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EMBO European Molecular Biology Organization

RESEARCH CONFERENCES

ESF-EMBO Research Conference

Functional Neurobiology in Minibrains

Hotel Eden Roc, Sant Feliu de Guixols (Costa Brava) • Spain

17-22 October 2010

Chair by: Matthieu Louis, Centre for Genomic Regulation, EMBL-CRG Systems Biology Unit, ES

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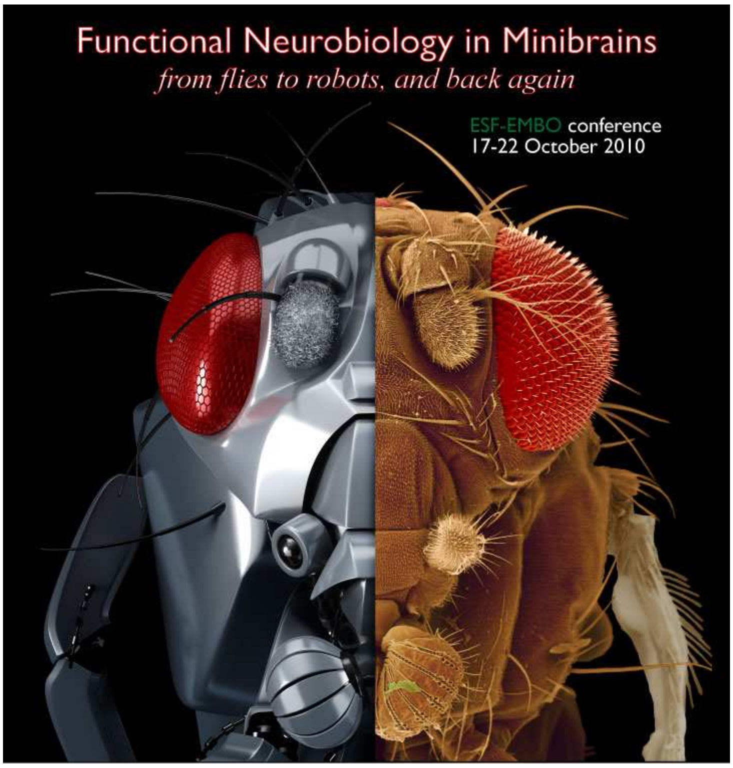
Highlights & Scientific Report



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)

An understanding of the 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 development of robotics. In turn, we asked whether emerging properties of robots equipped with biologically-inspired behaviour control circuitry can provide testable hypotheses for neurobiological experiments.

As a biological system, the fruit fly, *Drosophila melanogaster* has 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 therefore centred on researchers working with *Drosophila*, but featured a number of speakers working on other insect model systems, in addition to representation by roboticists.

We focused on several questions at the forefront of current research: what are the neuronal circuits and physiological coding mechanisms underlying sensory perception (vision, smell, taste, hearing and touch)? How does internal state (such as starvation) or previous experience influence behavioural decisions? How can behaviours be quantitatively recorded and described? Which aspects of these respective analyses offer perspective for robotics?

The participants of this ESF-EMBO symposium reported numerous findings addressing these questions. Even though we are still far from a comprehensive understanding of the fly brain, our knowledge about the design and function of simple sensory systems has already been a rich source of inspiration to device sensorimotor algorithms controlling autonomous aircrafts. We believe that establishing a genuine dialogue between insect neurobiology and cybernetics will provide a fertile ground for the development of future technologies. This ESF-EMBO symposium positively promoted such a dialogue across Europe and beyond.

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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 ESF-EMBO symposium was to discuss these mechanisms and to explore whether the principles of behaviour control can be exploited for robotics. The contribution of several speakers illustrated that robots equipped with biologically-inspired sensorimotor algorithms provide a powerful test bed for neurobiological experiments.

To maintain thematic integrity throughout the symposium, we focused on one model organism: the fruit fly *Drosophila melanogaster*. As a biological system, *Drosophila* has emerged as a powerful system offering the power of a numerically simple but sophisticated nervous system with significant molecular and circuit conservation with mammals. In addition, the fly brain is amenable to genetic tools to visualise and manipulate neuronal activity, and to access the physiological properties of circuits by imaging and electrophysiology. We invited a small number of speakers using other insect organisms, such as ants and houseflies. Their input provided stimulation for further developments in the fly neuroscience community. Finally, we brought together researchers of the insect community with experts in modelling and robotics.

The symposium was organized into nine sessions, each focusing on one “functional problem” (e.g., format of sensory input, sensory motor integration). Most sessions comprised contributions from various fields – molecular genetics, electrophysiology, behavioural quantification, mathematical modelling and robotics. Oral presentations, panel discussion and poster sessions promoted discussion about how to quantitatively describe working hypotheses about brain functions and behaviour control. They provided an interdisciplinary platform to discuss recent findings in terms of models. The participants outlined a state of the art of our current understanding of the molecular and cellular bases of processes as diverse as sensory coding, learning, attention and decision making. They reported examples where modelling and robots are used to test the validity and limits of our current understanding of brain functions.

The symposium tackled three types of issues. The first pertained to fundamental biological questions of sensorimotor control: what are the mechanisms underlying perception? What is the nature of a ‘decision’, and how is the emergence of a decision controlled neurobiologically? How is complementary and conflicting sensory information treated in the brain? Our meeting highlighted recent advance in deciphering the principles of peripheral sensory coding. At the same time, we measured how little we know about the integration of multisensory signals. Where and how multimodal information is processed remains elusive. Over the past couple of years, a series of cutting-edge assays have been created to address these questions. For instance, miniaturized treadmills allow neurophysiologists to characterize activity in the brain of walking flies stimulated by visual and olfactory cues. Several presentations indicated that the central complex, and more specifically the ellipsoid body, plays an important role in orientating decision in response to directional sensory cues.

The second issue we considered was technological: can we achieve a systematic mapping of neuronal circuits (connectomics) in the *Drosophila* brain? How can we reliably characterize the activity in neuronal ensembles? How can we artificially manipulate neuronal processing? Which quantitative methods are best suited to describe behaviour?

The results presented during this symposium rely on gigantic technological leaps that have taken place

during the past decade. Fly neurobiologists have now access to an unprecedented toolkit. New genetically encoded sensors have been developed to reliable measure calcium and chloride signals in identified populations of cells. In the near future, the sensitivity and temporal accuracy of these sensors might allow us to detect single action potentials. In parallel, several groups have engineered optical actuators to manipulate neuronal activity by light in a non-invasive manner. Fly geneticists have used an “enhancer bashing” strategy to generate very large collections of driver lines. It is hoped that every neuron in the brain will be labelled by a set of driver lines. Several laboratories have already combined these tools to establish an atlas of the fly brain and define causality relationships between circuits and behaviour.

Another major breakthrough in the field has been the development of machine vision algorithms to monitor the movement of freely moving flies at high spatial and temporal resolutions. Such software will be critical to study the behaviour of flies in naturalistic conditions. In particular, it should allow us to investigate social interactions more systematically – a promising topic touched on by two speakers.

Finally, we examined a more conceptual issue: can knowledge from different disciplines be integrated in a common framework, and can informatics/robotics approaches help in this regard? Can neuroscience learn anything from robotics and/or from the emerging properties of bio-inspired robots? Our symposium witnessed fruitful exchanges between the fly and robotics communities. By and large, research involved a high degree of interdisciplinarity where experimental data were discussed in light of qualitative and/or quantitative models. The fly neuroscience community has integrated modelling as a tool to combine data from different scales of description in a unique conceptual framework. Neuro-informatics is bound to play a key important role in the future of neuroscience. Whereas biology clearly inspires robotics, discoveries made from bio-inspired robots do not permeate so much the fly community. The field of altitude control in flight based on optic flow detection stands as a notable exception. We think this exception should become a rule.

The primary goal of this symposium was to improve our understanding of how behaviour is organised in the brain. We were guided by the idea that this problem requires a conceptual framework where hypotheses can be articulated and tested on the basis of a common set of rules and constraints. Our meeting demonstrated that mathematical and computational modelling coupled with robotics provides a basis for such a framework.

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*

ASSESSMENT OF THE RESULTS: It was recognized that given the societal problems associated with an ageing population, as well as in the context of warfare, robotics and biologically-inspired hardware in general, will have an increasing role to play. Exploiting the knowledge from biological sensing and behavioural control was judged to be potentially useful in the long term. It became clear that in a number of cases (e.g. autonomous navigation, movement detection, detection of volatiles, olfactory memory formation), the state of the neurogenetic analysis is ripe for modelling approaches and subsequent implementation into physical hardware. In the case of the altitude control of flight, the leap towards technical implementations seems imminent.

Still, we judge that the possibilities of bio-inspiration for robotics are far underexploited and thus offer rich possibilities for the future. Among other things, successful brain-machine interfacing will likely require a much closer cooperation between brain and behavioural scientists and engineers. To overcome this, the participants clearly voiced two major problems to be overcome:

i. The need to be able to recruit engineers into their biological research groups ("embedded engineers") in order to fruitfully pursue their research in this direction. A dedicated funding scheme to do so would have a major, positive influence in this emerging field of bio-inspired robotics. Potentially, a PhD student-level education program to attract young engineers early in their careers seems warranted, too.

ii. The need to develop tools for data analysis on all levels of the problem (DNA sequence, protein structure, brain anatomy, behaviour). Again, there is the need to be able to recruit software engineers into biological research groups, both in terms of competitive salary, and in terms of early exposure to the fascinating field of the brain sciences

EMERGING TROPICS:

1. Analysis of the representation of ethological relevant sensory cues. The fly nervous system is typically studied upon stimulation by simple and crude stimuli. It is timely to consider dynamical signals having similar statistical properties as those encountered in the wild. Fly vision has led the way in this direction. Other sensory modalities should follow this example. Any progress made in this direction will be relevant to the design of artificial sensors.

2. Development of artificial sensors and integrated circuits to integrate composite unimodal and multimodal signals. Electric noses can be created to detect single chemical with high accuracy. Still, most attempts to create sensor arrays capable of classifying complex odors have failed. Flies excel at discriminating between distinct odor mixtures. Their olfactory system appears to be simple enough to serve the purpose of bio-mimetics.

3. Brain-machine interfaces to test specific hypotheses about structure-function relationships. These interfaces will benefit from our progress in optogenetics, bioluminescence and electrophysiology in behaving insects. It would also require the miniaturization of multiunit electrodes for adult flies, and even larvae.

4. Expanded tools for mathematical modeling and data analysis. A clear need was expressed to integrate more engineers and computer scientists in wet labs. Neuro-informatics is an emerging field, which requires support from the life science community. The participants also discussed that implementing *in silico* models into actual robots may have the advantage of probing under conditions of natural levels of noise; in this context, the role and potential biological function of noise/chance for trial and error learning was debated. This discussion opened new vistas to the roboticists.

In addition, we believe that fly systems neuroscience and robotics should be in positions to address the following questions in the coming 10 years: 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?

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

Need to hire engineers in biological labs. This can be complicated as salaries are not competitive. The only chance to succeed is to integrate engineers in research environment very early on. It would be good to see the EU support these initiatives across countries.

Given the generation of an extremely large pool of data, there is a necessity to hire people highly trained in the analysis of complex dataset. Training program and financial support toward a bioinformatics of neuroscience, which includes behavioral quantification and connectomics. Lab-course programs to allow graduate students and post-docs to build robots

Inclusion of brain-machine interfaces in future symposium on the same topic.

Atmosphere and Infrastructure

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

From informal conversations with participants throughout the meeting, we felt there to be overall very positive responses regarding both the location and organization. The relatively intimate nature of the meeting (due to the small size, and on-site housing/meals) was thought to be highly conducive for scientific and social interactions throughout the meeting. In particular the Phd students were apparently happy with the extensive “access” to the senior scientists. There were no apparent major problems in organisation. Some minor concerns voiced included:

- some participants were unable to locate the bus shuttle to the hotel on the arrival day
- the seminar room was good, but not optimal, due to absence of raked seating
- there was inadequate lighting for the posters; serving coffee during poster sessions would help participants maintain a high level of energy
- request of scientific abstracts to all invited speakers at a month before the conference

Date & Author:

December 1, 2010

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