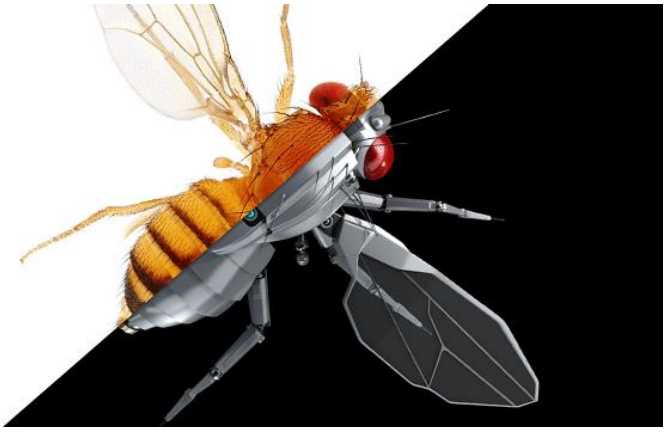
RESEARCH CONFERENCES



ESF-EMBO Conference

Flies, Worms and robots: combining perspectives on minibrains and behaviour

8 – 13 November 2014
Sant Feliu, Spain

Chaired by: Matthieu Louis
Co-chaired by: Barbara Webb

http://minibrains.esf.org/

Highlights & Scientific Report

Conference Highlights

Please provide a brief summary of the conference and its highlights in non-specialist terms (especially for highly technical subjects) for communication and publicity purposes. (ca. 400-500 words)

In the continuity of the 2010 ESF-EMBO minibrains symposium, this conference provided a valuable opportunity to link an integrated understanding of the genetic, molecular, and neuronal mechanisms of behaviour to emerging approaches in robotics. The focus was on the 'miniature' brain of the fruit fly, with complementary insights from work on other model organisms, in particular the nematode worm. This was chosen as an example system where closely related questions about how to exploit knowledge of the full 'connectome' for the brain have long been explored using genetic tools.
The conference revealed the highly significant advances in mapping the Drosophila connectome in adult and larvae and the rapid development and exploitation of precise tools for individual neural recording and control in the behaving animal. This was reflected in reports that showed a step change in our understanding of circuits underlying escape, sensory taxis, integration of internal states and learning. Several presentations showed that whole brain individual neural imaging in both tethered and freely moving *C. elegans* is becoming a reality. This work paves the way for the adaptation of similar techniques to *Drosophila*. Modelling and computation have contributed significantly to developing the analysis tools, particularly for automating the identification of behaviour. New developments in robotics, in particular the use of soft materials and novel actuation methods, were reported, and look set to provide unique insights into behaviour from an embodied perspective. The conference was particularly successful in fostering a real dialogue between engineers and biologists, including activities to enhance a shared perspective. Roboticists had the opportunity to participate in demonstrations of a range of current methods in molecular genetics and behaviour, and biologists could build and investigate the behaviour of a light-sensing robot.

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Scientific Report

Executive Summary

(2 pages max)

An integrated understanding of the genetic, molecular, and neuronal mechanisms of behaviour remains one of the most challenging problems in biology. The goal of this research symposium was to discuss these mechanisms and to explore whether the principles of biological behaviour control can be exploited for robotics. In turn, we asked whether emerging properties of robots equipped with biologically-inspired behaviour control circuitry can provide testable hypotheses for neurobiological experiments. We focussed on several questions at the forefront of current research: how can behavioural decisions draw upon multisensory information? How do functional behavioural patterns actually arise in terms of motor-neuron activation and muscle coordination? How is a balance achieved between sensitivity and adaptation? Under which conditions and at which stage of the circuitry does neuronal plasticity come into play? The conference provided an interdisciplinary platform where recent findings were discussed in terms of quantitative models.

As a biological system, the fruit fly *Drosophila melanogaster* has clearly emerged as a suitable model, offering the combined power of a numerically simple but sophisticated nervous system with significant molecular, cellular and circuit conservation with those of mammals, powerful genetic tools to visualise and manipulate neuron structure and function, and access to the physiological properties of circuits by imaging and electrophysiology. The symposium was thus focussed on *Drosophila*, but brought in a small number of selected speakers using other model organisms, whose input complemented the current strengths in *Drosophila* and provided stimulation for further technological and conceptual developments in the fly neuroscience community. Also invited were experts in modelling and robotics, to promote discussion about how to quantitatively describe working hypotheses about brain functions and behaviour control, and how bio-inspired robots may be used to test the validity and limits of our current understanding of biological behaviour control. Thus, the symposium's topics included the following disciplines: genetics, molecular biology, electrophysiology, behavioural analysis, neuroinformatics, computational modelling and robotics.

To maximise interaction of researchers from these disciplines, the sessions of the symposium were based on 'functional problems' (e.g. format of sensory input, format of motor output, sensory-motor integration, see scientific content below) rather than traditional disciplines. The symposium tackled three types of issues. The first pertains to fundamental biological questions of behaviour control. We examined the neural mechanisms underlying the encoding of olfactory, thermosensory and visual stimuli by multi-layered neural networks. Moving down to the control circuits, progresses were discussed about our understanding of the emergence of action selection and 'decision making' in the context of escape and orientation behaviours in sensory gradients. Some speakers also touched on how the brain organizes the integration of complementary and conflicting sensory information in the brain. The second type of challenge is technological. Several talks reported groundbreaking advances in the systematic mapping neuronal circuits (connectomics) in *C. elegans* and *Drosophila*, and the characterization of the activity in neuronal ensembles during free behaviour. These technical achievements were simply unthinkable during the first minibrains meeting in 2010. The meeting established the state of the art in the manipulation of neural processes by means of optogenetics. Another reported feat was the development of multiple computer-vision and machine-learning technique to quantify behaviour at a fine-resolution and in a high-throughput manner. The third type of challenge the meeting touched on is conceptual: we defined whether the field of systems neuroscience has reached a sufficient maturity to integrate knowledge from different disciplines in a common quantitative platform. One conclusion that was reached is that, even though powerful tools exist to analyse behavioural responses, we are still missing a modelling framework to account for complex sensorimotor processes involving multiple neurons ad motor actuation. The meeting described a couple of recent attempts (e.g. Neurokernel led by Aurel Lazar) to promote the creation of a joint environment for *in silico* simulations of neural functions achieved by specific circuits the fly brain. Robotics is also opening up new exciting prospects to test mechanistic hypotheses formulated by biologists. In the near future, we anticipate witnessing concrete cases where neuroscience learns from the emerging properties observed in bio-inspired robots.

Scientific Content of the Conference

(1 page min.)

- *Summary of the conference sessions focusing on the scientific highlights*
- *Assessment of the results and their potential impact on future research or applications*

Session 1: Sensing in living and artificial systems

The following questions were addressed during this session:

- How much computation already takes place in first order sensory neurons? For example, how much of the adaptability of natural systems is in the early sensory processing layers?

- Are artificial sensory systems still missing some of the tricks we can learn from nature? What types of sensorimotor computations that we know worms and flies must perform are hard for robots?

Scientific highlights of this session included: some of the first investigation of the olfactory pathway to the lateral horn in adult flies with segregation of representations associated with attractive and repulsive behaviours; important new insights unravelling the actual underlying components of the Hassenstein- Reichardt visual motion detector as implemented in the layers of the fly optic lobe; and demonstration of an analog VLSI implementation of this detector; dual role of a single thermosensory neuron in positive and negative thermotaxis.

Session 2: Sensory-motor integration for simple and complex behaviors

The following questions were addressed during this session:

- Do we have any examples of a complete sensory-motor control loop understood at a quantitative level? If not, what is needed to complete our understanding?

- How do motor systems, including body morphology and mechanics, shape behaviour, and is this a constraint for transferring ideas from biology to robotics?

- How should we describe behavior? As stimulus-response relationships? As composed of discrete motor primitives/motifs? As feedback systems shaped by proprioception/self-sensation?

Scientific highlights of this session included: complete brain recordings in *C. elegans* in fixed and free moving conditions; application of whole-brain imaging to study responses to oxygen gradient, concluding that sensory representations and motor outputs are encoded by separate neurons; description of the neural implementation of “economic” behaviour in *C. elegans* with emphasis on the role of neuromodulation; novel robotic mechanisms for increasing acuity in a low resolution ommatidia sensor by copying micro-movements observed in fly eyes; successful computational methods for unbiased classification of large corpora of freely moving animal data into distinct actions; rapid progress in using a functionally motivated reconstruction approach to trace circuits in high resolution EM data; description of a hierarchy of natural and stereotyped behaviours composing the escape responses and odour source location during flight in *Drosophila*, evidence for internal representations of orientation in the central complex in behaving flies; new soft robotic technologies.

Session 3: Circuit mapping, connectomics, functional inference and modelling

The following questions were addressed during this session:

- What are the best approaches to get from a connectome to function? Is it more efficient to start from a function and look for its neural substrate? How much connectome detail is "enough"?

- What can we hope to learn from unbiased behavioural screens?

- How can modelling help circuit mapping and functional characterization? What is the value, particularly to robotics but also to neuroscience, of learning precise mechanistic implementations of circuit operations that are already well described by theoretical models?

Scientific highlights of this session included: use of combined anatomical and neurogenetic tools to uncover complete neural circuits for escape and to characterize locomotor interneurons in Drosophila larvae; large-scale structure-function brain mapping; discussion about the high degree of correlation between synaptic and gap junction networks in *C. elegans*, leading to the notion that the connectome should be seen as a large multiplex circuit; using Ca imaging, identification of novel classes of neurons in the ventral nerve cord involved in peristaltic contraction and description of spatio-temporal activity patterns evolving in these neurons; high-resolution dissections of the neural circuits underlying the control of (1) grooming behavior in the adult fly and (2) feeding behavior in the larva; discussion about the role of the MBs in the integration of contextual information in the release of innate sensory behaviors; description of CAMPARI, a new genetically encoded sensor to monitor neural activity integration in Drosophila.

Session 4: Plasticity and internal states

- What learning capabilities do flies and worms share, and how do they differ? Can we understand these similarities and differences in terms of the neural circuits?

- How do motivational factors control behaviour and interact with learning?

Scientific highlights of this session included: substantial and significant new information about the organization of output neurons from the key learning area in the Drosophila brain, the mushroom bodies; description of context dependent effects in innate and learned behavior that implicate this pathway; role of the Mushroom bodies in the control of sleep in *Drosophila*; description of a new paradigm to study how different internal states (satiation, mating status) affect the microstructure of feeding behaviours in *Drosophila*.

Session 5: Circuit and behaviour in ecology and evolution

- Are there important natural behaviours in flies and worms that have been experimentally neglected to date? What are the ecologically relevant behaviours? How can we introduce a tractable level of environmental complexity to our experimental design in the lab?

- How much variability is expected in the circuit-function relationships across individuals, strains and species of the same group? Is it best to focus on fully understanding a genetic model species before studying variants?

- Do we need a genetic understanding of behaviour, or is a circuit understanding sufficient?

- Should evolution matter to robotics?

Scientific highlights of this session included: a systematic approach to interpreting nutritional choices in Drosophila; evolutionary considerations in the variation of olfactory receptor mechanisms and song production closely linked to genetic loci; differences in the timescale of the detection of olfactory signals by odorant receptors and ionotropic receptors; using the ionotropic receptor as a case study, a report on the evolution of the peripheral organization of the olfactory system across species to achieve olfactory specialization.

Forward Look

(1 page min.)

- *Assessment of the results*
- *Contribution to the future direction of the field – identification of issues in the 5-10 years timeframe*
- *Identification of emerging topics*

It is clear that the functional understanding of neural circuits will progress faster in animals for which the full range of genetic tools are available, and many more in rapid development, some described during the conference. There is nevertheless still a role for study of 'non-genetic' species, particularly those species displaying extraordinary performances at behaviours studied in 'genetic' species. This might also include specialization for a specific task that is of interest to robotics (e.g. dragonflies for flying robots and interception) or for which study of the behaviour in the real ecological situation is possible and perhaps necessary to understand their behavioural mechanisms. On the other hand it may be important to better communicate to engineers the difference and the possibilities offered by using 'genetic' species as a model, and perhaps more serious consideration of what the process of development from a genetic specification might offer to produce truly novel devices. It is possible to develop genetic tools for new organisms – in principle this requires only sequencing of genome, interfering with the genome in embryos and/or germ lines, and raising the animals in the lab – but it was noted from participant experience that it can still be extremely difficult to do in practice. Nevertheless new opportunities may well arise in this direction with the advance of new genome editing tools (e.g. CRISPR). It was also noted that to date genetic methods have perhaps been underexploited in biomechanics, but this could be also particularly significant for the interaction with robotics, where the limitations of conventional hardware are a major stumbling block.

Engineering and computational methods are changing the kinds of experiments possible, with the most striking examples at this meeting including high-throughput behavioural paradigms, closed loop optogenetic control and bottom-up or trainable methods for classifying behavioural states. Many of these are the result of more active attempts for biological researchers to introduce researchers with more computational or engineering backgrounds to their labs — a trend that we consider a successful development that was seeded at the previous minibrains meeting. Looking to the future, important advances might be made by developing more tools for automated animal handling. This could help towards another issue, which is the lack of standardization of methods and documentation and, as a consequence, inconsistencies in results generated by different labs. Other issues important to improving experimental investigations include devising additional or better means to understand the mapping of muscle activations to behaviour, how environmental factors (such as seasons) can affect animals even in the lab, and trying to develop paradigms with more ecological validity.

At a more abstract level it was noted that full understanding of neural circuits may require conceptual and theoretical developments. It should be appreciated that the 'computation' of complex non-linear system is not well understood. Moreover, 'morphological' computation can be a crucial part of adaptive behaviour. Perhaps insufficiently considered are how these systems have evolved under strong energy and metabolic constraints: as well as guiding biological theory, this may be crucial to exploitation of bio-inspired methods for low energy computation and robotics. Another issue discussed was whether the variability of biological systems – so often considered just a problem of noise for experimentation – may in fact be fundamental.

There are still barriers to be overcome in fostering the continued and extended interactions of biologistsand roboticists. These include maintaining a dialogue (as in this meeting) where the flow of information is not one way (biology to engineering ideas) but much more interactive. Roboticists can pose entirely novel questions that cast new light on the organisms, or by trying to implement hypotheses raise important new issues about function and neural implementation.

- Is there a need for a foresight-type initiative?

None in particular were identified during the forward-looking session.

Business Meeting Outcomes

- *Election of the Organising Committee of the next conference*
- *Identified Topics*
- *Next Steps*

Committee: two PIs spontaneously offered to assist the organization of the 3rd minibrains meeting.

Topics: In the future, we could consider including wider range of other 'small brain' animals, e.g. bees, but feel important that focus is not diluted too much. We will try to increase representation of robotics.

Next steps: in the absence of the ESF, there will be a need for us to identify funding scheme or umbrella that will allow similar conference arrangements.

Atmosphere and Infrastructure

- *The reaction of the participants to the location and the organisation, including networking, and any other relevant comments*

There was a very positive atmosphere, e.g. poster sessions spontaneously continuing till midnight, high attendance at all talks throughout the conference, strong involvement of more junior researchers, and good gender balance considering numbers in the field. There was a palpable sense of excitement at the rapid advances evident in the field since the previous conference.

The participants agreed it was very beneficial to have extended from fly to worm, as there is a large overlap in methods and problems. But also good not to have made it too much wider, so that all participants still had a good proportion of talks that were of direct relevance to them. It was also appreciated that the topics were mixed (worms, flies, robots) while organized thematically to represent commonality and this is a format to be maintained.

A general sense at the conference was that the increase (since the previous conference) in talks from a robotic perspective was good, but the proportion could be increased in future meetings.

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