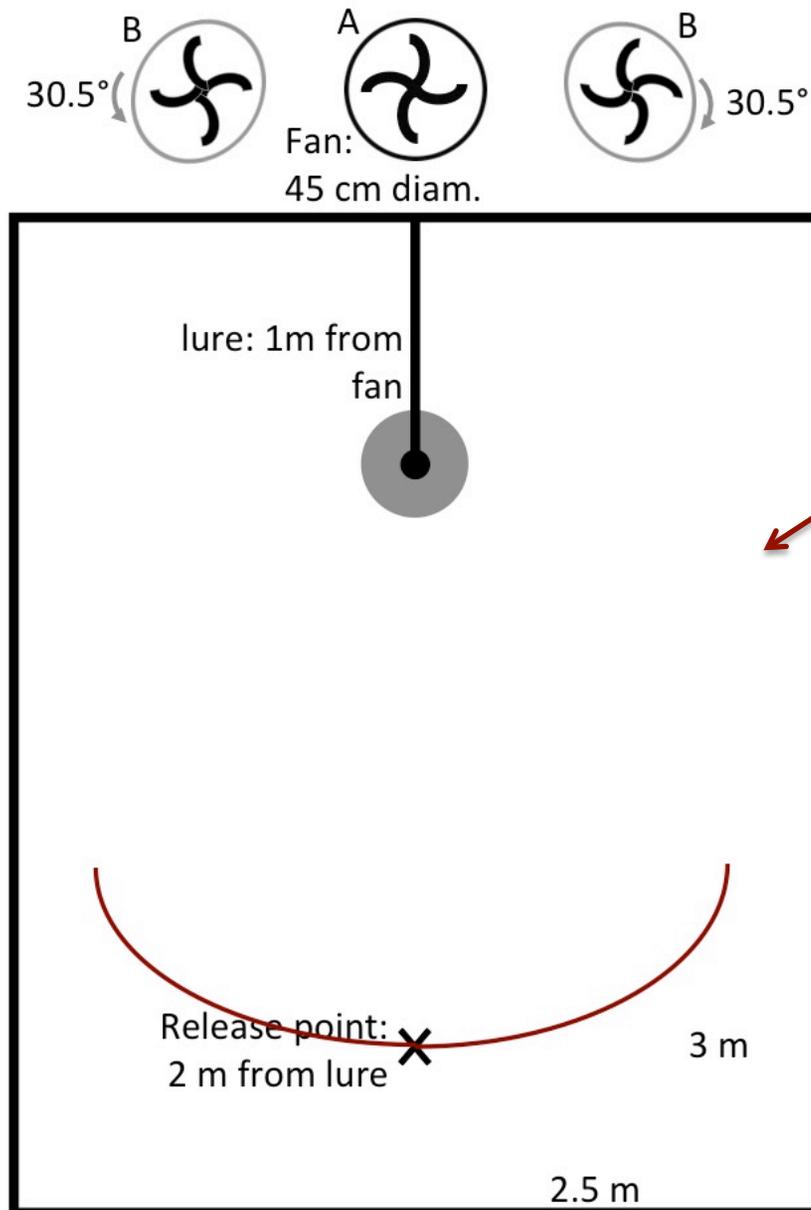
- PID not sensitive enough
- Measure with double EAGs:
 - One Agrotis (Black)
 - One Spodoptera (Red)



Setup

Quantitative elements

- $U = 0.3 - 2 \text{ m.s}$
- $\delta v / U \approx 0.05 - 0.3$
- $Re \approx 10^3 - 10^4$
- $Pe \approx 10^6$
- (Z)-7-dodecenyl acetate
(Agrotis Pheromon)
1-10 μg in 10 μl Hexane
EAG(10m) $\approx 300 \mu\text{V}$
- 4-méthyl-5-nonanol
(ferrugineol)
1 μg in 10 μl Hexane



Trajectory and Pheromone Detection

- Complex temporal dynamics
- Multi-scale peaks, Multi-duration peaks and peaks in peaks
- Peak detection using Random Forest
- Ground-Truthing on double EAG experiments (Manual correction)
- Out of Bag Error = 5.10^{-3}

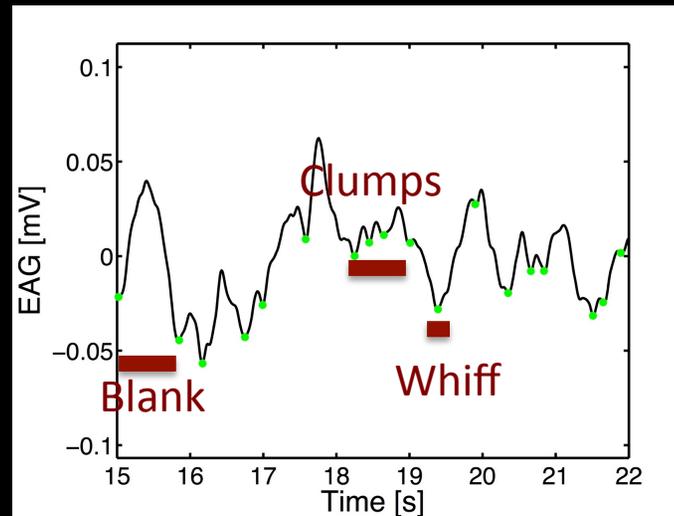
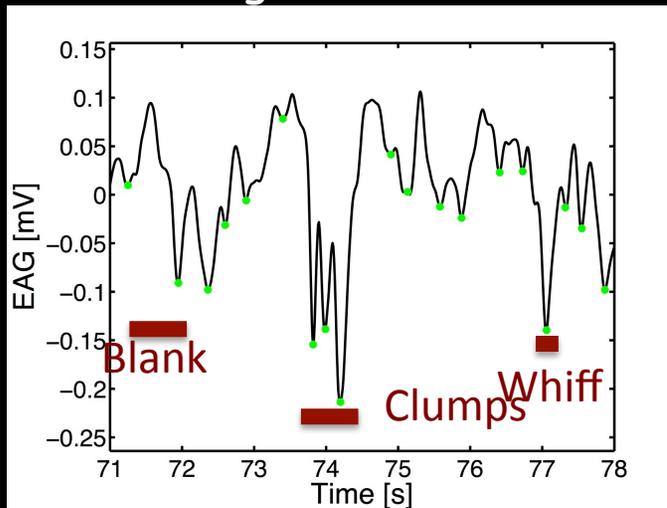
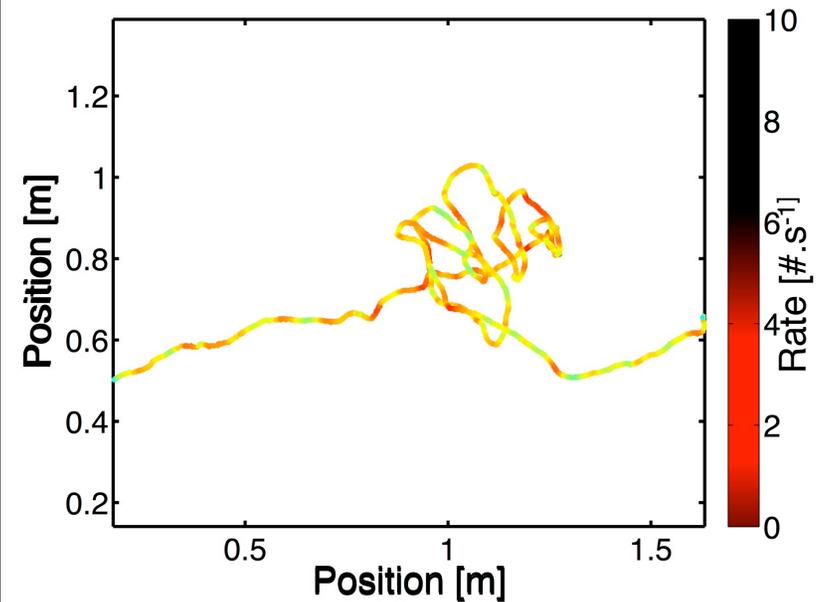
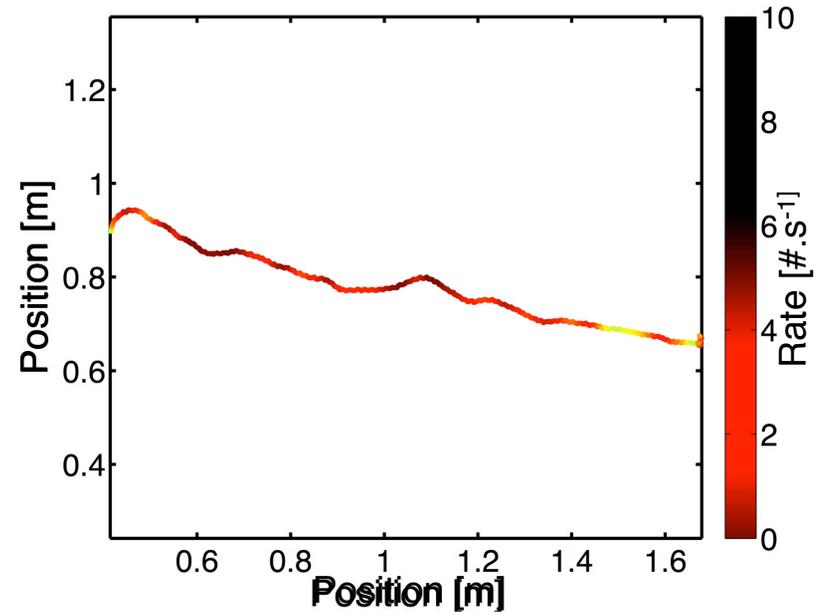
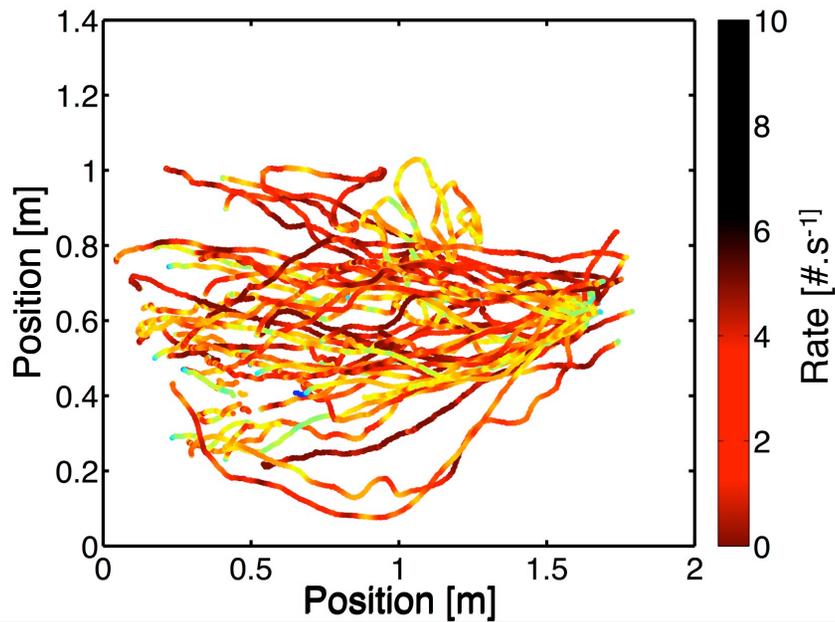


Image Analysis Using Robust PCA

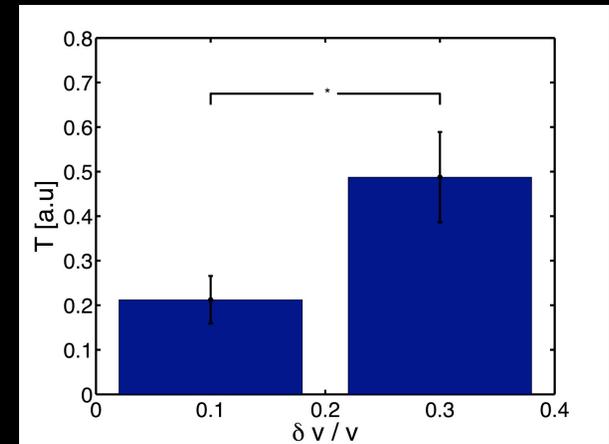
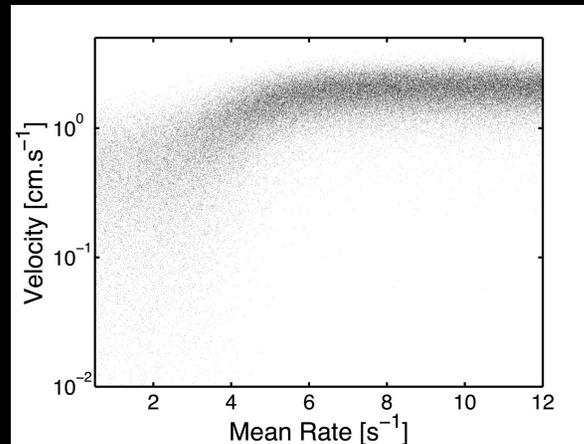
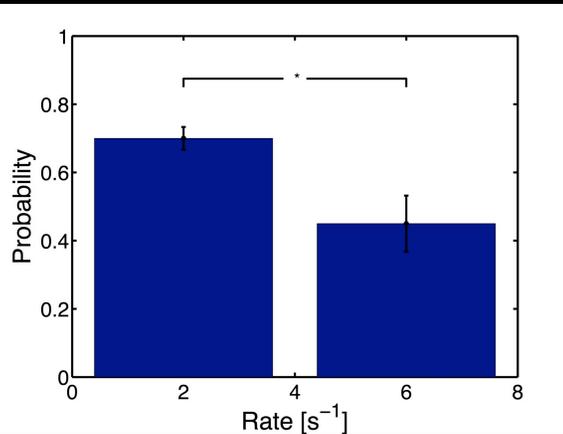


Trajectory/Detections



The surprising, disappointing and inefficient strategy of the Rhynco: Key elements

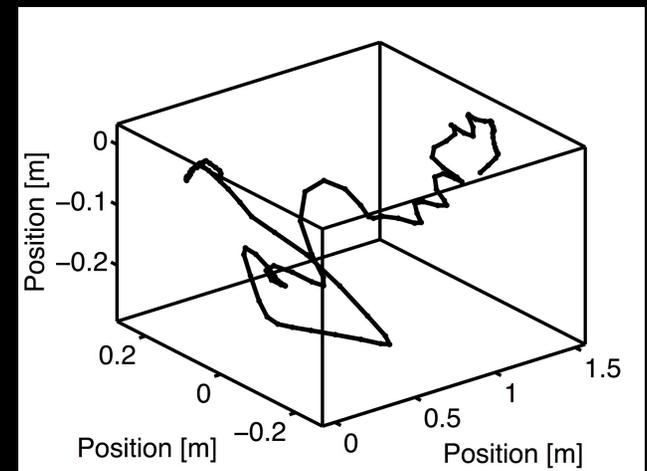
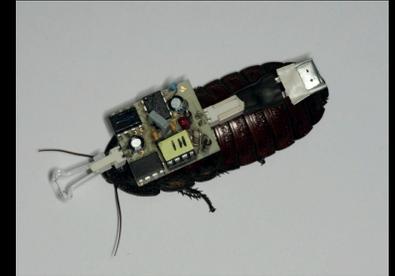
- Correlated Two Mode Poisson motion: Run-Stop ($0.08s^{-1}$, $0.1s^{-1}$)
- Decorrelation of characteristic scales
 - $T_{\text{turbulence}} \sim 100 \text{ ms}$ - $1s$
 - $T_{\text{rhynco}} \sim 10s$



- Velocity-Rate correlation: non-adapted chemotaxis (Bacteria)
 $v_{\text{chemotaxis}} \sim 0.7 \pm 0.2 \text{ cm.s}^{-1}$
- Stop-Rate correlation: Exploiting rather than exploring

Conclusion and Perspective

- Neural substrate to play the Bandit Game (Mushroom body?)
- Q-Learning for olfactory search
- Disentangling cue statistics and other cues
 - Pheromone detection statistics and wind dynamics
 - The Bandit Game for thermal (chiral thermal Gradient)
- *Agrotis Ipsilon* turbulent searches
 - Challenge: adding the extra antenna setup without modifying flight pattern
 - Clear Patterns during flight



Acknowledgments

Pasteur Institute

- Massimo Vergassola (now at UCSD)
- Jerome Wong-Ng (now at UCSD)
- Guillaume Voisinne (now at Sloan Kettering)
- Christopher Wheeler
- Ziqi Zhang
- Alexandre Touche

Janelia Research Campus

- **Marta Zlatic** Lab
- Vivek Jaryaman Lab
- Albert Cardona Lab

LORIA-INRIA

- Dominique Martinez

John Hopkins University

- Carey E. Priebe Lab

EMBL/CRG Research Unit in Systems Biology

- Mathieu Louis Lab

EPFL

- Thomas Lochmater

Physiologie de l'Insecte Signalisation et Communication

- Philippe Lucas
- Jean-Pierre Rospars
- Didier Rochat
- Christelle Monsemprasse
- Vincent Jacob
- Khalid Khfif

NYU

- Mark Gershow Lab

Grants:

ANR Grand Emprunt: Pherotaxis (2011-2015), ANR 07 NANO 062 03 (2010-2013), ANR 09 PIRI 0025 01 (2011-2014), C'NANO Ile de France (2010-2012), Masson Visiting Project Janelia Research Campus (2014-2016)