
Champalimaud
Foundation

# CNP

CHAMPALIMAUD
NEUROSCIENCE PROGRAMME

2011
ANNUAL
REPORT

Champalimaud
Foundation


# THERE ARE NEW WORLDS

TO BE VISITED

# WORDS FROM THE DIRECTOR

The year 2011 was a special one for the members of Chamaplimaud Neuroscience Programme, as it was our first year at the Champalimaud Centre for the Unknown. Not only the physical building, but the name itself is significant to us, for the Unknown is a concept that speaks to us directly as scientists.

The Centre stands at almost exactly the site where some 500 years ago the great Discoverers set sail for the Unknown, and I can think of few metaphors more apt for scientific research. Those explorers set off to expand the frontiers of knowledge very much as we scientists do now. They loaded their ships with equipment; we pile it into our laboratories. They drew maps for their voyages out of what was known and guessed about what was not; we construct theories and hypotheses based on models and experiments. In the end, the goal remains much the same: to go out into the unknown and discover something that has not been glimpsed yet but which will change us forever.

In this age, there are few frontiers in the physical earth to be discovered. The deep sea remains an uncharted "land" and the frontiers of outer space of course remain. But the inside of the head, the brain, which could not be more near, is a place of the deepest mysteries, a place where fantastic voyages and discoveries still await. For all the knowledge we already possess of its inner workings, we still remain deeply ignorant how this "organ of thought" plays its songs. There are new worlds to be visited.

But these new worlds cannot be discovered by a single person. Success in this type of journey rests upon the spirit and fortitude of a dedicated team. I imagine the members of the Programme as a crew of those would-be-discoverers of yore. We exchange stories from our voyages, compare maps and tell tales of people and creatures glimpsed on far-away shores. We share a kind of ship and we count on each other to make our quest a successful one. Together, we are mapping out the route to the discovery of the Unknown.

Zach Mainen
*Director, Champalimaud Neuroscience Programme*

# CHAMPALIMAUD FOUNDATION

The Champalimaud Foundation, based in Lisbon, Portugal, was created at the bequest of the late Portuguese industrialist and entrepreneur, António de Sommer Champalimaud. At the end of 2004 it was officially incorporated as the Anna de Sommer Champalimaud and Dr. Carlos Montez Champalimaud Foundation, in honour of the benefactor's parents. As stipulated by António Champalimaud prior to his death, Leonor Beleza, former Portuguese Minister of Health, is the Foundation's President.

The Champalimaud Foundation supports individual researchers and research teams working at the cutting edge of biomedical science. It aims to stimulate novel theoretical and practical methodologies by utilising the experience of both research scientists and medical practitioners.

The impact of progressive research - basic, applied and clinical - is far-reaching, affecting how illnesses and diseases are diagnosed and treated throughout the world. By supporting these active research programmes, The Champalimaud Foundation intends to stimulate further clinical research, particularly in the non-profit sector. By doing so, the Foundation aims to make a significant contribution to reducing the global burden of illness and disease.

Board of Directors:
**João Silveira Botelho** (left), **Leonor Beleza** (middle) and **António Horta-Osório** (right).

## CHAMPALIMAUD FOUNDATION

### Board of Directors

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ANTÓNIO HORTA-OSÓRIO

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MARIA BLASCO

RONALD BLASBERG

BARRY DICKSON

PAUL MARKS

J. ANTHONY MOVSHON

KEITH PETERS

MARTIN RAFF

SUSUMU TONEGAWA

# CHAMPALIMAUD CENTRE FOR THE UNKNOWN

The Champalimaud Centre for the Unknown is a multidisciplinary centre for neuroscience research, translational cancer research and clinical practice. The Centre contains state-of-the-art facilities for basic and clinical research that hold cutting edge technological tools and equipment. In the short time since its inauguration in October of 2010, the Centre has hosted multiple international scientific events attended by world-renowned scientists. Furthermore, work at the Centre has received both national and international recognition, including multiple prestigious awards accepted by Champalimaud investigators.

In addition to harbouring clinical and scientific excellence, the Centre is also designed to induce proximity and interaction between researchers, clinicians, patients, families and professionals. This singular mix of individuals at the Centre encourages the generation of new collaborations; Collaborations that may be the key to the development of novel solutions to long-standing problems.

Beyond its practical value, the Centre also offers beauty and inspiration to the people of Lisbon, as free access is allowed to the landscaped areas of the building that run along the Tagus waterfront. This unique combination of stunning river views and exceptional architecture draws people of all ages to the Centre, where they are invited to breathe-in this graceful meeting of science and nature and join us in imagining the Unknown.

ZVI FUKS
Director


# THE CHAMPALIMAUD NEUROSCIENCE PROGRAMME

AIMS TO UNRAVEL THE NEURAL BASIS OF BEHAVIOUR

# THE CHAMPALIMAUD NEUROSCIENCE PROGRAMME

"OUR IMAGINATION IS STRETCHED TO THE UTMOST, NOT, AS IN FICTION, TO IMAGINE THINGS WHICH ARE NOT REALLY THERE, BUT JUST TO COMPREHEND THOSE THINGS WHICH ARE THERE."

Richard Feynman, *The Character of Physical Law* (1965)

Through evolution, the process of life has organised matter into a myriad of interlinked forms from molecules to ecosystems. Neuroscience attempts to understand the behaviour of individual organisms within this web in terms of the structure and function of their nervous systems.

A major current challenge in neuroscience is to understand how properly functioning neural circuits support intelligent, adaptive behaviour and how the dysfunction of these circuits can be prevented. Based on work over the last century, this appears to be a problem ripe for progress but which may demand a paradigm shift in current thinking and approaches.

The Champalimaud Neuroscience Programme (CNP) seeks to facilitate the quest of scientists to forge new links between nervous system function and behaviour. The scientific goals of the programme are represented not by a particular field within neuroscience, but by the full intellectual scope of the scientists of the programme. The aspiration of the CNP as an organisation is to help those scientists to reach their full creative potential and to promote collective achievements beyond those reachable by individual scientists or laboratory groups. This is a challenge that we believe demands that we examine, question and attempt to improve the scientific processes itself. Toward this end, the vision of the CNP seeks to promote an institutional culture based on the following aims:

- To maximise cooperation without sacrificing independence and diversity of thought;
- To foster good life quality, recognising that well-being and productivity go hand in hand;
- To be a hub for scientific interaction, engaging our peers in productive exchange rather than competition;
- To share our knowledge not only within the scientific community but with the community at large;
- To continually renew the organisation itself, nurturing new scientific approaches and the organisational structures that encourage them.

If we are successful, the legacy of the CNP will be not only advances in scientific knowledge but advances in the scientific process itself.

# ORGANISATION OF THE CNP

ZACH MAINEN
CNP / INDP Director

RUI COSTA
Deputy Director

ALFONSO RENART
INDP Coordinator

## SCIENTIFIC ADVISORY BOARD

The Scientific Advisory Board (SAB) of the CNP is composed of internationally recognised neuroscientists who meet annually with CNP researchers whose work is scheduled for review. In this meeting the SAB provides input and advice on current and future research directions with the purpose of facilitating optimal research advances.

The SAB consists of regular members who also reside on the Scientific Committee of the Champalimaud Foundation, and additional SAB members who join on a yearly basis.

### Regular SAB members

J. ANTHONY MOVSHON
Visual Neuroscience Laboratory
Centre for Neural Science
New York University
New York, USA

BARRY DICKSON
Austrian Institute of Molecular Pathology
Vienna, Austria

MARTIN RAFF
MRC Laboratory for Molecular
Cell Biology & Cell Biology Unit
University College of London
London, UK

### 2011 SAB members

DARCY KELLEY
Department of Biological Sciences
Columbia University
New York, USA

PETER DAYAN
Gabsy Computational Neuroscience Unit
University College of London
London, UK

YADIN DUDAI
Department of Neurobiology
The Weizmann Institute of Science
Rehovot, Israel

# PUTTING TOGETHER THE CNP - 2007 TO PRESENT

## 2007

The CNP is created through a collaborative agreement between the Champalimaud Foundation and the Calouste Gulbenkian Foundation;

Zach Mainen appointed CNP coordinator;

Investigators Marta Moita and Zach Mainen join the CNP and open labs at host institution Instituto Gulbenkian de Ciência (IGC);

The International Neuroscience Doctoral Programme (INDP) begins under the direction of Zach Mainen.

*First CNP retreat group picture*

## 2008

Luísa Vasconcelos (IGC), Domingos Henrique (Instituto de Medicina Molecular, Lisbon, Portugal) and Rui Oliveira (Instituto Superior de Psicologia Aplicada, Lisbon, Portugal) join the CNP as associated investigators.

*3-5 June*
First CNP retreat in Azarujo.;

*5 October*
Corner stone of Champalimaud Centre for the Unknown (CCU) is laid;

Investigators Joe Paton, Rui Costa, and Susana Lima join the CNP.

## 2009

Investigators Ribeiro and Israely join the CNP.


*CCU Inauguration*

*Zach Mainen*

## 2010

Zach Mainen appointed CNP Director;

Researchers Megan Carey and Michael Orger join the CNP;

*1 September*
Zach Mainen made life-long member of the European Molecular Biology Organisation (EMBO);

*5 October*
Inauguration of the CCU.

*CCU*

## 2011

Investigators Christian Machens, Leopoldo Petreanu, Alfonso Renart, Adam Kampff and Luísa Vasconcelos join the CNP;

*January*
Labs begin operating at the CCU;

*18-21 September*
First Champalimaud Neuroscience Symposium;

*28 October*
First Ar event.

*First Ar event*

*First Ar event*


*First Champalimaud Neuroscience Symposium*

# GROWTH AND DIVERSITY

Since its establishment in 2007 until December 2011, CNP grew to include 113 members.

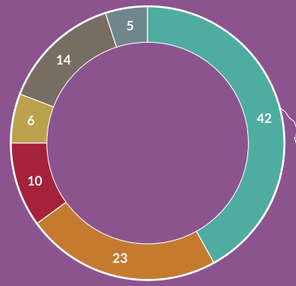
CNP Growth

2007-2011


- Principal Investigators
- Postdoctoral Fellows
- PhD Students
- Lab Technicians
- Platforms
- Administration

Educational Background of CNP Members

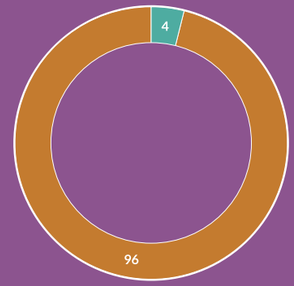
2011




- Biology
- Computer Science, Math, Physics and Engeneering
- Neuroscience
- Psychology
- Medical Sciences
- Other

Personnel Distribution (%)

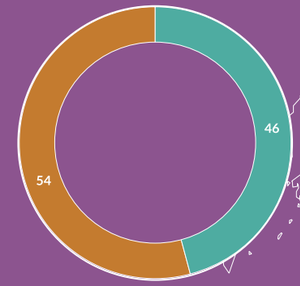
2011




- Non-Scientific
- Scientific

Gender Distribution (%)

2011




- Male
- Female


# TO FORGE NEW LINKS

## BETWEEN NERVOUS SYSTEM FUNCTION AND BEHAVIOUR

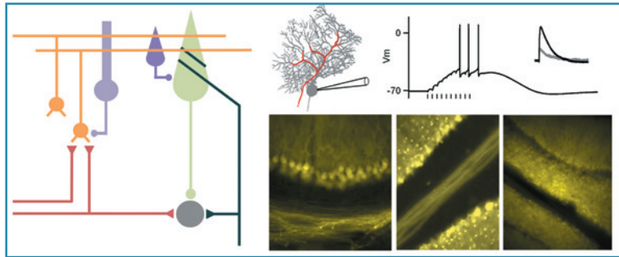
# NEURAL CIRCUITS AND BEHAVIOUR

Research Groups

## MEGAN CAREY

Principal Investigator

Understanding how cellular and synaptic mechanisms interact within neural circuits to control behaviour is a fundamental goal of neuroscience. To achieve that goal, we need a thorough understanding of behaviour as well as a detailed knowledge of the underlying neural circuit. With this in mind, we focus our research on the cerebellum, a brain area that is critical for coordinated motor control and motor learning and whose circuitry is relatively simple and well understood. Many of the neuron types in the cerebellum are molecularly identifiable, and existing technologies allow us to target transgenes to specific neuronal populations. By comparing specific aspects of behaviour and neural activity across mice in which we have targeted genetic perturbations to different cell types, we hope to determine links between cellular function, circuit activity, and behaviour.




KEY PUBLICATIONS

Carey MR (2011) *Synaptic mechanisms of sensorimotor learning in the cerebellum.* **Curr Opin Neurobiol 21:609-15**.

Carey MR, Myoga MH, McDaniels KR, Marsicano G, Lutz B, Mackie K, Regehr WG (2011) *Presynaptic CB1 receptors regulate synaptic plasticity at cerebellar parallel fiber synapses.* **J Neurophysiol 105:958-63**.

Kim JC, Cook MN, Carey MR, Shen C, Regehr WG, Dymecki SM (2009) *Linking genetically defined neurons to behaviour through a broadly applicable silencing allele.* **Neuron 63:305-315**.

Carey MR, Regehr WG (2009) *Noradrenergic control of associative synaptic plasticity by selective modulation of instructive signals.* **Neuron 62:112-122**.

Carey MR, Medina JF, Lisberger SG (2005) *Instructive signals for motor learning from visual cortical area MT.* **Nat Neurosci 8:813-819**.

# LAB MEMBERS

**Ana Machado**
MIT - Portugal
PhD student

**Catarina Albergaria**
External PhD Student

**Daniel Schlacks**
Research Assistant

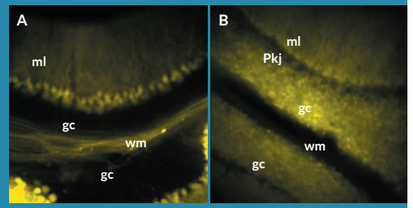
**Claire Monroy**
Technician

FUNDING

CHAMPALIMAUD FOUNDATION

## Dissecting the role of endocannabinoids in eyeblink conditioning

Delay eyelid conditioning is a simple form of classical conditioning that depends critically on an intact cerebellum. Multiple synaptic plasticity mechanisms within the cerebellum have been identified and proposed as cellular substrates of learning for this behaviour. One class of molecules that appears to be important is endocannabinoids. Both cannabis users and cannabinoid receptor (CB1) knockout mice exhibit impairments in delay eyelid conditioning. However, endocannabinoids are important for multiple plasticity mechanisms at many synapses, and it is not clear exactly where or how they act to modulate eyeblink conditioning. We are taking a genetic approach to this problem, by deleting CB1 receptors selectively from identified cell types within the brain. Through behavioural and electrophysiological experiments in these mice, we hope to constrain both the candidate sites and mechanisms of action for CB1 receptors in eyelid conditioning.




**DRIVING GENE EXPRESSION IN IDENTIFIED CELL TYPES USING VIRAL VECTORS.**
**A.** In L7-Cre mice, cell bodies (Pkj), molecular layer dendrites (ml), and white matter axons (wm) of Purkinje cells express YFP following virus injection. Note the absence of fluorescence in the granule cell layer (gc). **B.** In Gabra6-Cre mice, the same virus drives YFP expression in granule cell bodies (gc) and their axons in the molecular layer (ml), but not the Pkj cell layer and white matter.

FUNDING

CHAMPALIMAUD FOUNDATION

## Understanding the role of the cerebellum in gait coordination

The cerebellum is important for coordinated motor control. Gait ataxia, which is a lack of coordination during walking, is one of the most prominent symptoms of cerebellar damage. However, the precise role of the cerebellum in controlling gait is not well understood. Although sophisticated genetic tools exist to manipulate the cerebellar circuit in mice, analyses of mouse gait have typically been limited to gross performance measures and lack detail about precision and timing of limb movements. Here we are developing high-speed video methods for measuring and analysing mouse gait to identify specific gait parameters that are cerebellum-dependent. We will use genetic tools, including cell-type specific expression of tetanus toxin and optogenetics, to manipulate activity in individual cerebellar cell types and examine their contributions to gait control.

FUNDING

CHAMPALIMAUD FOUNDATION

## Endocannabinoids and motor performance and learning

Endocannabinoids are powerful neuromodulators that act through CB1 receptors to modulate synaptic transmission and activity throughout the brain. While a role for endocannabinoids in synaptic plasticity is clear, the importance of endocannabinoid signaling for motor control and learning is less well understood. Several studies have shown that CB1 receptor knockout mice show decreased locomotion and exploratory behaviour, but do not exhibit severe coordination deficits or ataxia. This is perhaps surprising, since many forms of endocannabinoid-dependent synaptic plasticity have been described at various synapses within the cerebellum and other structures known to be important for coordinated motor control. However, most previous studies have been limited to open field behaviour and rotarod performance and may have missed more subtle phenotypes. Here, we are combining sensitive assays of mouse motor performance and learning and using a cell-specific knockout approach to elucidate the role of endocannabinoids in motor control and learning.


# NEUROBIOLOGY OF ACTION

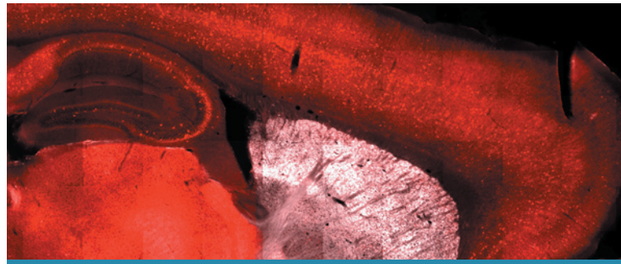
## Research Groups

## RUI M COSTA

Principal Investigator

We are interested in the neural bases of action in health and disease. Our overall goal is to understand how changes in molecular networks in the brain modify neural circuits to produce experience-dependent changes in actions. We are particularly interested in investigating the corticostriatal mechanisms underlying the learning and flexible use of actions, e.g. how novel actions and skills are learned, how they are voluntarily initiated, how they can be used to obtain particular outcomes, and how eventually they can become automated and habitual. We seek to investigate these problems using an integrative approach spanning from molecules to circuits, where we monitor and manipulate the activity of molecules, neuronal circuits, and behaviour. We chose to implement this integrative approach in mice because they combine the power of genetics, a mammalian brain with layered structures that can generate oscillatory activity, the possibility of accurately quantifying simple behaviours like action initiation and stereotypic skill learning, and also more elaborate behaviours like goal-directed actions.

KEY PUBLICATIONS



Jin X, Costa RM (2010) *Start/stop signals emerge in nigrostriatal circuits during sequence learning.* **Nature 466 (7305):457-62**.

Dias-Ferreira E, Sousa JC, Melo I, Morgado P, Mesquita AR, Cerqueira JJ, Costa RM*, Sousa N* (2009) *Chronic stress causes frontostriatal reorganisation and impairs decision making.* **Science 325 (5940):621-5**.

Yin HH, Prasad-Mulcare S, Hilario MRF, Clouse E, Davis MI, Lovinger DM, Costa RM (2009) *Dynamic reorganisation of striatal circuits during the acquisition and consolidation of a skill.* **Nat Neurosci 12:3**.

Costa RM, Lin SC, Sotnikova TD, Cyr M, Gainetdinov RR, Caron MG, Nicolelis MAL (2006) *Rapid alterations in corticostriatal ensemble coordination during acute dopamine-dependent motor dysfunction.* **Neuron 52 (2):359-69**.

Costa RM, Federov NB, Kogan JH, Murphy GG, Stern J, Ohno M, Kucherlapati R, Jacks T, Silva AJ (2002) *Mechanism for the learning deficits in a mouse model of neurofibromatosis type 1.* **Nature 415 (6871):526-30**.

* equal contribution

# LAB MEMBERS

**Cristina Afonso, PhD**
Postdoctoral Fellow

**Catherine French, PhD**
Postdoctoral Fellow

**Fatuel Tecuapetla, PhD**
Postdoctoral Fellow

**Gabriela Martins, PhD**
Postdoctoral Fellow

**Rodrigo Oliveira**
Postdoctoral Fellow

**Thomas Akam, PhD**
Postdoctoral Fellow

**Vítor Paixão, PhD**
Postdoctoral Fellow

**Eduardo Ferreira**
External PhD Student

**Pedro Ferreira**
2007 INDP PhD Student

**Ana Vicente**
2008 INDP PhD Student

**Fernando Santos**
2008 INDP PhD Student

**Ana Vaz**
Research Technician

## CLINICAL RESEARCH FELLOWS

**Albino Maia, MD, PhD**
Clinical Research Fellow

**Rosalina Fonseca, PhD**
Clinical Research Fellow

FUNDING

EUROPEAN RESEARCH COUNCIL (ERC);
MARIE CURIE IRG;
CHAMPALIMAUD FOUNDATION

## Neural mechanisms of skill and sequence learning

Understanding how novel actions are learned and consolidated as sequences of movements and skills are the main aims of this project. We have uncovered neural activity in basal ganglial circuits that are related to the learning and execution of sequences of movements. We also used optogenetics to identify and manipulate the neurons mediating this activity.

FUNDING

EUROPEAN RESEARCH COUNCIL (ERC);
FUNDAÇÃO PARA A CIÊNCIA
E A TECNOLOGIA (FCT);
CHAMPALIMAUD FOUNDATION

## Corticostriatal mechanisms underlying goal-directed actions and habits

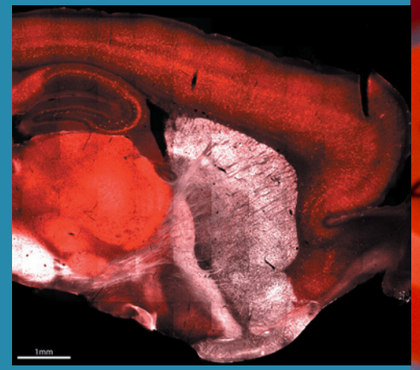
Our goal is uderstanding the difference in the brain between intentional actions and habits or routines. We have uncovered that the dopamine transporter is a critical gate for habit formations; and also that different corticostriatal circuits dynamically interact during the shift between goal-directed actions and habits.

FUNDING

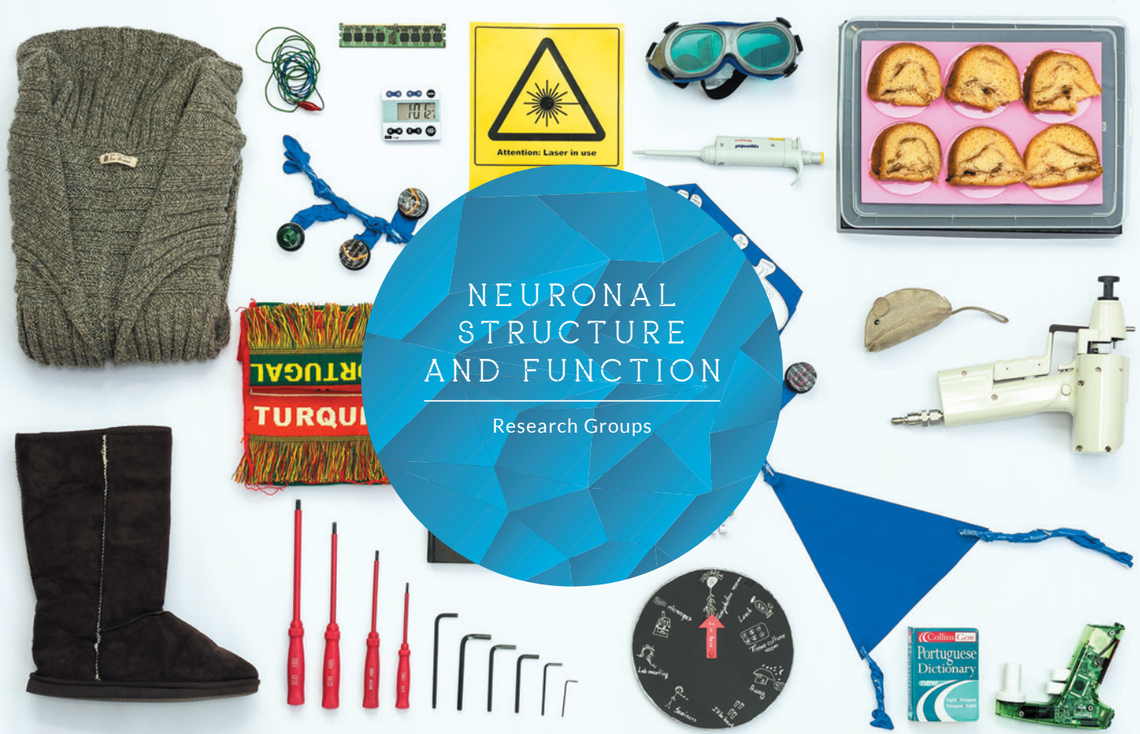
CHAMPALIMAUD FOUNDATION

## Neural mechanisms underlying the generation of novel actions

This project aims to understand how new self-initiated actions are generated and how this ability is hampered in Parkinson´s disease. We have developed a new methodology to classify in an unbiased manner different behavioural and neural states.




**VISUALISATION OF DIFFERENT BASAL GANGLIA CIRCUITS USING A REPORTER LINE.**
The ROSA26-YFPreporter mouse line was crossed with an RGS9L-cre line. The striatum and its projections toglobus pallidus and substantia nigra reticulata are visualised in white. For contrast, immunoreactivity for parvalbumin labeling heavily cortex, thalamus and hippocampus is depicted in red. Scale bar = 100um.



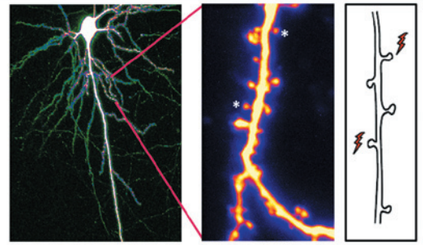

# NEURONAL STRUCTURE AND FUNCTION

## Research Groups

## INBAL ISRAELY

Principal Investigator

We are interested in understanding how activity can lead to specific structural changes in neurons that may be important for learning, and how such changes affect connectivity within neural circuits. It is unknown how the diverse forms of activity that a neuron receives are physically stored and regulated at the level of individual spines, the sites of neuronal connections. Does long lasting depression lead to structural changes at synapses? What types of structural and electrophysiological modifications take place at spines following complex patterns of naturally occurring activity? Several mental retardation disorders in humans are characterised by abnormal spine morphology, and studying neurons from animal models may further our understanding of the relationship between structure and function. We aim to combine molecular and genetic tools with imaging and electrophysiological methodologies, to determine how information is physically stored in the brain.



KEY PUBLICATIONS

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Arikkath J, Peng IF, Ng YG, Israely I, Liu X, Ullian EM, Reichardt LF (2009) *Delta-catenin regulates spine and synapse morphogenesis and function in hippocampal neurons during development.* **J Neurosci 29 (17):5435-42.**

Arikkath J, Israely I, Tao Y, Mei L, Liu X, Reichardt LF (2008) *Erbin controls dendritic morphogenesis by regulating localisation of delta-catenin.* **J Neurosci 28 (28):7047-56.**

Israely I, Costa RM, Xie CW, Silva AJ, Kosik K, and Liu X (2004) *Deletion of the neuron-specific protein delta-catenin leads to severe cognitive and synaptic dysfunction.* **Curr Biol 14 (18):1657-63.**

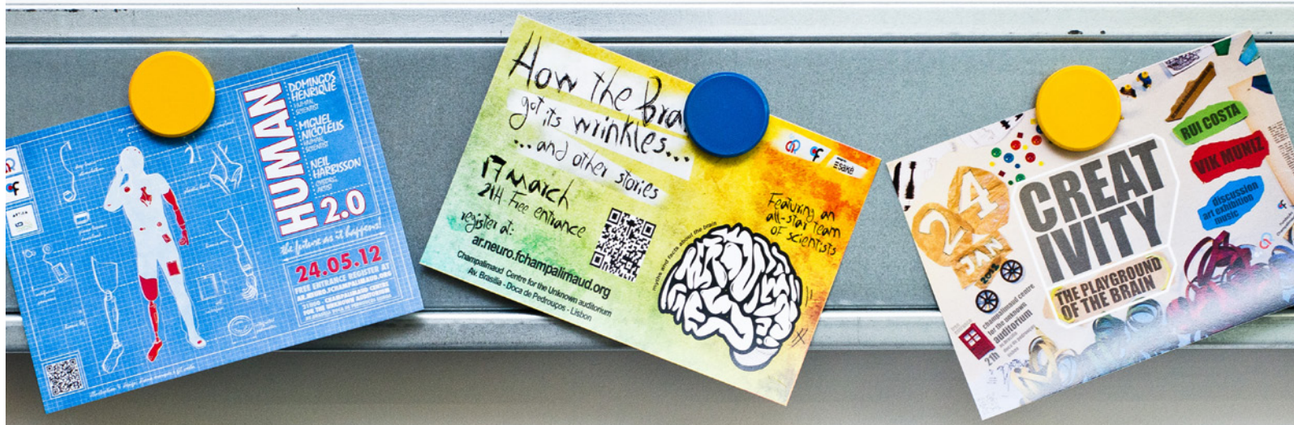
* equal contribution

# LAB MEMBERS

**Yazmín Cortés, PhD**
Postdoctoral Fellow

**Ali Argunsah**
2009 INDP PhD Student

**Anna Hobbiss**
2009 INDP PhD Student



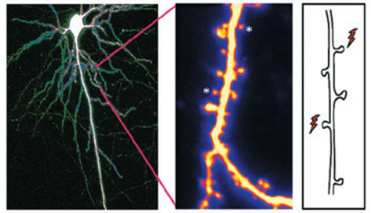
FUNDING

BIAL FOUNDATION;
CHAMPALIMAUD FOUNDATION

## Dendritic compartmentalisation of protein synthesis-dependent synaptic plasticity

We found that protein synthesis dependent stimulation of spines can facilitate plasticity at neighbouring spines for up to an hour and over long distances (70 um). Through 2-photon imaging and uncaging of glutamate at individual spines, we aim to visualise structural changes that occur in response to protein synthesis dependent forms of activity. We will examine how activity at multiple spines leads to structural changes and changes in synaptic weights within a dendritic branch. We aim to determine whether competition for proteins during synaptic plasticity can shape the organisation of inputs within a dendrite, leading to the physical clustering of synapses. We also investigate whether the clustering of synapses can be observed following the development of neural circuits, by examining the endogenous distribution of spines within dendrites of the hippocampus.

We find that the stimulation of multiple spines closely together in time can lead to competition for cellular resources, and that new proteins are required for this process. These findings demonstrate that synaptic plasticity may be biologically constrained, and provides a potential mechanism through which synapses could be spatially clustered. We are examining the parameters over which competition is regulated, in order to define the learning rules for protein synthesis dependent plasticity.



**INDUCING ACTIVITY AT SINGLE DENDRITIC SPINES TO STUDY STRUCTURAL DYNAMICS.**
Using 2-photon microscopy in living brain slices together with photoactivation of caged glutamate, we can examine how neurons physically store information at synapses. We can vary the type of stimulation delivered at a given input to mimic different forms of activity, and study what are the structural and functional correlates. We also examine how a neuron integrates information arriving at multiple synapses.

FUNDING

BIAL FOUNDATION;
CHAMPALIMAUD FOUNDATION

## Structural correlates of synaptic depression at dendritic spines

Synaptic potentiation leads to an enlargement of spine head volumes at individual synapses, however the structural correlates of synaptic depression are poorly understood. Long term depression can be initiated through a variety of receptors, and it is unknown whether the structural correlates of this form of plasticity apply generally to any decrease of synaptic weight, or whether there are specific modifications depending on which signaling pathway is activated. We aim to determine what are the structural correlates of synaptic depression at dendritic spines. In particular, we are interested in exploring long lasting forms of synaptic depression that depend on new protein synthesis. We will determine what are the parameters which govern these changes following activity at specific inputs. Additionally, we will probe whether new proteins serve to constrain plasticity at multiple spines similarly to the case for long term potentiation.

We have induced long lasting synaptic depression through the activation of metabotropic glutamate receptors (mGluRs) in hippocampal organotypic slice cultures. We have quantified the structural changes which correlate with this form of plasticity through 2-photon imaging of subsets of spines for up to four hours. Additionally, we recorded electrophysiological responses from these cells in order to monitor the changes following synaptic plasticity.

FUNDING

CHAMPALIMAUD FOUNDATION

COLLABORATORS

THOMAS MCHUGH
(Riken Brain Science Institute, Japan)

## Plasticity consequences of naturalistic spike trains at single synapses

Naturally occurring patterns of activity are complex in structure and have an irregular distribution of action potentials. Thus far, synaptic plasticity at individual inputs has been assessed through delivery of regular patterns of activity. We aim to mimic the varied input patterns observed in vivo with glutamate uncaging at individual spines, in order to determine what are the structural and plasticity correlates of these forms of activity. We will determine how such complex trains of activity interact across multiple synapses within a dendritic branch. We will use this information to model neuronal information processing in order to develop an understanding of the learning rules which govern synaptic weight changes.

We have established a collaboration in order to obtain in vivo electrophysiological recordings from hippocampal CA3 neurons. Experiments in which electrophysiological recordings are coupled with 2-photon imaging in hippocampal organotypic slice cultures are underway in order to monitor the structural and plasticity correlates of spike timing dependent plasticity. This form of plasticity depends on the integration of events at single inputs, similarly to what is observed endogenously.


FUNDING

CHAMPALIMAUD FOUNDATION

COLLABORATORS

DEVRIM ÜNAY
(Bahcesehir University Istanbul, Turkey)

## Automatic dendritic spine detection and analysis

The combination of live 2-photon imaging and glutamate uncaging allows us to investigate how neuronal structure and function are correlated at the level of individual spines following synaptic activity. In addition to changes in the volume of the spine head, many other changes in spine structure have been observed, for example, changes in the length of the spine neck. Such changes are difficult to quantify with existing methodologies, and therefore we aim to develop automated data analysis tools for handling both the large data sets and the many variables to be analysed. We aim to achieve greater precision and flexibility in the quantification of structural changes, as well as to significantly enhance the efficacy of data analysis.

Thus far, we have developed an automated, multi-level, region based segmentation method to detect dendritic spines from two-photon laser scanning microscopy images. Identified structures in two-photon images of dendritic spines are used to train the segmentation algorithm. This is the first step towards a broader automated dendritic spine detection and analysis framework.

# INTELLIGENT SYSTEMS

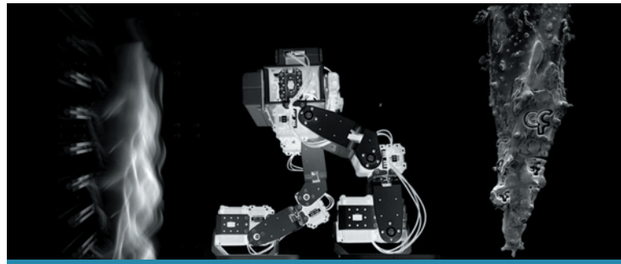
## Research Groups

ADAM KAMPFF
Principal Investigator

The goal of the Intelligent Systems Lab is to understand how a nervous system constructs a model of the world. How do brains learn about the statistics of their environments? How is this information encoded in networks and used to control intelligent behaviour? To answer these fundamental questions, two major technical advances must occur:

1. The development of virtual worlds in which the statistics and physics of the environment can be manipulated, providing experimental control over the model formed by an animal's nervous system.
2. The design and construction of novel devices for simultaneously recording from large populations of neurons throughout the brain of a behaving animal.

My research group strives to address both of these problems.



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* equal contribution

# LAB MEMBERS

**Gonçalo Lopes**
2010 INDP PhD Student

FUNDING

CHAMPALIMAUD FOUNDATION

COLLABORATORS

NICCOLÒ BONACCHI
AND JOE PATON (CNP)

## Bonsai: A general purpose data stream processing framework for experimental neuroscience

Modern techniques in experimental neuroscience require the combination of many different technologies and software algorithms for data acquisition, analysis and instrument control. The development of such systems is often a time-consuming and challenging task. We present Bonsai, an open-source framework for rapidly prototyping and composing asynchronous data stream processing workflows, which is built on top of the Reactive Extensions for the .NET framework. The development of a Bonsai workflow revolves around two simple concepts: sources and combinators. Sources represent different data stream generation processes and devices, such as cameras, microphones and other data acquisition systems. Combinators provide ways to transform, filter, and otherwise manipulate these asynchronous data streams. We present the general architecture of Bonsai as well as the currently available packages for computer vision, audio and signal processing, data acquisition and instrument control. We also demonstrate several practical applications of the framework to the design of paradigms commonly used in experimental neuroscience.

FUNDING

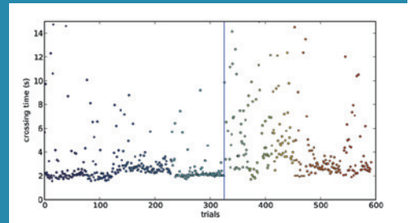
CHAMPALIMAUD FOUNDATION

COLLABORATORS

JOE PATON (CNP)

## Moving with motor cortex: A fine-scale analysis of rodent behaviour in unpredictable environments

Mammals excel at using statistical regularities to predict their environment, but the neural algorithms and representations underlying this ability to learn and use a predictive model are far from understood. In order to study this question in rodents, we designed a "modular" shuttling paradigm. In this task, rats are alternately rewarded at opposite ends of a U-maze and their crossings recorded using high-speed, high-resolution video. The walls and floor of the maze are composed of modular elements outfitted with programme sensors and actuators, the rules of which specify the statistics of the environment. We performed a systematic exploration of behaviour in non-stationary environments and identified fine-scale metrics that will be paired with electrophysiology and lesion studies in cortical motor areas. Here we present the assay design and behaviour data collected during crossing of a series of obstacles, some of which change their configuration on a trial-by-trial basis. We show how rats quickly learn to navigate this environment and provide a detailed characterisation of behavioural responses to unpredictable reconfigurations.




**PERFORMANCE DATA FROM ONE RAT DURING THE SHUTTLING TASK BEFORE AND AFTER UNEXPECTED CHANGES TO THE ENVIRONMENT.**
The blue vertical line indicates the beginning of environment manipulations. Different colors indicate distinct sessions.

FUNDING

CHAMPALIMAUD FOUNDATION

COLLABORATORS

PEDRO BARQUINHA
AND ELVIRA FORTUNATO
(CENIMAT-Faculdade de Ciências
e Tecnologia of Universidade Nova de
Lisboa, Monte de Caparica, Portugal)

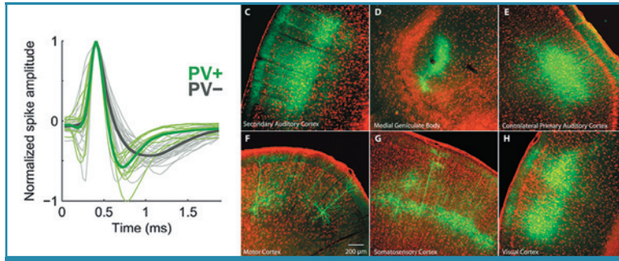
## Nanostructuring strategies for improving the performance of neural electrodes

Extracellular electrical recording of neuronal activity is an important technique for understanding the function of nervous systems. However, major discrepancies have been observed when the signals detected with extracellular electrodes are compared to those recorded with other techniques (e.g. functional imaging). We hypothesised that the smooth, metallic surfaces commonly used for extracellular recording may be sub-optimal for detecting and isolating the activity of neurons in the vicinity of the probe. We are thus investigating novel electrode materials and structures, aiming to improve the electrode-tissue interface, optimise the SNR, and increase selectivity for dense signals. We used material processing techniques to make "nanostructural" changes to the microelectrode: a focused ion-beam (FIB) with 10 nm resolution and surface deposition of metallic oxides and conductive polymers. The effects of these structural and surface modifications were first verified by impedance and cyclic voltammetry measurements. We then evaluated the performance of the modified devices during acute recordings from mammalian brain structures.


# NEUROETHOLOGY LABORATORY

## Research Groups

The main goal of our laboratory is to gain mechanistic insights into the neuronal processes underlying fundamental behaviours in females: the choice of a suitable mate and how to initiate and terminate sexual behaviour. To do so, we use mice as model system and a combination of approaches that include physiological, anatomical and molecular tools to dissect the contribution of candidate brain areas to the emergence of these natural behaviours. Our long-term goal is to investigate if (and how) mates of different attractiveness differentially modulate the course of a sexual interaction.




KEY PUBLICATIONS

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# LAB MEMBERS

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**Léa Zinck, PhD**
Postdoctoral Fellow

**Susana Valente**
External PhD Student

**Vanessa Urbano**
Research Technician

FUNDING

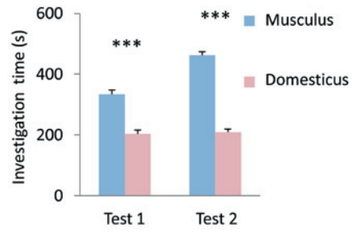
BIAL FOUNDATION;
CHAMPALIMAUD FOUNDATION

## Assortative Mate Choice

Along with finding food and avoiding predators, selecting sexual partners is one of the primary functions of the brain. Choices serve a variety of functions, from avoiding familial inbreeding to avoiding inter-species mating, all of which generally serve the goal of maximising the fitness of the resulting offspring and thereby providing the best investment of ones genes. Our goal is to understand the neural mechanisms underlying this fascinating behaviour. Very little is known about how the criteria for mating are represented in the brain, how the decision-making process works, how it is influenced by internal state. In order to study those processes it would be ideal to reproduce mate choice in the laboratory under controlled, repeatable conditions. Inspired by the natural situation of the hybrid zone between the two subspecies of house mouse, Mus musculus musculus and Mus musculus domesticus, we have developed a behavioural paradigm to study assortative mate choice in the lab.

We have established a mate choice paradigm with M. m. musculus and M. m. domesticus, where musculus females exhibit a strong and reliable preference for their own subspecies. We have also established that this preference is influenced by early imprinting mechanisms and it increases with multiple testing. Furthermore, the preference for a specific male is not absolute, but rather flexible and dependent of the alternatives that are available. Papers in preparation: A reliable paradigm to study assortative mate choice in the laboratory. Zinck, Urbano and Lima; Assortative mate choice in the house mouse is learned during early life.

A




**THE GRAPH IN PANNEL A SHOWS THE RESULTS OF LIMITED CONTACT EXPERIMENTS, WHERE MUSCULUS FEMALES CAN CHOOSE BETWEEN SPENDING TIME WITH A MUSCULUS OR A DOMESTICUS MALE.**
**A.** As shown, musculus females prefer to spend their time interacting with musculus males, and this preference is stable because if the same females are retested on a subsequent session 3 days apart, the preference is maintained (Paired t-test: ***p<0.001 (N=54).

FUNDING

MARIE CURIE IRG;
CHAMPALIMAUD FOUNDATION

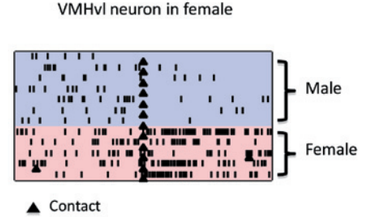
## Female Receptivity and the Hypothalamus

Female rodent behaviour is heavily influenced by sex hormones. While, for example, females are sexually receptive during proestrous phase, they reject copulation during all other phases of the reproductive cycle. It is well accepted that the ventromedial hypothalamus (VMH) plays a critical role in the control of sexual behaviour. However it is unclear how the orchestrated activity of neurons in the VMH mediates behavioural changes across the estrous cycle in neurophysiological terms. Our hypothesis is that activity within the VMN is underlying the sexual receptivity changes observed in females across the estrous cycle. To test this, our aims are:

1. Record the electric activity of single neurons in the VMN of freely behaving females;
2. Investigate the contribution of different neuronal populations within the VMN using optogenetic tools;
3. Test the causal relationship between the activity observed and the different neuronal populations using optogenetics.

We found gender-responsive VMH neurons, in agreement with a previous study in the VMH of male mice. Furthermore, our results showed that the proportion of male-inhibited neurons during proestrous (7/22, 32%) was higher than those during the estrous and diestrous (5/34, 15% and 4/33, 12%, respectively). These results suggest that changes in the balance of excitation and inhibition in VMH neurons may underlie behavioural changes across the estrous cycle.

B




**B.** In pannel B we have the electrophyisiological response of a single neuron in the female´s ventromedial hypothalamus in response to female or male stimuli. This particular neuron is inhibited during contact with male. The activity of the neuron is aligned to the contact of the stimulus female to the focal animal.

FUNDING

CHAMPALIMAUD FOUNDATION

## Female sexual behaviour: neuronal pathways for arousal termination

Like all behaviours, sexual arousal has a beginning and an end during the course of a normal sexual interaction. Sensory genital stimulation received by the female during copulation (sensed by mechanoreceptors present in the cervix and clitoris) is relayed to the brain and is important for the rewarding effects of copulation and for its termination. Despite being a fundamental aspect of sexual behaviour, very little is known about how the brain integrates the genital stimulation received during copulation and how the brain might use this information to inhibit further sexual arousal.

We have started by establishing a protocol to trace the genital input to the brain, by using pseudo rabies viruses (PRV) expressing green fluorescent protein. PRV infects axon terminals of neurons and after infecting a neuron, jumps to synaptically connected neuronal partners. By employing this method we are investigating which brain areas are synaptically connected to the genital organs that receive stimulation during copulation.

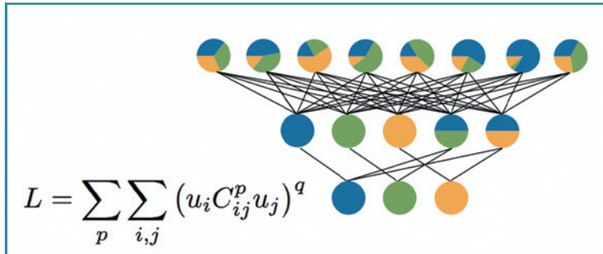

# THEORETICAL NEUROSCIENCE

Research Groups

## CHRISTIAN MACHENS

Principal Investigator

We construct mathematical theories to understand the operation of the brain. Our main interest lies in understanding how the millions of neurons inside the brain coordinate their activity to make sense of the world and create behaviour. Whereas many experimental labs address the question by measuring the behaviour of animals, the electrical activity of neurons, or the anatomical details of neural connectivity, our main aim is to put order into these observations using the language of mathematics. To this end, we collaborate closely with experimental labs recording from thousands of neurons and develop methods to visualise and interpret these recordings. We form theories of the computations implemented by neural circuits based on optimisation principles and apply these theories to the recorded data. We also construct neural network models designed to elucidate the circuit mechanisms underlying the measured behaviours.

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# LAB MEMBERS

**Florian Dehmelt**
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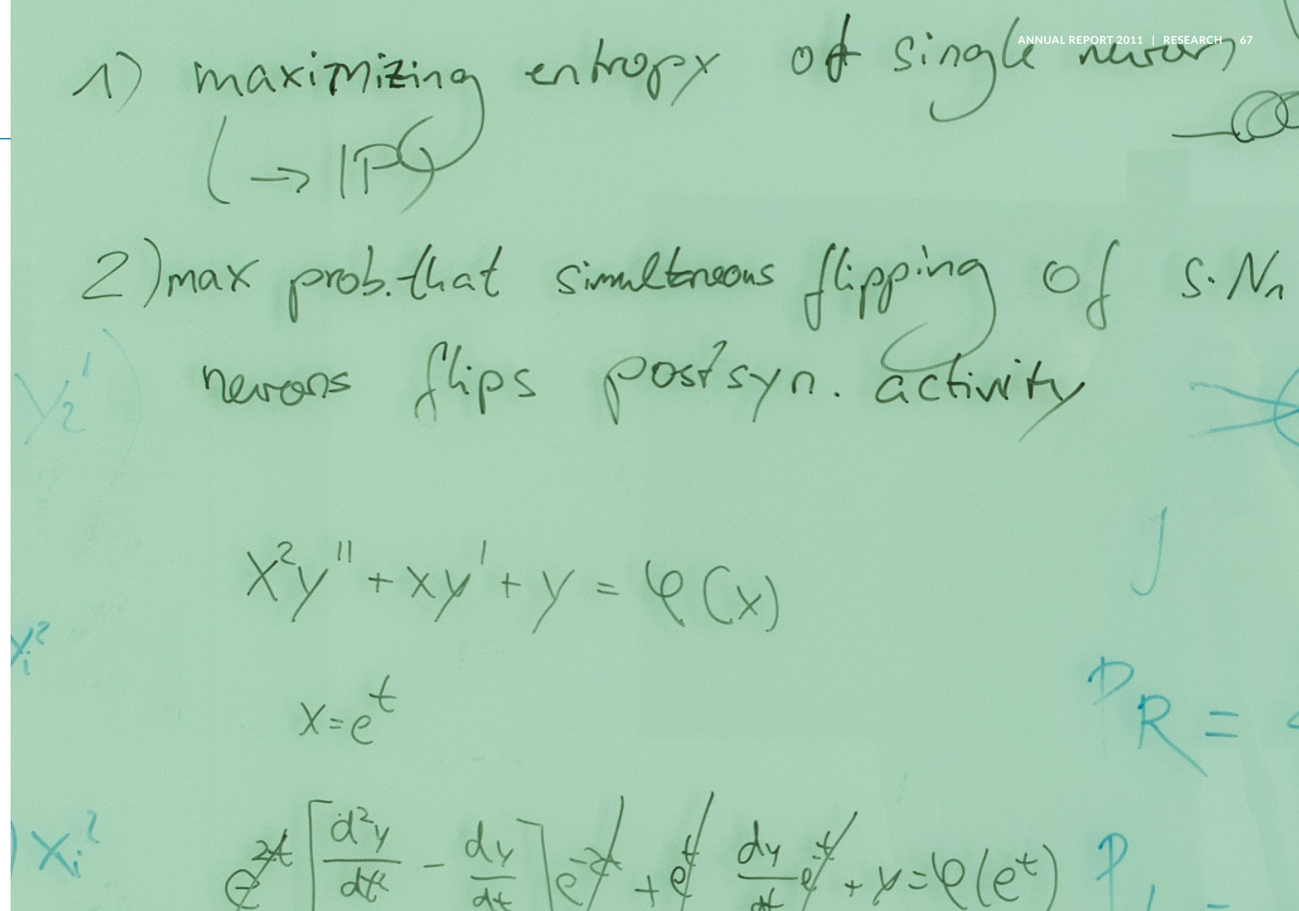
**Pedro Gonçalves**
External PhD Student

**Wieland Brendel**
External PhD Student

**Nuno Calaim**
Research Technician



FUNDING

ECOLE NORMALE SUPERIEURE, PARIS, FRANCE

COLLABORATORS

CHRISTOS CONSTANTINIDIS (WAKE FOREST UNIVERSITY);
RANULFO ROMO (UNIVERSIDAD NACIONAL AUTONOMA DE MEXICO);
NAOSHIGE UCHIDA (HARVARD UNIVERSITY)

## Analysis of neural population data

Higher brain areas receive inputs from many parts of the brain. The activity of neurons in these areas often reflects this mix of influences. As a result, neural responses are extremely complex and heterogeneous, even in animals performing simple tasks. In this project, we analyse neural population data and develop new data analysis tools to understand neural population recordings. We specifically follow probabilistic approaches, in which the goal is to characterise a (multi-variate) probability distribution that represents the likelihood of finding a given neural response in a specific area. Our study of the population response in the PFC of monkeys and rodents during 2AFC tasks suggests that independent inputs like time, stimulus and reward are consistently represented in separate orthogonal subspaces.

We have continued analysing data and recruited new collaborators. We have finalised a new method for the analysis of population data ("Demixed principal component analysis", published in the NIPS proceedings) and have submitted a review which is currently under revision: Wohrer A, Humphries M, Machens CK (2012). Population-wide distributions of neural activities during perceptual decision-making tasks.

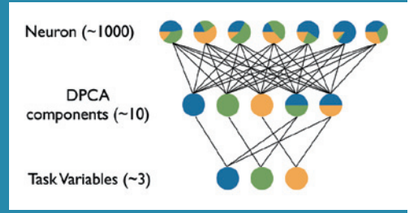



**ILLUSTRATION OF DEMIXED PRINCIPAL COMPONENT ANALYSIS (DPCA).**
A central problem in understanding activity in the brain is that neurons often mix information, especially in higher-order areas. If an animal is engaged in a task that involves a stimulus, a decision, and a time interval between the two, then each neuron will generally represent a different amount of information about the stimulus (yellow), the decision (green), and the time (blue). Given that brain areas consist of millions of neurons, thousands of which can be recorded with modern-day technique, the complexity of these mixtures severely impedes our ability to understand what the respective area is computing or contributing to the task. We have developed a new method (DPCA) that allows us to represent this data in a far more compact format, using only a few components (or 'representative cell responses') that demix the information about the relevant task variables as much as possible.

FUNDING

ECOLE NORMALE SUPERIEURE, PARIS, FRANCE

COLLABORATORS

SOPHIE DENEVE (Ecole Normale Superieure, Paris)

## Spiking network dynamics

Neural networks are capable of performing an incredible variety of difficult tasks, but how they manage to do this is poorly understood. We study how spiking neural networks can implement arbitrary linear dynamical systems - these encompass a huge variety of computations. We follow an approach in which the membrane potential of a neuron is reinterpreted as a 'prediction error' between a network's actual and desired output. Neurons only fire when this prediction error (membrane potential) exceeds a certain value. These assumptions naturally explain several mysterious properties of neural systems, such as the tight balance between excitation and inhibition, and irregular, asynchronous firing. We are specifically interested in the oculomotor system, which controls eye position.

We have made progress in understanding the main properties of the networks developed under the new assumption. A paper has been written and is currently in revision: Boerlin M, Machens CK, Deneve S (2012). Balanced spiking networks can implement linear dynamical systems with predictive coding.

FUNDING

CHAMPALIMAUD FOUNDATION

## The role of time in behaviour

Reinforcement Learning in its classical setting is based on Markov Decision Processes which assume discrete state representations and transitions. When time, an intrinsic continuous quantity, becomes a relevant variable for the learning process this discrete setting becomes inadequate. We use continuous reinforcement

learning to model a classical conditioning paradigm of trace conditioning, where reward is given at a fixed time interval after a cue presentation. In this paradigm, the timing of reward delivery becomes a relevant variable for the learning process. We study how the agent can learn the timing of the reward, given that the tracking of time is uncertain. We assume that the perceived time evolves according to a stochastic (drift-diffusion) process. We discuss different scenarios of how learning could work under these constraints, and compare the resulting behavioural predictions.

## Control of cerebral energy metabolism

FUNDING

ECOLE NORMALE SUPERIEURE, PARIS, FRANCE

Maintaining homeostatic ATP concentration in brain tissue is a major challenge to an organism, and failure results in neuronal injury and possible neurodegeneration. Nutrients required for ATP synthesis are extracted from blood, and changes in blood flow and oxygenation correlate well with changes in neural activity. While action potentials can be generated with remarkable efficiency, it is not known whether this parsimony is mirrored by a similarly efficient regulation of blood flow. To quantify its contribution to the cost of energy homeostasis, we are studying a minimal metabolic model linking metabolite supply from blood to ATP synthesis in brain tissue. The model incorporates both oxidative and a non-oxidative pathways consuming glucose, oxygen and pyruvate, and accounts for the removal of waste products such as carbon dioxide. Preliminary results predict that the metabolic supply observed experimentally represents the fastest possible return to homeostasis.

## Dynamics of an oculomotor integrator revealed by instantaneous optogenetic perturbations

FUNDING

ECOLE NORMALE SUPERIEURE, PARIS, FRANCE

COLLABORATORS

ARISTIDES ARRENBERG (University of Freiburg);
HERWIG BAIER (Max-Planck-Institute for Neurobiology, Martinsried)

The oculomotor integrator (OI) in the hindbrain transforms incoming horizontal eye movement commands into position signals to maintain stable eye fixations after saccades. Previous electrophysiological and pharmacological investigations of the system have shown that neurons in the OI have firing rates that can persist at a continuum of levels, with each level corresponding to a particular fixation. These findings have led to the hypothesis that the OI has a continuum of stable stationary states, giving rise to a continuous attractor network. Here we test this hypothesis by performing optogenetic perturbations in the OI of zebrafish expressing halorhodopsin (or channelrhodopsin). The resulting instantaneous eye movements confirm that the system features continuous attractor dynamics, and suggest previously unsuspected dynamics around the attractor after channelrhodopsin stimulation. These results pose new constraints on the circuit connectivity of the system, and highlight the potential of the combination of optogenetics with theoretical models to unveil neural circuit dynamics.

We have finalised both theory and data analysis. A paper is currently under preparation and should be submitted soon: Goncalves P, Arrenberg A, Baier H, Machens CK (2012). Dynamics of an oculomotor integrator revealed by instantaneous optogenetic perturbations.

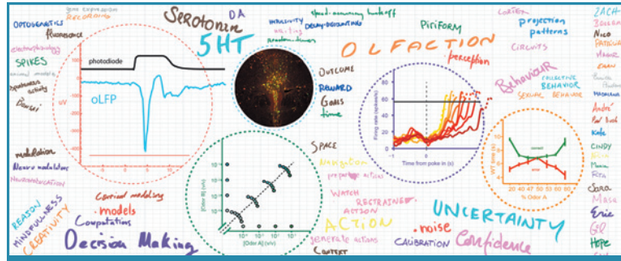

# SYSTEMS NEUROSCIENCE

## Research Groups

ZACH MAINEN
Principal Investigator

We are interested in understanding the principles underlying the complex adaptive behaviour of organisms. Starting with quantitative observations of animal behaviour, we aim to integrate quantitative cellular and systems level experimental analysis of underlying neural mechanisms with theoretical, ecological and evolutionary contexts. Rats and mice provide flexible animal models that allow us monitor and manipulate neural circuits using electrophysiological, optical and molecular techniques. We have made progress using highly-controlled studies of a simple learned odour-cued decision task and are extending our focus toward more complex behaviours. Projects in the lab are wide-ranging and continually evolving. Current topics include:

1. Olfactory sensory decision-making.
2. The function of the serotonin system.
3. The role of uncertainty in brain function and behaviour.
4. The neural dynamics of choice.




KEY PUBLICATIONS

Miura K, Mainen ZF, Uchida N (2012) *Odour Representations in Olfactory Cortex: Distributed Rate Coding and Decorrelated Population Activity.* **Neuron 74 (6):1087-1098**.

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Uchida N, Mainen ZF (2003) *Speed and accuracy of olfactory discrimination in the rat.* **Nat Neurosci 6:1224-1229**.

# LAB MEMBERS

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**Niccolò Bonacchi**
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**Patrícia Correia**
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**Thiago Gouvêa**
2009 INDP PhD Student

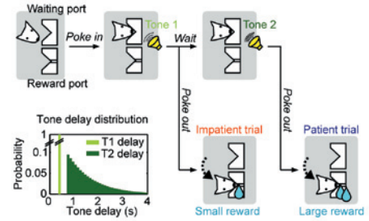
FUNDING

EUROPEAN RESEARCH COUNCIL (ERC)

## Optogenetic identification and control of serotonin neurons in behaving animals

Serotonin (5-HT) is an important neurotransmitter implicated in a wide variety of physiological functions and psychopathologies, but whose function is not well understood. Critically, very little is known about the activity of serotonin-releasing neurons in the brain. This problem is greatly exacerbated by the difficulty in identifying these neurons during physiological recordings. To address these problems, we will develop and validate optogenetic methods that target 5-HT neurons, gaining access to record and perturb this system optically with high temporal and genetic specificity. We will combine these tools with behavioural analysis and electrophysiological recordings toward understanding the role of 5-HT in adaptive behaviour. Our aims are to use these approaches to stimulate, silence and monitor 5-HT function in the context of spontaneous behaviours, value-related decision-making, sensorimotor function and behavioural timing.

We continued to validate techniques for stimulating light-gated channelrhodopsin-2 in 5-HT neurons, using slice physiology, pharmacology, microdialysis, in vivo recordings and demonstrated a light-activated field potential as a measure of 5-HT stimulation (manuscript in preparation). We found effects of 5-HT stimulation on olfactory neural activity in the piriform cortex. We demonstrated a new system for chronically monitoring neural activity in genetically-defined neuronal populations.




**THE ROLE OF THE NEURAL ENSEMBLES IN THE FRONTAL CORTEX IN DECIDING WHEN TO GIVE UP WAITING (M. MURAKAMI).**
The behavioural task used to study waiting time. A trial begins with a rat inserting its snout in a nose poke and waiting for two tones. If it succeeds in waiting for the second tone, which has a long delay, then it gets a large water reward; if it gives up before tone two it gets only a small reward. In these conditions, rats give up waiting at random times between the first and second tone (not shown).

FUNDING

HUMAN FRONTIERS SCIENCE PROGRAMME (HFSP)

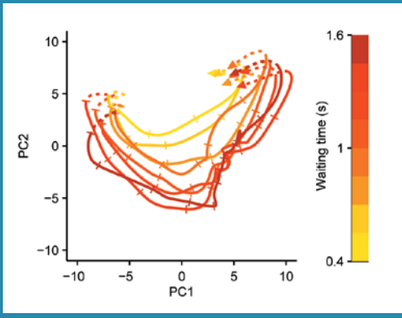
COLLABORATORS

ALEX POUGET
(Department of Brain and Cognitive Sciences, University of Rochester, USA);
MATTHIEU LUIS
(Centre for Genomic Regulation (CRG), Barcelona, Spain)

## Olfactory objects and decisions: from psychophysics to neural computation

Object recognition is an important and difficult problem solved by the nervous system. According to theoretical accounts, object recognition can be understood as a process of probabilistic inference. Under this hypothesis, complex stimuli are represented using a probabilistic population code. To link these normative ideas to specific neurophysiological and behavioural predictions, we are formalising them using computational models. Experimentally, our primary goal is to monitor and perturb object representations in the functioning, computing brain. To this end, we deploy olfactory psychophysical tasks in rats, which formalise complex real-world problems. By combining such quantitative paradigms with large-scale neural ensemble recordings in the olfactory cortex, we can study how populations of neurons encode and process complex odour scenes, attempt to account for behavioural performance, and test the predictions of our theoretical models.

We compared speed-accuracy trade-offs (SATs) in odour detection and categorisation and found large differences between tasks, demonstrating that SAT is problem-specific and suggesting that the locus of performance-limiting noise is a critical variable (manuscript in preparation). We developed a computational model of these tasks, which can be fit to the data, and which has allowed us to formalise these hypotheses.




The dynamics of activity representing a population of 188 frontal cortex neurons during the waiting period. Activity was averaged over a group of trials with similar waiting time (as indicated by the color code) and principal component analysis was used to reduce the number of dimension into two (PC1 and PC2). Tic marks on each trajectory indicate 150 ms time intervals and arrows indicate the direction of time. Notice that trajectories all begin within a tightly defined region corresponding to initiation of waiting and end within another region corresponding to the initiation of withdrawal from the nose poke. With increasing waiting time, the trajectories formed larger arcs between these subspaces.

FUNDING

CHAMPALIMAUD FOUNDATION;
FUNDAÇÃO PARA A CIÊNCIA
E A TECNOLOGIA (FCT), PORTUGAL

## Action selection and action timing in the premotor cortex

Executing the right action at the right moment is important for adaptive behaviour. Thus, not only how we choose one action among multiple options but also how we determine the timing of actions are fundamental questions.

Our goal is to understand what features of future actions are represented in the neuronal firing patterns in these areas, and how the interaction between neurons gives rise to the action selection and action timing processes.

To achieve this goal, we are using multiple single-unit recording techniques in behaving rodents. By correlating the activity of neurons with the animal's behaviour, we are seeking to understand the internal representation of future actions in the motor cortex. Furthermore, by analysing the relationships of spiking activity amongst multiple neurons, we hope to gain insight into computations within the microcircuits in the motor cortex. Finally, we will apply optogenetic techniques to perturb specific circuits and observe the impact on behaviour.

We analysed neural correlates of action timing in the preomotor cortex, documenting two classes of waiting-time predictive neurons and a dynamical systems analysis of the ensemble activity (manuscript submitted). We also developed a task in which we can manipulate the availability of potential action options. We began testing optogenetic interventions in these contexts.


FUNDING

CHAMPALIMAUD FOUNDATION

COLLABORATORS

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(Cold Spring Harbor Laboratory, USA)

## Evaluating the reliability of knowledge: neural mechanisms of confidence estimation

Humans and other animals must often make decisions on the basis of imperfect evidence. What is the neural basis for such judgments? How does the brain compute confidence estimates about predictions, memories and judgments? Previously, we found that a population of neurons in the orbitofrontal cortex (OFC) tracks the confidence in decision outcomes. We are seeking to extend these observations by testing whether confidence-related neural activity in the OFC is causally related to confidence judgments. We are also addressing how the uncertainty about a stimulus in the course of decision-making is computed in olfactory sensory cortex. We are currently establishing similar confidence-reporting tasks in humans and testing them in a range of behaviours. These experiments will give us further insights into the nature of the neural processes underlying confidence estimation.

In rats, we used chronic multi-electrode recordings to assay neural ensemble function in the olfactory tubercule of rats performing a confidence reporting task (study in progress). We also found that inactivation of the rat orbitofrontal cortex impairs confidence reporting but not choice behaviour (manuscript under review). In humans we tested confidence reporting tasks similar to those we deployed in rats under several different psychophysical paradigms.


MARTA MOITA
Principal Investigator

We are interested in understanding the neural mechanisms underlying behavioural plasticity using a combination of behavioural, pharmacological, molecular and electrophysiological tools. In particular, we are studying how prior experience and how social interactions shape behaviour. To this end, we are studying fear; both how animals learn to fear cues that are predictive of aversive events or threats, and how fear can be socially transmitted, i.e. how animals respond to the distress of con-specifics. We chose fear learning because it is conserved across species, entailing fast robust learning and very long lasting memories. We are also studying decision-making in the context of social interactions, using game theory to test how rats learn and evaluate the payoffs that result from the interaction with another individual.


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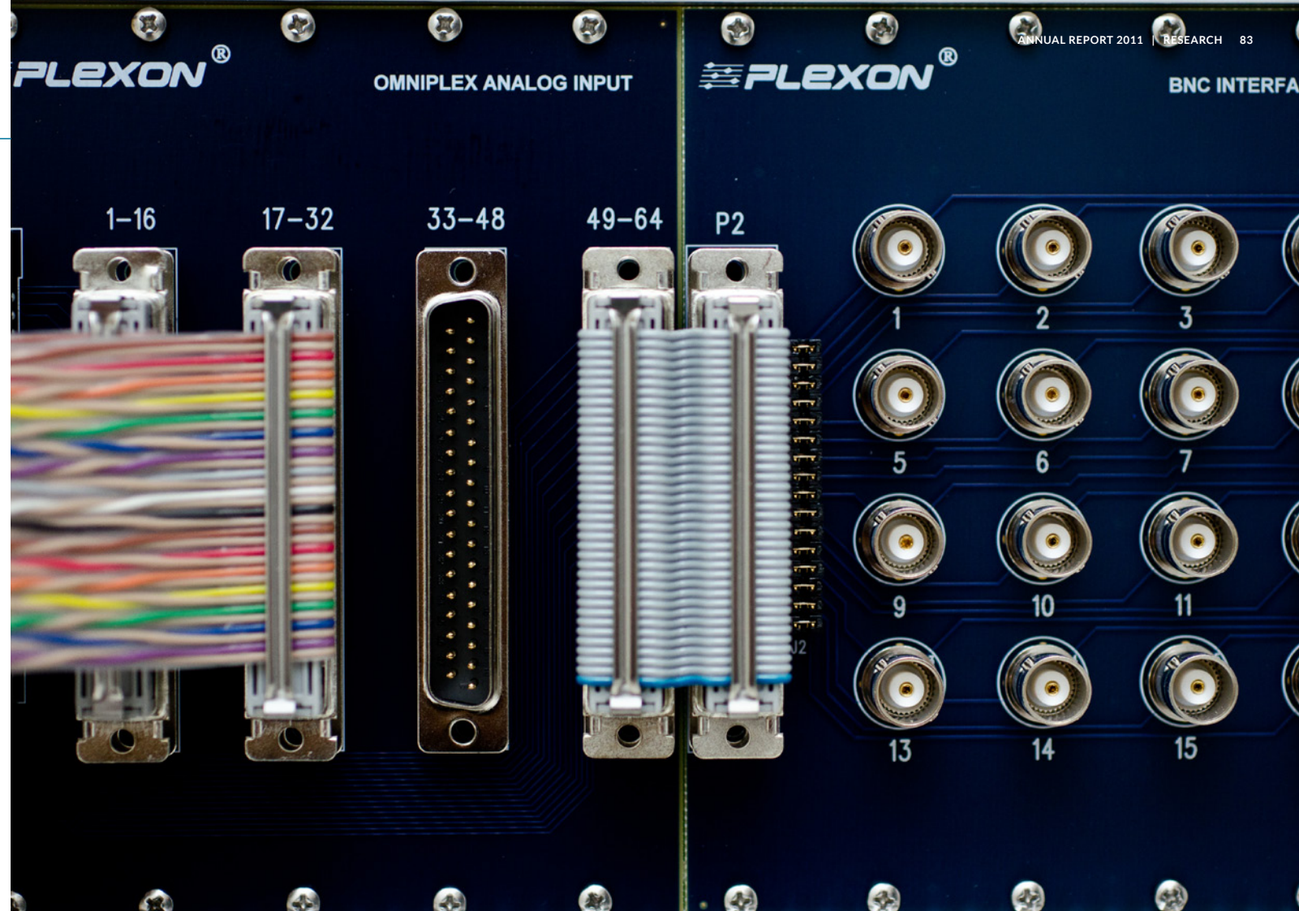

FUNDING

FUNDAÇÃO PARA A CIÊNCIA E A TECNOLOGIA (FCT), PORTUGAL

COLLABORATORS

HUGH BLAIR
(University of California Los Angeles (UCLA),USA);
ALFONSO RENART
(Fundação Champalimaud, Portugal)

## Neural Mechanisms of trace auditory fear conditioning

This project focuses on the role of different memory systems in trace auditory fear conditioning (tAFC). We hypothesised that the mechanism underlying the association between a tone and a shock depends on the length of the trace interval. In the case of long intervals it relies on episodic memory between the two stimuli, whereas in the case of a short interval it relies on working memory.

We have tested the role of contextual learning in auditory trace fear conditioning. We found that decreasing the saliency of the training environment disrupts learning to fear a tone that precedes shock by several seconds and that inactivating the hippocampus does not decrease it further. In addition we are studying the role prefrontal cortex in trace conditioning by performing single-unit recordings in this structure during learning.

## Cooperation in social dilemmas in rats

FUNDING

CHAMPALIMAUD FOUNDATION

Game theory has constituted a powerful tool in the study of the mechanisms of reciprocity. Having shown that, in a Prisoner's Dilemma game, rats shape their behaviour according to the opponent's strategy and the relative size of the payoff resulting from cooperative or defective moves, we now aim at dissecting the mechanisms.

We tested whether rats learn to coordinate in a game where coordination with a conspecific leads to highest number of rewards. We have found that rats learn to coordinate and that they are not simply following the other rat, since decreasing the reward for coordinating leads to a significant decrease in coordination.

FUNDING

CHAMPALIMAUD FOUNDATION;
BIAL FOUNDATION

COLLABORATORS

SUSANA LIMA
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## Neural mechanisms of social transmission of fear in rats

This project aims at investigating the mechanisms underlying social transmission of fear (STF) in rats, i.e. how rats respond to the fear displayed by a con-specific. In order to unravel the neural circuit underlying STF, we will first determine how prior self-experience with shock contributes to STF and what are the sensory cues that mediate this process.
We found that rats do not rely on visual cues, alarm calls or short range chemical signals to detect fear in a conspecific. Instead, they use auditory cues which are likely to signal the sudden transition from motion to immobility. Through sound playback experiments, we found that the absence of movement-evoked sound was necessary and sufficient to induce fear in rats. In addition we have found that prior experience with shock is necessary, but not sufficient for vicarious fear.

FUNDING

CHAMPALIMAUD FOUNDATION

## Social Buffering of Fear

Social interactions can decrease anxiety and fear in a variety of circumstance, a phenomenon known as social buffering. Even though oxytocin has been implicated in this process, its underlying neural mechanisms remain poorly understood. We use auditory fear conditioning, during which an animal can learn to fear a neutral tone when it is paired with aversive footshocks, to test the effect of social buffering on fear conditioned rats. Our goal is to test whether social interactions decrease conditioned fear responses in a lasting manner and to unravel the neural mechanisms of this process.

We conditioned rats to fear a tone and the next day, we exposed them to the tone in the presence or absence of their cagemate. We found that rats tested in the presence of their cage-mate showed less freezing than if tested alone. In addition, when tested again, now alone, rats that were previously exposed in the presence of their cagemate still froze less than the ones exposed alone showing that social buffering has long lasting effects on fear. Finally, we are currently testing the role of oxytocin in the central nucleus of the amygdala (CeA), a major output station that controls several defense responses. Preliminary data suggests that blocking oxytocin in CeA blocks the immediate and long lasting effect of social buffering on freezing.

FUNDING

CHAMPALIMAUD FOUNDATION

## Prosocial behaviour in rats

Most of the studies on cooperation until now used tasks that focus on cooperative acts where the focal animal obtained a benefit for cooperating. Even though the ability to help other individuals in the absence of self-interest was thought to happen only in humans, it was recently shown that non-human primates engage in this form of cooperation, provided the recipient of help displays clear signals of intention. Moreover, rats respond to the distress of a restrained conspecific by opening the restrainers' door. We aim to establish a paradigm to study prosocial behaviour in rats that allows the dissection of the motivations that drive rats to help a conspecific and the investigation of the underlying neural circuits.

We developed a new behavioural task to measure the ability of rats to cooperate, when the decision to cooperate does not involve a direct reward to the focal animal, and with no interference of stress on the cooperating animals. Rats were trained in a double T-maze, where the animals have to nose-poke to access the rewarded arms. The focal rat has the opportunity to choose to reward a conspecific or not, depending on the arm where it nose-pokes. Rats engaged in this task showing high levels of cooperation, suggesting that rats can show instrumental helping and might be sensitive to vicarious reward.

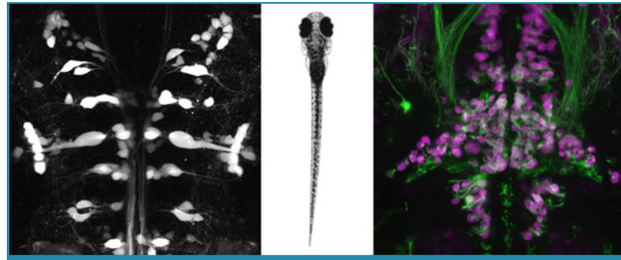

## MICHAEL ORGER

Principal Investigator

Our goal is to understand how the brain integrates sensory information and selects and executes appropriate actions. In particular, we aim to determine the organisation and function of neural circuits underlying visually guided behaviours. We use zebrafish as a model organism because it allows us to visualise and manipulate activity in neural circuits throughout a vertebrate brain. At just one week old, zebrafish can following moving patterns, avoid predators and track and capture live prey. With their small, transparent head, the entire volume of the brain can be imaged non-invasively at single cell resolution. Our approach has three main themes:

1. Quantitative analysis of behaviour.
2. Whole brain imaging of neural activity dynamics.
3. Perturbation of identified neurons to reveal their role in sensorimotor processing.

In parallel, we are developing genetic tools that allow specific targeting and manipulation of identified cell types.



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Ahrens MB, Li JM, Orger MB, Robson DN, Schier AF, Engert F Portugues R (2012) *Brain-wide neuronal dynamics during motor adaptation in zebrafish.* **Nature 485 (7399):471-7.**

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* equal contribution

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**Felix Ludwig**
MSc Student

FUNDING

CHAMPALIMAUD FOUNDATION

## Understanding the Neural Mechanisms that Control Swimming Speed in Zebrafish Larvae

Animals often use distinct gaits to move at different speeds, and this requires the engagement of distinct neural circuits. Zebrafish larvae use different motor patterns, and recruit different spinal interneurons, during slow and fast swimming. Currently, it is not known how the brain computes desired speed or relays this information to the spinal cord. We have developed a system to perform high-speed online analysis of tail kinematics in freely swimming fish, while presenting visual stimuli. We find that zebrafish will adjust their swim speed to track different moving patterns, and they do this by switching between two discrete motor patterns. We intend to discover the neural substrates responsible for this behaviour by imaging whole brain neural activity in restrained fish, during visually evoked swimming at different speeds in a closed-loop virtual reality environment. By thoroughly investigating the mechanisms of speed control in zebrafish larvae, from visual inputs to spinal circuits, we hope to uncover general principles of vertebrate locomotor control.


Zebrafish reticulospinal neurons.

FUNDING

MARIE CURIE CAREER INTEGRATION GRANT

COLLABORATORS

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(Department of Molecular and Cellular Biology, Harvard University, USA)

## Neural circuits underlying the optokinetic response in larval zebrafish

How neural circuits integrate sensory information to produce appropriate actions is a fundamental question in neuroscience. We aim to address this question using optokinetic behaviour, reflexive eye movements in response to whole field motion. Even these simple responses can involve coordinated activity in hundreds of neurons distributed in areas throughout the brain. We image the pattern of neural activity in the brains of transgenic fish, which express a genetically encoded calcium indicator in all of their neurons, while they track visual stimuli with their eyes. Since this behaviour is very repeatable, we can systematically record responses from the whole brain with single cell resolution. We determine what sensory or motor signals are represented at each point, by showing stimuli designed to dissociate the two, such as monocularly presented or binocularly conflicting gratings. Neuronal tracing using photoactivatable GFP reveals potential connectivity of the circuit. These experiments will provide us with the most complete description, in a vertebrate, of the whole brain neural circuit underlying a sensorimotor behaviour.

FUNDING

CHAMPALIMAUD FOUNDATION

## Circuit mechanisms of visuospatial processing in the zebrafish brain

Complex visual behaviours, such as capturing moving prey or avoiding approaching predators, require animals to compute the location and salience of different objects moving in 3 dimensions. These computations depend on dynamic interactions between many interconnected visual areas in the brain. We use transgenic expression of optogenetic tools, and in vivo 2-photon functional imaging to reveal the cellular organisation of these circuits and the dynamics of visual processing in response to complex stimuli. We aim to:

Custom 2-photon microscope with integrated visual stimulation and high-speed behaviour tracking.

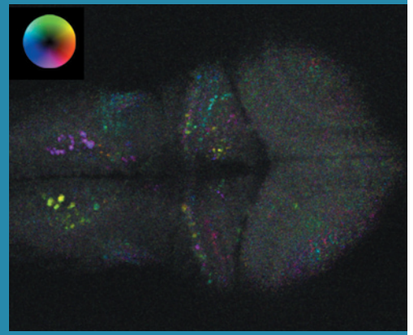
1. Generate driver lines that target gene expression to specific cell types within the fish visual system;
2. Characterise visual response properties and functional topography within these populations;
3. Analyse the interplay between population activity in the optic tectum and isthmic nucleus when the fish is presented with multiple visual targets. We further plan to apply optogenetic tools and laser ablations to interfere with defined units of the circuitry, and determine the link between circuit computations and behaviour.

FUNDING

CHAMPALIMAUD FOUNDATION

## From dusk till dawn - How zebrafish respond to changes in illumination

Larval zebrafish show a wide range of innate responses to spatial and temporal changes in illumination, from rapid orientation and taxis to sustained modulation of locomotor activity. However, little is known about the underlying neural circuits and how neuromodulators act on them to alter locomotor behaviour. Using high-speed video tracking in a custom-built arena we quantitatively assess the fishes' choice of swimming behaviour in response to visual stimuli such as whole field luminance changes and local light and dark patches. We aim to determine the neural activity evoked by the same stimuli using in vivo calcium imaging of transgenic fish expressing genetically encoded calcium indicators. In parallel, we are building a library of short promoter sequences that target expression to distinct neuronal types, with the aim of developing a comprehensive set of transgenic driver lines. These



Micron resolution whole brain functional imaging during optokinetic tracking. Color and intensity represent response tuning and magnitude.

FUNDING

CHAMPALIMAUD FOUNDATION

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(HHMI Janelia Farm Research Campus, Ashburn, Virginia, USA);
LEON LAGNADO
(MRC Laboratory of Molecular Biology, Cambridge, UK)

can be combined with different reporter lines to, for example, optogenetically activate or silence these populations, or record activity in the freely swimming fish using GFP-Aequorin.

## What the fish's eye tells the fish's brain

All visual information that the brain receives from the retina is transmitted via retinal ganglion cells. Understanding how visual information is encoded in this population and transmitted to the brain is key to understanding the computations that underlie visually guided behaviours. We aim to use in vivo calcium imaging in retinal ganglion cell terminals to reveal the spatiotemporal pattern of inputs to the brain when a fish is presented with behaviourally important visual stimuli. We are generating transgenic zebrafish expressing optimised GCaMP indicators in retinal ganglion cells, so that the whole population can be visualised in a single fish. To maximise temporal resolution, functional signals are recorded using a digital scanned light sheet microscope that allows thin optical sectioning, and high acquisition rates, even when imaging over very large areas. In particular, we will examine how small, moving spots that resemble the natural prey of the zebrafish are represented in the inputs to the optic tectum.

FUNDING

CHAMPALIMAUD FOUNDATION

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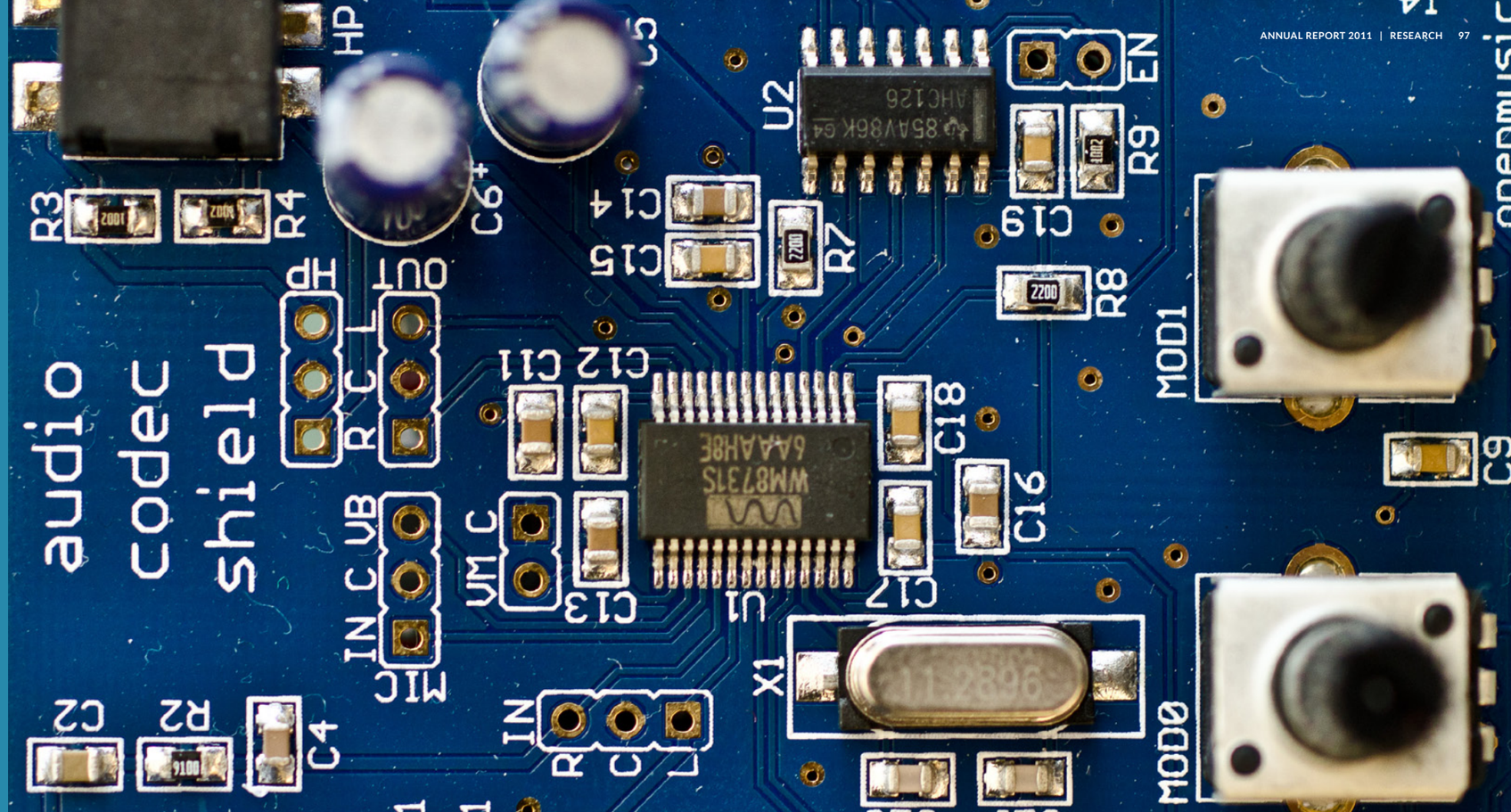
DOUGLAS S. KIM
(HHMI Janelia Farm Research Campus, Ashburn, Virginia, USA)

## In vivo characterisation of novel reporters of neural activity in the zebrafish visual system

The use of genetically encoded sensors, which report neuronal activity and signaling through fluorescence changes, has opened up new possibilities for the study of neural circuits. Measurements can be made with high spatial resolution, from spatially distributed and molecularly defined populations of neurons. However, different biological applications will require sensors optimised for different properties such as signal to noise ratio, brightness, sensitivity, or speed. We are characterising the in vivo performance of new calcium indicators developed by the GECI project team at HHMI Janelia Farm Research Campus. We have developed a system for fast and consistent expression of new constructs in neurons in the optic tectum of zebrafish. Using two-photon imaging, we record signals in the cell soma and dendrites in response to rapidly moving visual stimuli. This information is used to select the best variants for the development of stable transgenic lines, and to guide the design of future indicators.



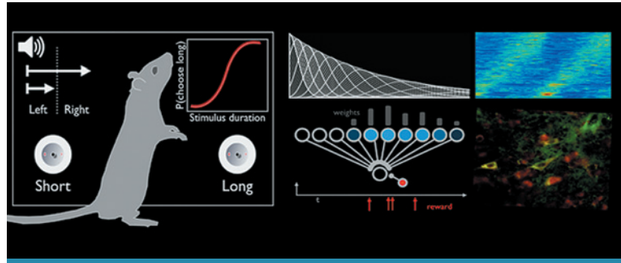

# LEARNING LABORATORY

## Research Groups

## JOE PATON

Principal Investigator

Learning to respond adaptively to cues in the environment that predict behaviourally relevant events is critical for survival. However, in the natural world, where animals are exposed to myriad sensory stimuli, learning the predictive value of cues is non-trivial. How do animals figure out which cues are predictive, and of what? This is called the credit assignment problem. Conceiving of this problem as statistical inference in the time domain offers a parsimonious account of animals' learning abilities. In other words, when cues occur relative to meaningful events is what determines their information content, their usefulness, and thus, whether they warrant learning about. However, we still do not understand how the brain might keep track of times. We aim to reveal neural mechanisms for time by observing and manipulating neurophysiology in behaving rodents performing tasks that lead them to estimate intervals.

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## Low dimensional, continuous monitoring of behaviour

Nervous systems evolved the ability to move before they could think, a fact that is likely to pose constraints on how cognitive functions are structured. However, cognition and action are often thought of as serial, largely segregated processes (i.e. decisions are followed by actions). An alternative view proposes that cognition and action rely on the same computations and are inextricably linked (i.e. decisions consist of actions and action planning). This alternative view may be particularly appropriate when the brain is faced with the challenge of representing and processing information over a time scale much longer than that of its component neurons and circuits. Most of the proposed solutions to this challenge rely on properties of structure and dynamics of disembodied neural networks, while actions are thought of as a subsequent process. However, it is plausible that in realistic situations the brain exploits the dynamics of the rest of the body to store and perhaps process information.

In addition, as neurophysiologists a major part of our job is to identify sources of variance in the firing patterns of neurons. In many parts of the brain, ongoing behaviour is a major source of neuronal firing variance.

However, experiments in cognitive neuroscience generally sample behaviour very sparsely (~0.1 Hz) as compared to the rate of neural data acquisition. As part of the HHMI Janelia Farm Visiting Scientist programme and in collaboration with Josh Dudman, we have developed a compact electronic device for measuring behaviour at the same timescale that we monitor neural activity. This "behavioural headstage" contains integrated circuitry for measuring acceleration and tilt along three axes, multiple coloured LEDs for video tracking, leads for electromyographs, and a small CMOS camera for capturing rat-centric video during cognitive tasks.

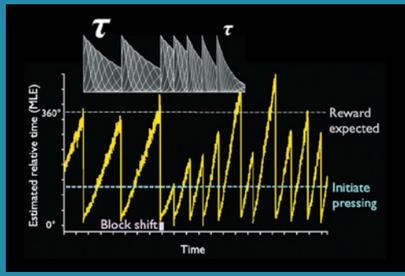
FUNDING

CHAMPALIMAUD FOUNDATION;
FUNDAÇÃO PARA A CIÊNCIA E A TECNOLOGIA (FCT), PORTUGAL

## Optogenetic investigation of interval timing in mice

In the past year, we have initiated a parallel set of timing studies in mice in order to take advantage the increased molecular power of the mouse relative to the rat. We have trained mice on a classic temporal reproduction task, called the peak interval task, and are currently training mice on the SFI task mentioned above. By combining viruses dependent on CRE recombinase activity for expression of transgenes, with mouse lines expressing CRE in specific basal ganglia cell types, we plan to express light sensitive channels and pumps in targeted locations within the basal ganglia circuit. Stimulating these proteins with light during experiments will provide us with two potentially powerful pieces of data. First, we will be able to ask what type of cell we are recording from in vivo much more easily and in higher volume than was available with older techniques. Second, we can test hypotheses about the role of activity in specific populations of neurons for timing behaviour.

In the past year Rui Azevedo has activated dopamine neurons using optogenetics in brain slices, and in behaving mice. He gained behavioural evidence of successful activation by showing that he could condition mice to prefer a particular spatial location by illuminating tranfected neurons specifically when mice entered a




**MODELING RATS' BEHAVIOUR USING MECHANISMS DERIVED FROM EXPERIMENTAL DATA.**
Output of a timing model running on a task that we have previously trained rats to perform. At the top are scalable temporal basis functions that resemble the activity profiles of neurons we have recorded in the striatum of rats during this task. These are used as rate functions to produce poisson spike trains. These spike trains are then decoded to estimate time (blue trace) and subsequently drive behaviour (red threshold).

particular region. He is currently training transgenic mice on a timing task, and will test whether manipulation of dopamine neuron activity affects interval timing.

FUNDING

CHAMPALIMAUD FOUNDATION;
FUNDAÇÃO PARA A CIÊNCIA
E A TECNOLOGIA (FCT), PORTUGAL

## Neurophysiology of time encoding in the rodent striatum

Lesion, pharmacology, and genetic studies all suggest that the ability to estimate the passage of time on the scale of seconds to minutes is produced in the striatum, a major input area of the basal ganglia. Thus, we trained rats to estimate time intervals and recorded from striatal neurons as they behaved and asked how the passage of time could be encoded in the firing patterns we observed. In addition, the basal ganglia is thought to implement reinforcement learning mechanisms, helping the animal learn how to act in response to a given situation based on past experience. We sought to place the neural signals we recorded into a computational frame work that reconciles interval timing and reinforcement learning. Towards that end, we are developing a computational model of interval timing that includes signals related to those we observe experimentally, but that also can solve reinforcement learning problems.

We currently have a manuscript in the final stages of preparation describing the neural signals we observe during an interval timing task. We are also actively extending these studies to gain more continuous measures of the animals' behaviour during our task. This will be important for continuing to rule out behavioural sources of variance in the firing of neurons we record.

FUNDING

CHAMPALIMAUD FOUNDATION;
FUNDAÇÃO PARA A CIÊNCIA
E A TECNOLOGIA (FCT), PORTUGAL

## Neurometric - Psychometric comparison of interval timing performance

Tasks in which subjects must categorise sensory stimuli whose characteristics are parametrically varied have been powerful tools for relating neural processing to sensation in a rigorous and quantitative manner. We are applying the same approach to an unconventional sensory modality, the ability to sense the passage of time, by training rats on a two alternative forced choice interval timing task. We can derive quantitative description of animals' interval timing abilities via the fitting of psychometric functions to their choice data and then compare this to the ability of neural activity to encode the passage of time. A tight correspondence between the animals' behavioural performance and the neuronal encoding of time would suggest involvement of those neural signals in the process of timing.

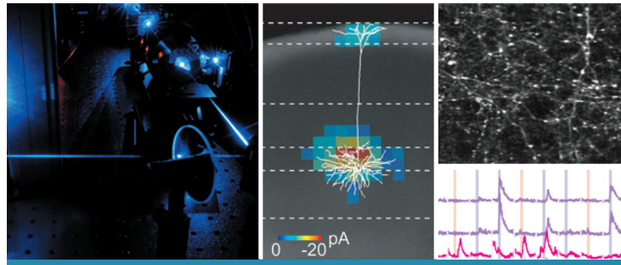
Thiago Gouvea has designed the behavioural apparatus, programmed the behavioural control required for the task, and has trained four animals. We will soon be initiating neural recordings during task performance.

# CORTICAL CIRCUITS

## Research Groups

LEOPOLDO PETREANU
Principal Investigator

The neocortex plays a key role in sensory perception and higher cognitive functions. Our overall goal is to understand the neural computations underlying cortical function, focusing on the functional role of cortico-cortical interactions. Cortico-cortical projections either terminate in the middle layers (feedforward inputs, FF) or innervate the lower and upper layers, avoiding the middle ones (feedback inputs, FB). The fact that these motifs are conserved across many cortical-connections suggests that FF and FB connections might have a common function across areas. In order to address functional role of cortico-cortical connections in cortical computation we are studying the structure and function of these circuits. Using novel optical methods we record the activity of cortico-cortical projections while the animal is engaged in behavioural tasks that depend on these circuits. We also characterise the connectivity and synaptic properties of identified neuronal populations constituting FF and FB circuits using optical circuit mapping methods.

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Petreanu L, Huber D, Sobczyk A, Svoboda K (2007) *ChannelrhodopsIn--2-assisted circuit mapping of long-range callosal projections.* **Nat Neurosci 10 (5):663-8.**

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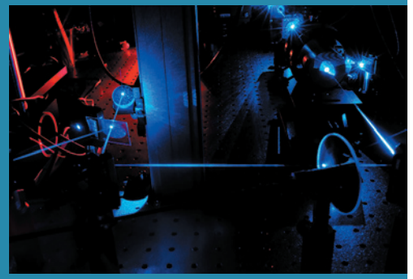
FUNDING

CHAMPALIMAUD FOUNDATION

## Optogenetic circuit mapping of long range cortical interactions

A comprehensive characterisation of the precise neuronal types constituting cortico-cortical circuits is necessary to understand their function. Feedforward connections terminate mainly from layer 2/3 to layer 6. In contrast, feedback connections terminate in all layers except layer 4. Thus, as the dendrites of cortical neurons usually span several layers, cortico-cortical axons can potentially make synapses with almost any neuronal type in the cortical column. However, as the overlap of axons and dendrites is not always a good predictor of actual connectivity, connections need to be probed with functional methods. Using channelrhodopsin-assisted circuit-mapping we are identifying the postsynaptic targets of afferents from different cortical areas. By mapping the connections linking cortical areas we aim at understanding the logic of feedfoward and feedback connectivity.



LASERS BEAMS ON THE OPTICAL TABLE OF A SLICE PHYSIOLOGY SETUP USED FOR MAPPING CORTICAL CIRCUITS.

FUNDING

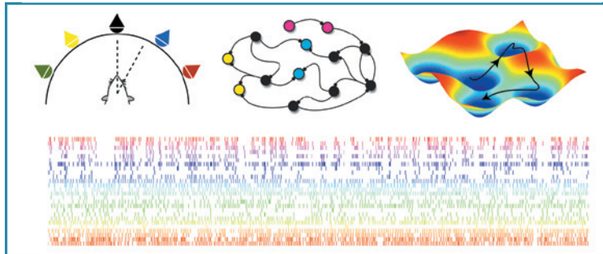
CHAMPALIMAUD FOUNDATION

## Optical recordings of feedforward and feedback cortical connections in behaving animals

In order to address the functional roles of feedforward (FF) and feedback (FB) circuits we plan to record from cortico-cortical projections in animals is engaged in behavioural tasks that depend on these circuits. Toward this goal, we are developing head fixed behaviours that require several interconnected visual areas. Head-fixed behavioural paradigms allow us to have precise stimulus control and motor readout over a large number of trials with high repeatability. Head-fixed behaviours also facilitate experimental access for the manipulation and recording of neuronal activity. In particular, they allow us to perform optical recordings of neuronal activity in behaving animals. Using two-photon microscopy and genetically-encoded calcium indicators we will record specifically from FF and FB projections by imaging afferent axons in their target area. Recordings cortico-cortical circuits together with precise measurements of sensory, motor and behavioural variables will help us in understanding the role of these connections in cortical computation


ALFONSO RENART
Principal Investigator

The overall goal of the lab is to identify generic principles governing the dynamics of cortical circuits and the way in which they produce function. We are interested both in identifying characteristic signatures of population organisation – through recordings of the simultaneous activity of neuronal populations during controlled behavioural tasks - as well as in understanding mechanistically how these patterns of population activity emerge – which we investigate by developing mathematical models of the underlying neuronal circuits. Our current work involves around two lines of research: sensory perception - with an emphasis on the relationship between the response variability of sensory neurons and the accuracy of perceptual discriminations - and working memory, with a focus on the mechanisms underlying the maintenance of information across time in the prefrontal cortex.



KEY PUBLICATIONS

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Moreno R, de la Rocha J, Renart A, Parga N (2002) *Response of spiking neurons to correlated inputs.* **Phys Rev Lett 89 (28):288101**.

* equal contribution

# LAB MEMBERS

**Job van der Voort**
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FUNDING

MARIE CURIE;
CHAMPALIMAUD FOUNDATION

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ALBERT COMPTE
(Institut d'investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain)

## Population dynamics during auditory perception

Although anatomy makes it certain that information processing in the brain is the result of the interaction of neurons organised in networks spanning multiple spatial scales, our knowledge about the patterns of population activity associated to specific computations and about the mechanisms that generate these patterns in recurrent neuronal circuits is very incomplete. We are interested in the computations performed by local cortical circuits during perception. We use the auditory modality because rodents naturally use auditory cues to guide their behaviour and because it allows us to deliver complex stimuli in a well-controlled and repeatable fashion. We are developing auditory discrimination tasks built around a basic sound localisation paradigm, which can easily and quickly be learnt by rodents. We record the simultaneous activity of multiple neurons from the auditory cortex during performance of these tasks in order to investigate questions such as the population structure of trial-to-trial variability and its relationship to the accuracy of perception, mechanisms for invariant processing of auditory information, or the interplay between feed-forward and feed-back influences in perception.

FUNDING

HUMAN FRONTIERS SCIENCE PROGRAM (HFSP)

COLLABORATORS

PAUL CHADDERTON
(Dept. of Bioengineering, Imperial College London, London, UK);
SEBASTIAN ROYER
(Centre for Functional Connectomics, Seoul, Korea)

## The dynamical basis of working memory in the prefrontal cortex

Actions, their consequences and the sensory stimuli that inform them do not occur simultaneously, therefore the brain must hold representations online so that they can be integrated, a capacity known as working memory. Single unit recordings in primates performing tasks with a delay period have shown the prefrontal cortex (PFC) to be a key brain area in this process. Based on this data a rich conceptual framework relying on the idea of dynamical attractors has been developed. However, key aspects of this framework appear at odds with recent data and some remain untested. In this collaborative project, we combine electrophysiology, quantitative anatomy, optogenetics and modeling to provide a dynamical foundation of working memory in mouse PFC. Our goals are:

1. To delineate the anatomical extent of circuits underlying working memory.
2. To assess the relative contributions of cellular vs. synaptic mechanisms to the ongoing memory traces.
3. To characterise the patterns of PFC activity at the population level during memory maintenance and to quantify their dynamical stability through delicate optical perturbations.
4. To gain a theoretical understanding of the mechanisms that allow recurrent networks to generate long-lasting, time-varying memory traces.

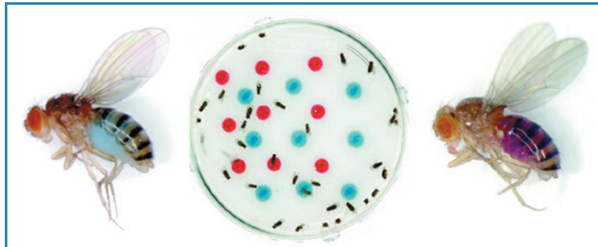

# BEHAVIOUR AND METABOLISM

## Research Groups

CARLOS RIBEIRO

Principal Investigator

We are interested in understanding how molecular and cellular mechanisms control complex biological processes at the level of the whole organism. For this we are focusing on how the internal metabolic state of the fruit fly *Drosophila Melanogaster* affects its behavioural decisions. Starting from novel behavioural paradigms we use molecular genetic techniques to identify and characterise molecular mechanisms and neuronal populations involved in producing the appropriate behavioural response to a specific metabolic need of the fly.



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Keleman K, Ribeiro C, Dickson B (2005) *Comm function in commissural axon guidance: cell-autonomous sorting of Robo in vivo.* **Nat Neurosci 8 (2):156-163**.

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Ribeiro C, Ebner A and Affolter M (2002) *In vivo imaging reveals different cellular functions for FGF and Dpp signaling in tracheal branching morphogenesis. Developmental.* **Dev Cell 2:677-683**.

# LAB MEMBERS

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**-Gonçalves, PhD**
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**Samantha Herbert**
PhD Student

**Verónica Corrales**
MIT - Portugal
PhD Student

**Célia Baltazar**
Research Assistant

FUNDING

CHAMPALIMAUD FOUNDATION;
BIAL FOUNDATION

## Molecular mechanisms of nutrient choice

We want to understand how *Drosophila* knows what type of nutrients it needs and which are the molecular mechanisms used by the nervous system to change the behaviour of the animal to allow it to find and eat the required nutrients.

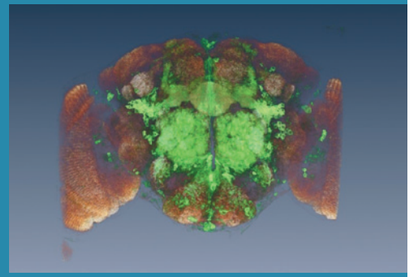
We are investigating how conserved nutrient sensing pathways act in the nervous system to control feeding. Furthermore analysing genes identified as being required for nutrient choice in a neuronal whole-genome RNAi screen we are investigating novel molecular mechanisms mediating nutrient homeostasis. Taken together these studies are providing us with an entry point for studying nutrient balancing and value-based decision making at the molecular level.

FUNDING

CHAMPALIMAUD FOUNDATION;

## Neuronal mechanisms of nutrient choice

We want to identify and analyse the neuronal networks used by *Drosophila* to change the behaviour of the animal to allow it to find and eat the required nutrients. We are using genetic approaches to identify neuronal populations which are required for the fly to decide which nutrients to eat. Currently we are analysing the identified neuronal substrates to understand how these neuronal populations act to guide feeding decisions.



**A 3D RENDERING OF A *DROSOPHILA* BRAIN WITH A MEMBRANE BOUND GFP IN GREEN AND THE REST OF THE BRAIN IN RED.**
A specific subset of neurons is labeled in this line, as visualised by the expression of the membrane bound GFP.

FUNDING

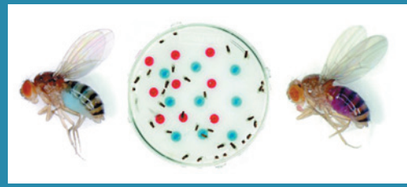
CHAMPALIMAUD FOUNDATION

COLLABORATORS

ALDO FAISAL
(Imperial College London, UK)

## Quantitative analysis of feeding behaviour in *Drosophila*

In collaboration with the laboratory of Aldo Faisal at Imperial College London we use automated video analysis to quantitatively link genetics to feeding behaviour in the fruit fly. These studies are providing us insights into the behavioural strategies used by the fly to maintain nutrient homeostasis as well as their biological implementation in the nervous system.



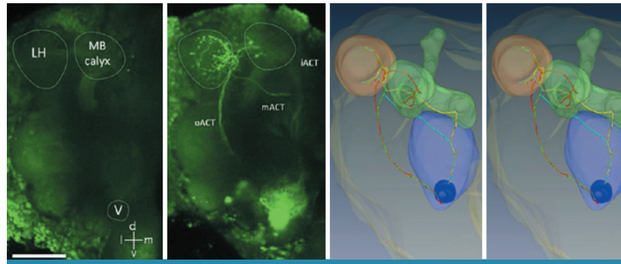
**FEEDING DECISIONS IN *DROSOPHILA* NUTRIENT BALANCING.**
Flies in the food choice setup (yeast is blue and sucrose is red). Food choice is revealed by the colour of the fly's abdomen after two hours of feeding, and a yeast preference index is calculated for the population.

# INNATE BEHAVIOUR

Research Groups

MARIA LUÍSA VASCONCELOS
Principal Investigator

Animals exhibit behavioural repertoires that are often innate and result in stereotyped sexual and social responses to their environment. Innate behaviours do not require learning or experience and are likely to reflect the activation of developmentally programmed neural circuits. We are interested in the nature of defined neural circuits: how activation of circuits elicits specific behaviours. In complex organisms it has been extremely difficult to study a circuit beyond the early stages of sensory processing. *Drosophila Melanogaster* is an attractive model system to understand a circuit because flies exhibit complex behaviours that are controlled by a nervous system that is numerically five orders of magnitude simpler than that of vertebrates. We use a combined behavioural, genetic, imaging and electrophysiological approach to determine how defined neural circuits and their activation elicit specific behaviours.




## KEY PUBLICATIONS

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* equal contribution

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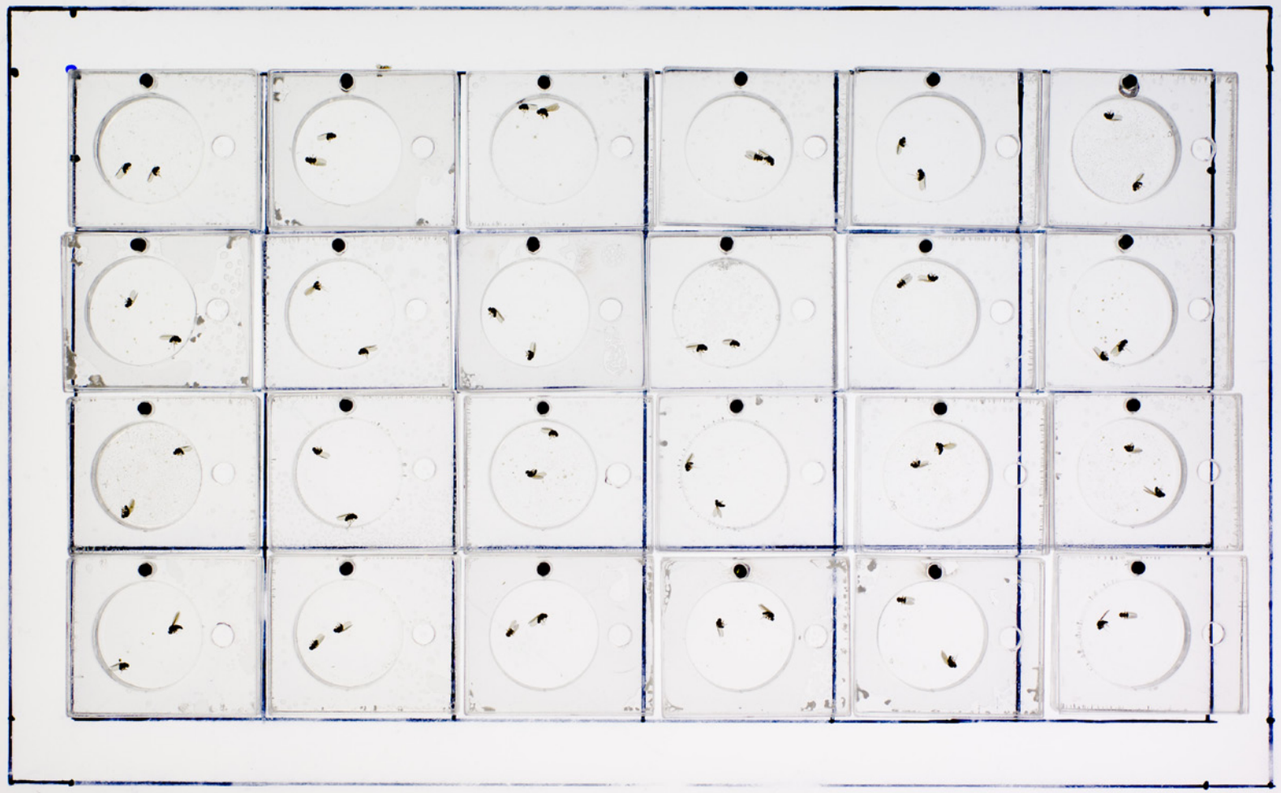
**Sophie Dias**
Research Technician



FUNDING

MARIE CURIE;
FUNDAÇÃO PARA A CIÊNCIA
E A TECNOLOGIA (FCT), PORTUGAL

## Female receptivity

Genetic studies have elucidated how *Drosophila* male courtship behaviour is specified and its circuit components are being dissected at a surprising speed. The circuit of female behaviour on the other hand has been largely uncharacterised. We use a behavioural protocol that allows us to selectively inactivate subsets of neurons in the adult flies only. We use this behavioural approach and combine it with anatomical and functional dissection of the circuit.

We explored further the involvement of apterous neurons (ANs) in receptivity: We verified that locomotion is unaffected, as well as the fly's attractivness. We characterised the pattern of ANs. We have masculinised the neurons and seen no phenotype indicating that ANs are not sexually dimorphic. We have tested females that have inhibited ANs for their egg laying. Egg laying in virgins is unchanged indicating that there is not an activation of the post-mating switch at least to the full extent.

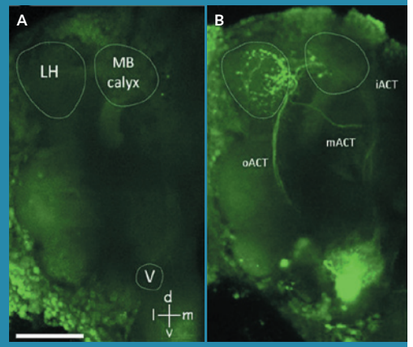
FUNDING

FUNDAÇÃO PARA A CIÊNCIA
E A TECNOLOGIA (FCT), PORTUGAL

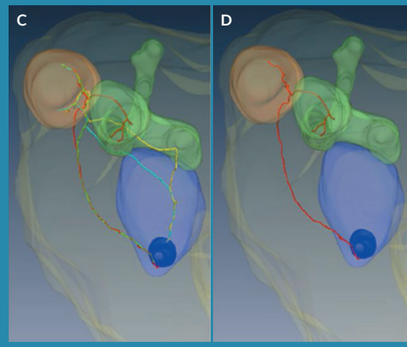
## Across species stress odour response

Stressed *Drosophila Melanogaster* release an aversive odourant that elicits a robust avoidance response in test flies. Our data indicate that stress odour avoidance is not common to all *Drosophilids*. This behavioural difference between melanogaster and some of its sister-species provides a powerful framework, amenable to genetic, developmental and anatomical dissection, to investigate how evolution has shaped distinct responses to an environmental cue.
We have traced the neurons that innervate the v glomerulus. We observed Three projection neurons connect solely with the lateral horn and one projection neuron that connects additionally to the Mushroom Body. This result suggests that the CO2 response can be modulated.

We tested the response of seven *Drosophilidae* to CO2. We observe a salt and pepper variation across the phylogenetic tree indicating multiple occurrences for gain/loss of behaviour.




**PHOTOACTIVATION ALLOWS VISUALISATION OF THE NEURONS INNERVATING THE V GLOMERULUS.**
**A.** Before photactivation. **B.** After photoactivation.




**C.** Schematic generated by automated filament tracing.
**D.** Schematic of the projection neuron thatconnect to lateral horn and mushroom bodies.

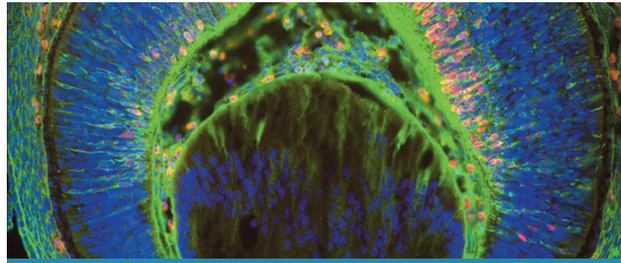
# NEURAL DEVELOPMENT

Associated Research Groups

## DOMINGOS HENRIQUE

Principal Investigator

Our main interest is to understand the molecular mechanisms that regulate the genesis of neurons in vertebrate embryos. A better knowledge of these mechanisms is a pre-requisite for the development of cellular replacement therapies to treat neurodegenerative diseases. Our research focus on the molecular events that control the generation of stem cells in the embryo, how these cells are maintained, and how they give rise to the multitude of neurons that compose the adult CNS.



KEY PUBLICATIONS


Vilas-Boas F, Fior R, Swedlow JD, Storey KG, Henrique D (2011) *A novel Reporter of Notch Signalling indicates regulated and random Notch Activation during Vertebrate Neurogenesis.* **BMC Biol 9:58**.

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Abranches E, Silva M, Pradier L, Schulz H, Hummel O, Henrique D, Bekman E (2009) *Neural Differentiation of Embryonic Stem Cells in vitro: a Road Map to Neurogenesis in the Embryo.* **PLoS ONE 4 (7):e6286**.

Afonso C, Henrique D (2006) *PAR3 acts as a molecular organizer to define the apical domain of chick neuroepithelial cells.* **J Cell Sci 119:4294-4304**.

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**Sara Ferreira**
Research Technician

FUNDING

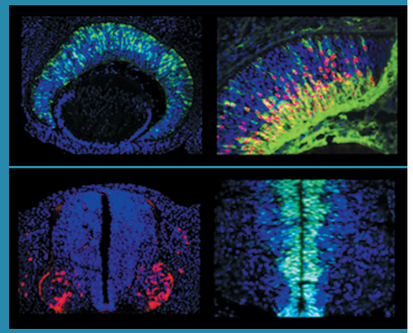
FUNDAÇÃO PARA A CIÊNCIA E A TECNOLOGIA (FCT), PORTUGAL

COLLABORATORS

ACHIM GOSSLER (U. Hannover);
A. Duarte (FMV, UTL, Lisbon)

## Understanding cell fate decisions in the embryonic neural retina

In this project, we aim to understand the principles underlying the generation of neuronal diversity in the developing retina. Lineage determination in the retina is governed mainly by cell-cell interactions, a process in which Notch signaling plays a central role. Our work focus on the function of two Notch ligands, Dll1 and Dll4, which are expressed in newborn retinal neurons and contribute for cell fate specification in the retina. We are also addressing how proneural bHLH genes act to prime multipotent retinal progenitors (RPCs) into different fates. We have found that different combinations of proneural bHLH genes are expressed not only in RPCs but also in differentiating neurons, overlapping with Dll4. Our working model is that the simultaneous expression of lineage-determination genes in retinal neurons is central to their multipotent character, with Dll4/Notch signaling acting to generate the observed spatio-temporal pattern of neuronal specification in the developing retina.



IMAGES OF DIFFERENTIATING NEURONS IN THE DEVELOPING RETINA AND SPINAL CORD OF MOUSE EMBRYOS.

FUNDING

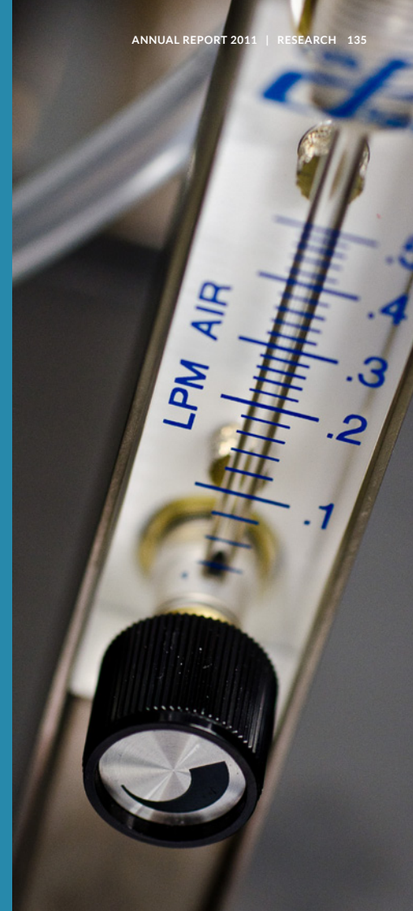
FUNDAÇÃO PARA A CIÊNCIA E A TECNOLOGIA (FCT), PORTUGAL

COLLABORATORS

ARJUN RAJ, (U.Penn);
ANA POMBO (Imperial College, London)

## The Key Role of the Dynamic Nanog Expression in pluripotent stem cells

Pluripotency in Embryonic stem (ES) cells is controlled by a dedicated gene regulatory network, at the top of which function a core of three transcription factors, Nanog, Oct4 and Sox2. Using a novel reporter mouse ES cell line, we performed a quantitative and dynamic analysis of Nanog protein and mRNA expression. Our results show that NANOG levels correlate with the degree of priming to differentiation shown by ES cells, and that fluctuations in NANOG levels are intrinsically driven and inherent to the pluripotent state. Our data is qualitatively and quantitatively explained in the framework of a fully stochastic model, where intrinsic noise combined with a positive feedback loop in NANOG regulation generates the observed heterogeneity in expression levels. This model allows us to infer unanticipated features of Nanog regulation and function in ES cells, suggesting novel perspectives about how pluripotency emerges from the inner workings of the NOS circuitry.



# SOCIAL NEUROENDO-CRINOLOGY

## Associated Research Groups

RUI OLIVEIRA
Principal Investigator

We are interested in understanding the neuroendocrine mechanisms of social behaviour and how the social environment may feedback on the neuroendocrine system. In particular we are interested in the role of hormones as key physiological mediators underlying social plasticity.

KEY PUBLICATIONS

Soares MC, Oliveira RF, Ros AFH, Grutter AS, Bshary R (2011) *Tactile stimulation lowers stress in fish*. **Nat Commun 2:534**.

Soares MC, Côté IM, Cardoso SC, Oliveira RF, Bshary R (2010) *Caribbean cleaning gobies prefer client ectoparasites over mucus*. **Ethology 116:1244-1248**.

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Oliveira RF (2009) *Social behaviour in context: hormonal modulation of behavioural plasticity and social competence*. **Integr Comp Biol 49:423-440**.

Antunes RA and OliveiraRF (2009) *Hormonal anticipation of territorial challenges in cichlid fish*. **Proc Natl Acad Sci USA 106:15985-15989**.

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**José Simões**
PhD Student

**Magda Teles**
PhD Student

**Rodrigo Abreu**
2007 INDP PhD Student

COLLABORATORS

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HANS HOFMANN,
Univ. Texas at Austin, U.S.A.

## Neurogenomics of social plasticity: rapid transcriptomic responses to social interactions

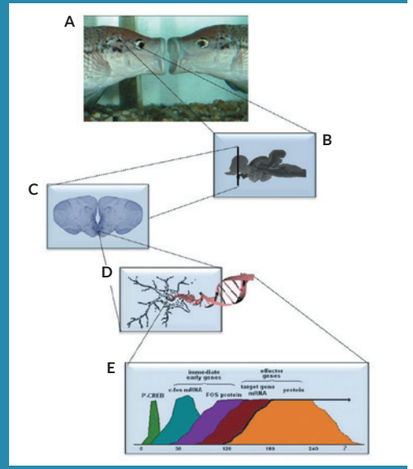
Social plasticity is a pervasive feature of animal behaviour. Animals must adjust the expression of their social behaviour to the nuances of daily social life and to transitions between life-history stages, and the ability to do so impacts on their Darwinian fitness. Social plasticity may be achieved by rewiring or by biochemically switching nodes of the neural network underlying social behaviour in response to perceived social information. Therefore, at the molecular level, it depends on the social regulation of gene expression, so that different neurogenomic states correspond to different behavioural responses and the switches between states are orchestrated by signaling pathways that interface the social environment and the genotype. We have been studying socially driven changes in gene expression in the brain in relation to adaptive social plasticity, both in cichlid fish and in zebrafish. So far we have shown that the perceived outcome of social interactions has a major impact in the brain transcriptome profile that mediate the effects of prior experience social experience on subsequent behaviour (i.e. winner and loser effects).

COLLABORATORS

GUNTHER ZUPANC,
Northeastern Univ., Boston, U.S.A.;
DANIEL PETERSEN,
U.S.A.

## Social modulation of adult neurogenesis: cichlid fish and zebrafish as study models

Social plasticity is predicted to rely on different neural plasticity mechanisms depending on its temporal expression. Transient and reversible changes in social behaviour driven by social experience and context are expected to depend on functional synaptic plasticity (e.g. LTP), whereas irreversible switches between discrete behavioural phenotypes driven by developmental processes in response to environmental cues are expected to rely on structural changes in the neural network underlying social behaviour. In this project we are using both zebrafish and cichlid fish to study how single vs. repeated sequential social interactions affect adult neurogenesis at different levels (proliferation, migration, differentiation, functional integration) in the nodes of the neural network underlying social behaviour. In cichlid fish, we are taking advantage of its well described chemical communication system and of the fact that we found high levels of both cell proliferation and neuropeptide levels (AVT, isotocin) in the olfactory bulbs (OB), to study olfactory modulation of neurogenesis and its regulation by neuropeptides in the OBs.




**MECHANISMS OF SOCIAL PLASTICITY:**
**A.** social living animals adjust the expression of their behaviour to social information collected in previous social interactions or by observing others. **B.** The cognitive appraisal of this information allows them to evaluate the stimulus/ event in terms of its valence and salience that will be encoded in a distributed neural network. **C-D.** At each node of this network neurons will change their neurogenomic state, that is, their gene expression profile in response to the perceived social information. **E.** Changes of gene expression are triggered by the activation of neuronal activity-regulated transcription factors (e.g. p-CREB) that regulate immediate early genes (e.g. c-fos) that can regulate synaptic proteins, therefore modulating neural plasticity that underlies behavioural flexibility.

COLLABORATORS

KOICHI KAWAKAMI,
Natl. Inst. Genetics, Japan

## Social learning in zebrafish

Social information can be collected on first-hand by directly interacting with other individuals, or by observing other behavioural agents (social learning). In this project we are investigating the mechanisms of social learning in zebrafish by contrasting it with equivalent asocial learning mechanisms in different social contexts (observational conditioning of predator avoidance vs. a classical fear conditioning paradigm; social eavesdropping in the context of aggressive encounters vs. stimulus enhancement; mate choice copying vs. independent mate choice). The comparison of the brain patterns of IEG expression across these studies will allow to test

if social learning in different functional domains share a common neural network, or if in contrast each social learning type shares its neural mechanism with that of its corresponding asocial learning form. These comparisons are particularly relevant since prediction error that is considered a learning signal is not directly available when animals use public information.

## Cognitive appraisal and cognitive bias in zebrafish

COLLABORATORS

GEERT FLICK,
Nijmegen Univ. Netherlands

A central concept in social cognition is that what trigger a response to a stimulus are not only its intrinsic characteristics but rather the evaluation of what that stimulus or event means to that organism at that moment in time. Therefore, the exactly same event may elicit different responses, depending on the way it is appraised by different individuals or by the same individual at different moments in time. The involvement of appraisal in the activation of the physiological and genomic responses also opens the possibility for consistent evaluation biases to occur (i.e. some individuals will consistently evaluate ambiguous stimuli as negative, and others as positive). Thus, cognitive bias in the appraisal process can be a major factor in individual variation in the susceptibility to life events. In this project we aim to uncover the genetic pathways and neural circuits involved in cognitive appraisal and cognitive bias, using zebrafish (Danio rerio) as a model organism. So far we have been developing behavioural assays (CPP, contrast effect test) to test cognitive appraisal in zebrafish.


COLLABORATORS

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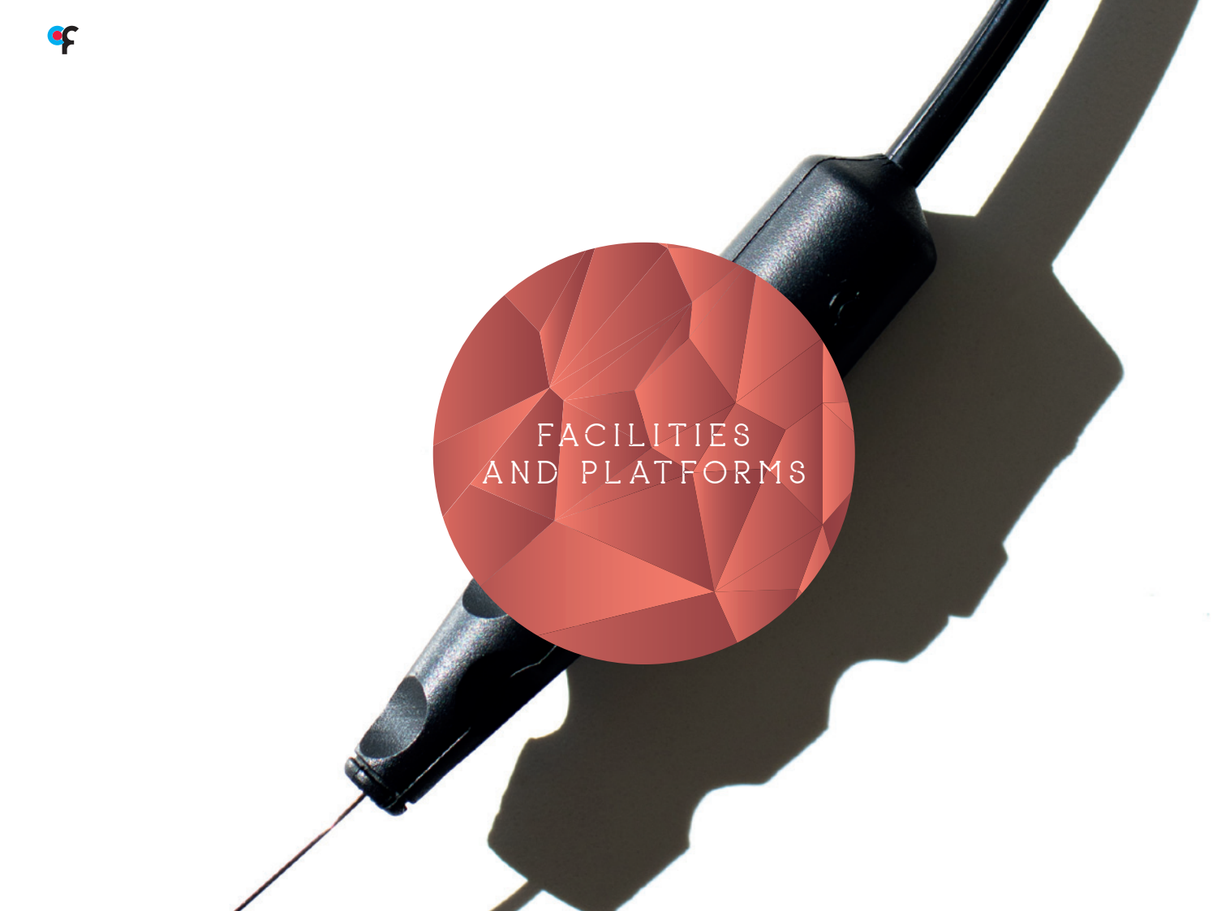
Univ. Saint Joseph, Macao, China;
ADELINO CANÁRIO,
Univ. Algarve, Portugal;
ALEX GOESMANN,
Univ. Bielefeld, Germany

## Neurogenomic and physiological mechanisms of adaptive behavioural plasticity in a fish with male alternative mating tactics

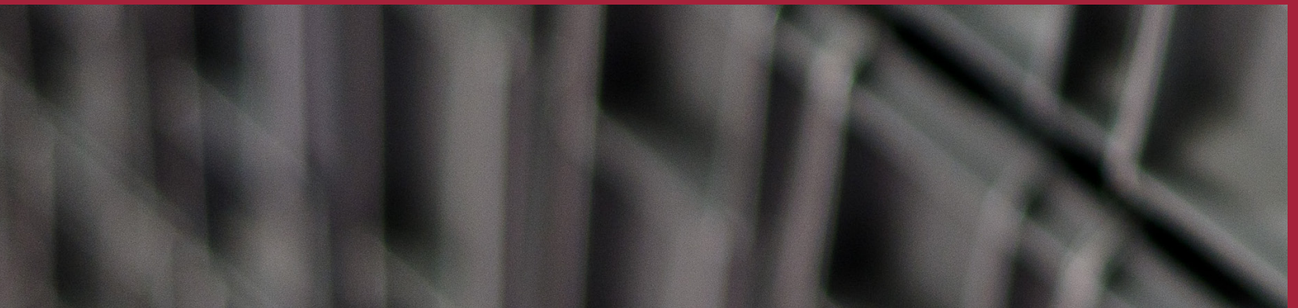
Species that present sequential alternative behavioural phenotypes so that the same individual expresses opposite behaviours at different life-history stages, are particularly well suited for studying the structural reorganisation of neural circuits underlying social behaviour. In this scope we are studying an intertidal fish (peacock blenny) where two developmental sequential male morphs occur that express divergent behaviours: female courtship behaviour in young female-mimicking males vs. male courtship behaviour in older territorial males. So far we have characterised the neuroendocrine correlates of these alternative mating tactics (i.e. circulating hormone levels, levels of steroid receptors, neuropeptides and steroidogenic enzymes in the brain, and the effects of steroids and neuropeptides on tactic expression), and the environmental cues that trigger the expression of these conditional tactics. More recently, we have deep-sequenced its transcriptome and we are now using RNA-Seq to compare alternative morphs and in order to identify the gene networks and signaling pathways underlying developmental social plasticity in this species.




# TO HELP OUR SCIENTISTS

REACH THEIR FULL CREATIVE POTENTIAL

SUCCESSFUL RESEARCH CANNOT EXIST WITHOUT A FIRM BASE OF TECHNICAL AND ADMINISTRATIVE SUPPORT. THE MEMBERS OF CNP FACILITIES AND PLATFORMS ARE A HIGHLY SKILLED GROUP OF INDIVIDUALS WHO, BEYOND PROVIDING EXCELLENT BASE SERVICES, TRAINING AND ADVICE, ARE ALSO COMMITTED TO KEEPING IN STEP WITH CHANGES IN INDIVIDUAL NEEDS OF CNP RESEARCHERS AND WITH METHODOLOGICAL AND TECHNICAL ADVANCES.





# ADMINISTRATIVE SUPPORT

The Administrative Office provides all the necessary aid, in all the fields from social, bureaucratic and technical, in order to ease the integration of new members and to provide all the necessary tools for the researchers to fully perform their priority goal - scientific research.

**Alexandra Piedade**
Meetings and Courses

**António Coelho**
Grants Manager

**Philipp Tsolakis**
Financial Manager / Controller

**Raquel Gonçalves**
Purchasing and Ordering

**Teresa Carona**
Project Manager

# FLY FACILITY

ISABEL CAMPOS, PhD
Manager

The core purpose of the CCU Fly Unit is to provide state of the art conditions for breeding, maintenance and manipulation of the fly *Drosophila Melanogaster*. The equipment of the Fly Unit includes temperature and humidity controlled chambers for *Drosophila* breeding and behavioural experiments, CO2 anesthesia stations, scopes for basic and detailed manipulation and a kitchen dedicated for fly food production. The unit has a committed expert staff that:

1 - Supports researchers in establishing, applying and developing advanced genetic methods; 2 - Is deeply involved in training activities; 3- Assures the proper functioning of the general CCU *Drosophila* infrastructure, currently serving a total of 19 researchers from three different laboratories (Chiappe, Ribeiro and Vasconcelos).

The CCU Fly Unit also offers services for external institutions and is currently responsible for the weekly production of fly media for 10 external labs from 3 different institutes: IGC, CEDOC and ITQB.

**Liliana Costa**
Research Technician

# GLASS WASH AND MEDIA PREPARATION PLATFORM

MARIA VITO
Manager

Glass wash and media preparation are core functions, essential in any research institution.

The Glass Wash & Media Preparation Platform supports investigators and laboratories at the Champalimaud Centre for the Unknown (CCU) by providing cleaning and sterilising services to lab-ware such as glass and plastic instruments and by preparing high quality tissue culture and bacteriological media required for standard research protocols.

# GENE EXPRESSION PLATFORM

TÂNIA VINAGRE, PhD
Manager

The Gene Expression Platform (GeneX) is an innovative concept of a scientific and technological platform aimed at providing the investigators of the CNP state-of-the-art molecular biology expertise, services and equipment.

The GenEx Platform offers a variety of technical services ranging from assuring the safe use and proper maintenance of shared equipment to the production - including design, synthesis and expression optimisation - of genetic constructs for a number of experimental applications and expression systems.

# HISTOLOGY PLATFORM

ANA SANTOS
Manager

In the Histology Platform, researchers work with highly trained staff members who share their expertise and provide support and services both in experimental design and procedures, according to the researchers' final objectives.

In the Histology Platform, biological samples originating from a range of animal models are processed and analysed with the use of sectioning equipment and histochemical and immunohistochemical techniques. These processed samples are then analysed in the Optical Imaging and Microscopy Platform where different structures, cells and microorganisms are identified.

**Leo Madruga**
Research Technician

# SCIENTIFIC HARDWARE PLATFORM

MATTHIEU PASQUET
Manager

The goal of the Scientific Hardware Development Platform is to design electronic hardware that supports and facilitates research at the CNP. This is an essential service that promotes progress in research on the individual, group and programme level.

The platform provides several classes of service that include general mechanics and electronics consulting and assistance, electronic hardware project development and the use of electronic equipment at various support levels. In addition, the hardware platform works in close contact with the scientific software development platform. This collaboration enables complex project development that encompasses electronic hardware, software (computer or embedded) and mechanic elements, providing researchers with specialised, custom made devices.

# SCIENTIFIC SOFTWARE PLATFORM

JOSÉ CRUZ, PhD
Manager

The goal of the Scientific Software and Development Platform is to provide high-quality software support, while controlling costs and reducing redundant effort. The platform provides three classes of service: 1 - Research, provisioning and support for existing software; 2 - Custom development by contract for individuals and groups; 3- Organisation-wide software and research support technology.

The Platform provides a professional level of service, development and support with the aim of reducing redundant effort, increasing reusability of software solutions, controlling costs and improving the ability of investigators to focus on research questions. The Platform could both utilize PhD students in computer science and engineering as well as contract any extra development services capacity to external clients to reduce costs and integrate the CF with the larger scientific community.

**Ricardo Ribeiro**
Software Developer

# VECTOR PRODUCTION PLATFORM

TATIANA VASSILEVSKAIA, PhD
Manager

The main goal of the Vector Production (VP) Platform is to provide research grade viral vectors to CNP members. Current focus is placed upon:

**VIRUS PRODUCTION AND CHARACTERISATION**
Since September 2011, 15 different AAV batches have been produced upon requests of CNP investigators. Every purified virus batch has been designed in order to meet the requirements of each individual researcher, and characterised by determination of the virus titer (Genome copies per ml, GC/ml) using qRT PCR.

**MANAGEMENT OF THE COMMON CNP VIRUS REPOSITORY**
The CNP virus registry contains 66 AAV lots, which were either acquired from outside sources by CNP groups (41), or produced by the VP platform (25). The data are currently being introduced to the more functional Vector Database, created by the Software platform on request of the VP platform.

Future plans of the VP Platform include optimisation of the quality/cost ratio for AAV production, development of protocols for manipulation, production, and amplification of different neurotropic viral vectors including Herpes simplex type1 virus, CAV-2 and others.

# VIVARIUM

NIKOL TSCHAEPPE
Manager

The Champalimaud Centre for the Unknown is a multidisciplinary centre for translational research in neurosciences and oncology with complementary facilities supporting biomedical activities. The vivarium has dedicated areas to rodents - mus musculus andrattus norvegicus, and zebra fish - danio rerio. The facility also incorporates procedural areas to enhance experimental work in a controlled environment.

The facility has transgenic & rederivation and aquatic units offering specialised services. These areas will continue to evolve on a needs basis. Operational procedures are being established to ensure the requirements of animal welfare and best practices of animal husbandry to promote completive scientific research.

**Rui Costa**
Veterinarian

**Joana Almeida**
Veterinarian

# (VIVARIUM) TRANSGENIC & REDERIVATION UNIT

The chief mission of the Transgenic & Rederivation Unit is to provide support to the research work of cancer and neuroscience investigators. The unit provides services of strain rederivation, cryopreservation, revitalisation and production of transgenic animals. Cryopreservation and Revitalisation of both embryos and sperm are crucial services that, in addition to other functions, provide the safeguarding of valuable mouse lines against loss through infection, disease, or breeding failure, with the possibility to revitalise the line as needed. These services facilitate the process of importing / exporting lines and reduce animal suffering. Rederivation is a generally accepted method for cleaning animals from infectious agents. The rederivation process is extremely important for the transfer of mouse lines produced elsewhere to the specific pathogen free (SPF) vivarium of the Champalimaud Foundation.

The unit also contains an in-house repository of genetically modified animal lines and offers the possibility of sharing equipment and know-how with other institutes with the purpose of promoting cooperation and higher profitability of resources across institutions.

In addition to the services provided, the unit strives to stay at the forefront of new technologies and the development of new tools.

**Rubina Caldeira**
Rederivation Unit

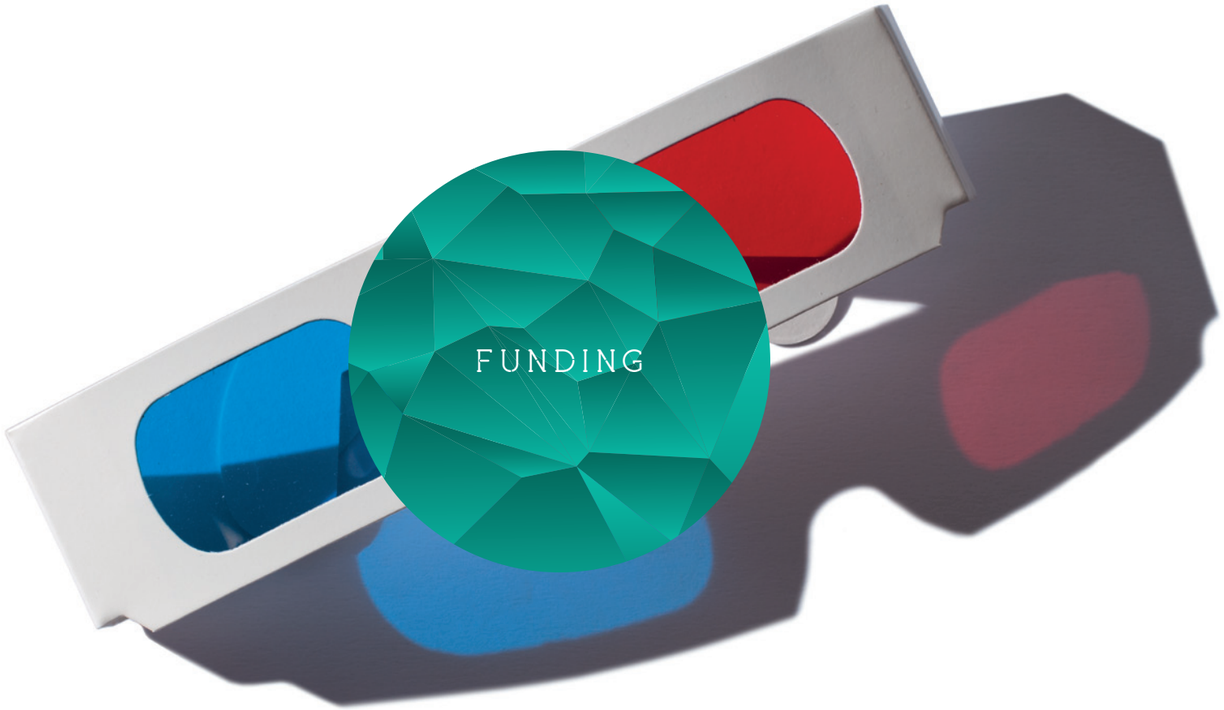
**Joana Almeida**
Transgenic Unit

# (VIVARIUM) AQUATIC UNIT

ANA CERTAL, PhD
Manager

The primary function of the Aquatics Unit is to house, breed and maintain wild-type, mutant and transgenic fish in accordance with the rigorous international health and welfare standards essential for cancer, neuroscience and biomedical research. The unit also provides state-of-the-art research support services including educational support, as advanced courses and workshops dedicated to the fish as a research model are held in the unit regularly.

The main fish species housed in the Aquatics Unit is Zebrafish, which emerged in the last decade as one of the key vertebrate model in biomedical, developmental and behavioural studies. Zebrafish are particularly valuable research tools because they develop rapidly, have transparent bodies and can be easily manipulated genetically and used for large-scale genetic screens. Their organ systems are very similar to those of humans, thus zebrafish mutants and transgenics provide excellent models of human disease.




# TO PROMOTE COLLECTIVE ACHIEVEMENTS

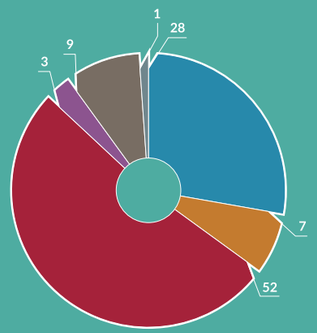
BEYOND THOSE REACHABLE BY INDIVIDUAL SCIENTISTS OR LABORATORY GROUPS

AS OF DECEMBER 2011, **64** ACTIVE GRANTS AND FELLOWSHIPS WERE RUNNING AT THE CNP FOR THE SUM OF NEARLY **7 MILLION EUROS**.

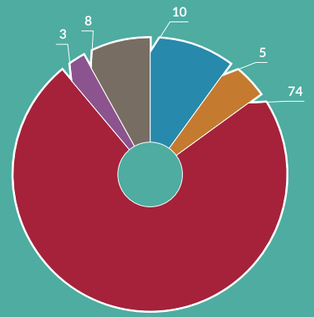
These sums were awarded by the following agencies and organisations:

All Funding (%)

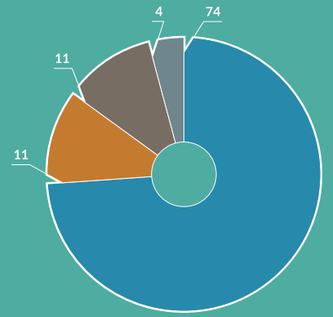
(Research Grants and Fellowships)




**15** Research Grants (%)




**49** Fellowships (%)




- Fundação para a Ciência e a Tecnologia
- International Human Frontier Science Program Organisation
- FP7-Ideas (European Research Council)
- Fundação Bial
- FP7-People (Marie Curie)
- Other (Uehara Memorial Foundation, Wellcome Trust)

## - RESEARCH GRANTS -

### FP7-COOPORATION

European Union

**Copewell**
*A new integrative framework for the study of fish welfare based on the concepts of allostasis, appraisal and coping styles*
2011-2015
AWARDED TO AN INTERNATIONAL GROUP OF INVESTIGATORS, INCLUDING RUI OLIVEIRA.

### FP7-IDEAS (EUROPEAN RESEARCH COUNCIL)

European Union

**ERC Advanced Grant, European Research Council**
*Optogenetic Analysis of Serotonin Function in the Mammalian Brain*
2010-2015
AWARDED TO ZACHARY MAINEN

**ERC Starting Grant, European Research Council**
*Neural mechanisms of action learning and action selection: from intent to habit*
2009-2014
AWARDED TO RUI COSTA

### FUNDAÇÃO BIAL

Portugal

**Bial Science Research Grant**
*Dopaminergic regulation of dietary learning in humans and rodents*
2011-2014
AWARDED TO RUI COSTA

**Bial Science Research Grant**
*Investigating the function of synaptic competition in memory formation and mental retardation*
2011-2014
AWARDED TO INBAL ISRAELY

**Bial Science Research Grant**
*Neuronal mechanisms underlying sex hormone-dependent switching of sexual receptivity*
2011-2013
AWARDED TO SUSANA LIMA

**Bial Science Research Grant**
*Neural Mechanisms of Social transmission of fear*
2011-2014
AWARDED TO MARTA MOITA

**Bial Science Research Grant**
*Elucidating the molecular mechanisms mediating feeding behaviour*
2011-2013
AWARDED TO CARLOS RIBEIRO

## FUNDAÇÃO PARA A CIÊNCIA E A TECNOLOGIA (FCT)
Portugal

**Research Project Grant**
*Dissecção das bases moleculares e dos circuitos envolvidos na intenção*
2011-2014
AWARDED TO RUI COSTA

**Research Project Grant**
*Unraveling the Neuronal Circuits Underlying Female Receptivity*
2010-2013
AWARDED TO MARIA LUÍSA VASCONCELOS

**Research Project Grant**
*From genes to behaviour:*
*dissecting the basis for CO2 response across Drosophilids*
2010-2013
AWARDED TO MARIA LUÍSA VASCONCELOS

**Research Project Grant**
*Alternative reproductive tactics in teleost fish:*
*the peacock blenny (Salaria pavo) as a study model*
2008-2011
AWARDED TO RUI F OLIVEIRA

**Research Project Grant**
*Neuroendocrine control of reproductive behaviour in the Mozambique tilapia: mechanisms and effects of the social environment*
2008-2011
AWARDED TO RUI F OLIVEIRA

## INTERNATIONAL HUMAN FRONTIER SCIENCE PROGRAM ORGANIZATION (HFSPO)
International

**Human Frontier Science Program**
*Olfactory objects and decisions: From psychophysics to neural computation*
2010-2013
AWARDED TO ZACHARY MAINEN, ALEX POUGET AND MATTHIEU LUIS

## FP7-PEOPLE (MARIE CURIE)
European Union

**Marie Curie International Reintegration Grant**
*Neural mechanisms of action learning in mouse models*
2009-2013
AWARDED TO RUI COSTA

**Marie Curie International Reintegration Grant**
*Neural mechanisms underlying mate preference and selection in mice*
2009-2013
AWARDED TO SUSANA LIMA

**Marie Curie International Reintegration Grant**
*Innate Neural Circuits*
2009-2013
AWARDED TO MARIA LUÍSA VASCONCELOS

**Marie Curie Intra-European Fellowship for Career Development**
2011-2015
AWARDED TO MICHAEL ORGER

# - FELLOWSHIPS -

## FP7-PEOPLE (MARIE CURIE)
European Union

**Marie Curie Intra-European Fellowship for Career Development**
2010-2012
AWARDED TO MAGOR LORINCZ

**Marie Curie Intra-European Fellowship for Career Development**
2009-2011
AWARDED TO LÉA ZINCK

## FUNDAÇÃO PARA A CIÊNCIA E A TECNOLOGIA (FCT)
Portugal

**Postdoctoral Fellowship**
2010-2013
AWARDED TO HOPE JOHNSON

**Postdoctoral Fellowship**
2010-2013
AWARDED TO MASAYOSHI MURAKAMI

**Postdoctoral Fellowship**
2008-2012
AWARDED TO CRISTINA AFONSO

**Postdoctoral Fellowship**
2011-2013
AWARDED TO FATUEL TECUAPELTA

**Investigation Fellowship**
2011
AWARDED TO JOÃO AFONSO

**Investigation Fellowship**
2011
AWARDED TO SILVANA ARAÚJO

**Investigation Fellowship**
2011
AWARDED TO JOAQUIM JACOB

**Investigation Fellowship**
2011
AWARDED TO RICARDO SILVA ZACARIAS

**Investigation Fellowship**
2011
AWARDED TO JENS BIERFELD

**Investigation Fellowship**
2011
AWARDED TO JACQUES BOURG

**Investigation Fellowship**
2011
AWARDED TO ROBERTO MEDINA

**Investigation Fellowship**
2011
AWARDED TO ANDRÉ LUZARDO

**Investigation Fellowship**
2011
AWARDED TO SOFIA SOARES

**Investigation Fellowship**
2011
AWARDED TO LUÍS MOREIRA

**PhD Fellowship**
2011-2014
AWARDED TO GONÇALO LOPES

**PhD Fellowship**
2011-2014
AWARDED TO GUSTAVO MELLO

**PhD Fellowship**
2011-2014
AWARDED TO SIMONE LACKNER

**PhD Fellowship**
2011-2014
AWARDED TO TIAGO MARQUES

**PhD Fellowship**
2011-2014
AWARDED TO RAIMUNDO LEONG

**PhD Fellowship**
2011-2014
AWARDED TO PATRÍCIA RACHINAS-LOPES

**PhD Fellowship**
2010-2013
AWARDED TO NICCOLÒ BONACCHI

**PhD Fellowship**
2010-2013
AWARDED TO ANDREIA CRUZ

**PhD Fellowship**
2010-2013
AWARDED TO ELIZABETH RICKENBACHER

**PhD Fellowship**
2010-2013
AWARDED TO THIAGO GOUVÊA

**PhD Fellowship**
2010-2013
AWARDED TO ALI ARGUNSAH

**PhD Fellowship**
2010-2013
AWARDED TO ANNA HOBBISS

**PhD Fellowship**
2010-2013
AWARDED TO SEVINÇ MUTLU

**PhD Fellowship**
2010-2013
AWARDED TO SUSANA VALENTE

**PhD Fellowship**
2010-2013
AWARDED TO ANA MACHADO

**PhD Fellowship**
2010-2013
AWARDED TO VERÓNICA CORRALES

**PhD Fellowship**
2009-2013
AWARDED TO ANA RITA FONSECA

**PhD Fellowship**
2009-2013
AWARDED TO ANDRÉ MENDONÇA

**PhD Fellowship**
2009-2013
AWARDED TO ANA PEREIRA

**PhD Fellowship**
2009-2013
AWARDED TO SCOTT RENNIE

**PhD Fellowship**
2009-2013
AWARDED TO FERNANDO SANTOS

**PhD Fellowship**
2009-2013
AWARDED TO ANA MAFALDA VICENTE

**PhD Fellowship**
2009-2013
AWARDED TO DENNIS HERRMANN

**PhD Fellowship**
2009-2013
AWARDED TO JOÃO MARQUES

**PhD Fellowship**
2008-2012
AWARDED TO PATRÍCIA CORREIA

**PhD Fellowship**
2008-2012
AWARDED TO MARIA INÊS VICENTE

**PhD Fellowship**
2008-2012
AWARDED TO SARA MATIAS

**PhD Fellowship**
2008-2012
AWARDED TO PEDRO FERREIRA

**PhD Fellowship**
2008-2011
AWARDED TO RUI AZEVEDO

## INTERNATIONAL HUMAN FRONTIER SCIENCE PROGRAM ORGANISATION (HFSPO)

International

**HFSP Long Term Fellowship**

*Serotonergic modulation of olfactory information processing*

2011-2014

AWARDED TO ERAN LOTTEM

**HFSP Long Term Fellowship**

*Cell-type specific features of identified serotonergic neurons in the raphe nucle in behaving rats*

2011-2014

AWARDED TO MAGOR LORINCZ

## UEHARA MEMORIAL FOUNDATION

Japan

**Research Fellowship**

2011

AWARDED TO KENSAKU NOMOTO

## WELLCOME TRUST

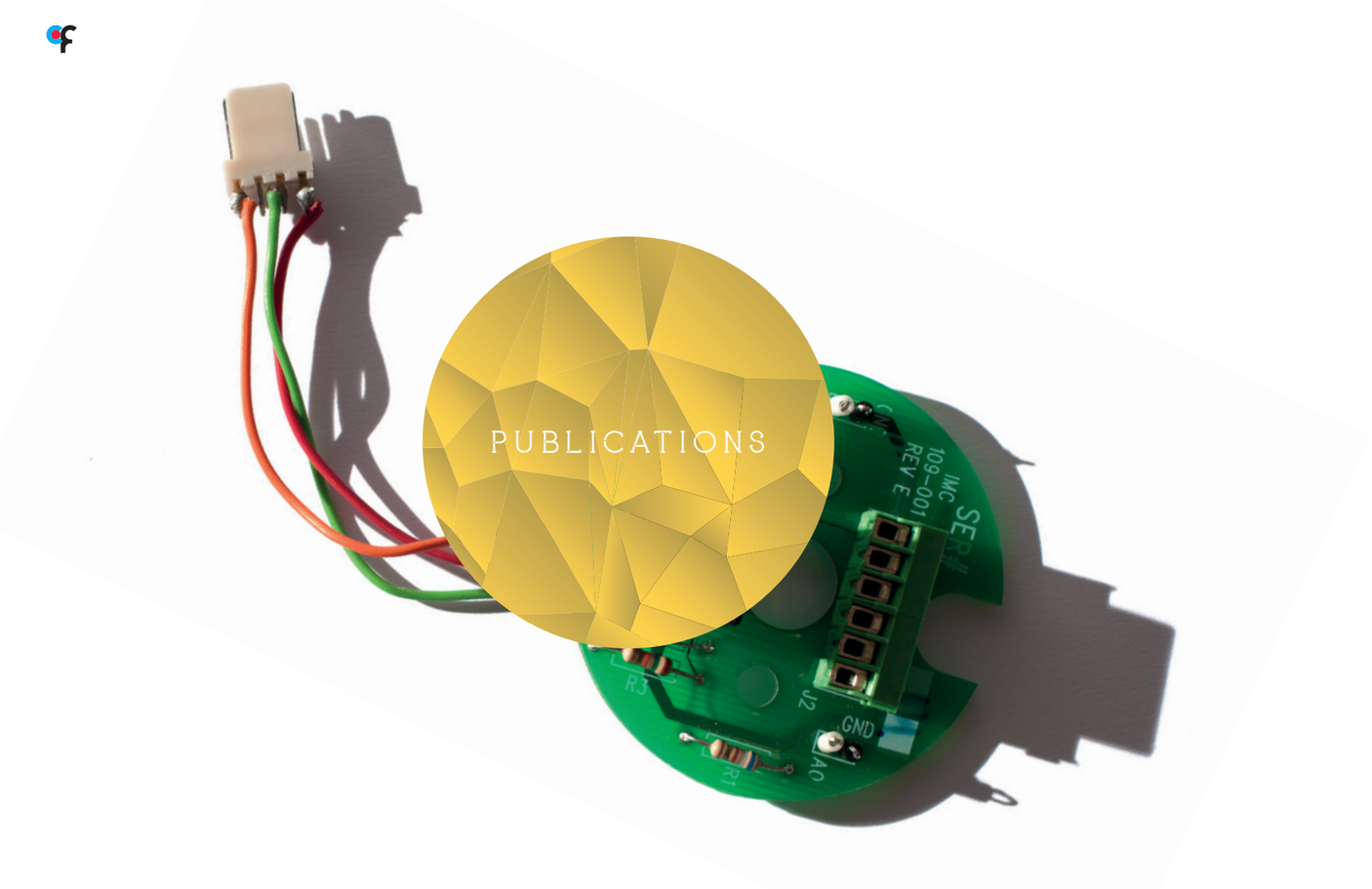
UK

**Postdoctoral Fellowship**

*The neural basis of goal-directed behaviour*

2011-2015

AWARDED TO THOMAS AKAM

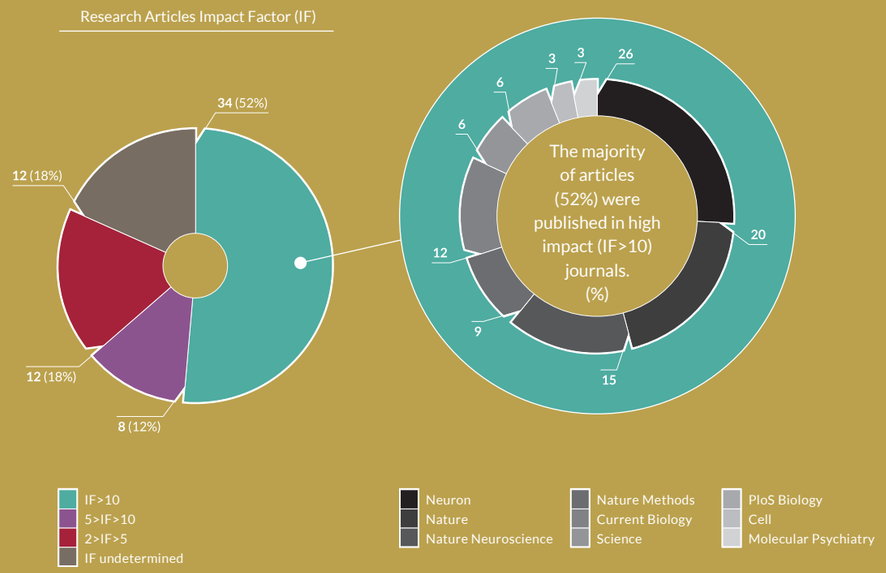



# TO MAXIMISE COOPERATION

WITHOUT SACRIFICING INDEPENDENCE AND DIVERSITY OF THOUGHT

A TOTAL OF **66** RESEARCH ARTICLES WERE PUBLISHED BY CNP INVESTIGATORS DURING **2007-2012**.

The Impact Factor (IF) is used as an estimate of the effect a research article may have on the scientific community based on how often articles in the journal where the article was published are cited.




## PEER-REVIEWED RESEARCH ARTICLES


Atsak P, Orre M, Bakker P, Cerliani L, Roozendaal B, Gazzola V, Moita M, Keysers C. (2011). *Experience Modulates Vicarious Freezing in Rats: A Model for Empathy*. PLoS ONE 6(7):e21855.

Bianco IH, Kampff AR, Engert F (2011) *Prey capture behaviour evoked by simple visual stimuli in larval zebrafish*. Front Sys Neurosci 5:101.

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Geiger JA*, Carvalho L*, Campos I, Santos AC, Jacinto A (2011). *Hole-in-one mutant phenotypes link EGFR/ERK signaling to epithelial tissue repair in Drosophila.* PLoS One 6 (11):e28349.
(*authors contributed equally).

Govindarajan A*, Israely *, Huang SY, Tonegawa S (2011) *The dendritic branch is the preferred integrative unit for protein synthesis-dependent LTP.* Neuron. 69:132-146.
(*authors contributed equally).

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Itskov PM, Vinnik E, Diamond ME (2011) *Hippocampal representation of touch-guided behaviour in rats: persistent and independent traces of stimulus and reward location.* PLoS One. 6 (1):e16462.

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Luan JB, Li JM, Varela N, Wang YL, Li FF, Bao YY, Zhang CX, Liu SS, Wang XW (2011). *Global analysis of the transcriptional response of whitefly to Tomato yellow leaf curl China virus reveals their relationship of coevolved adaptations.* J Virol :3330-3340.

Mao T, Kusefoglu D, Hooks BM, Huber D, Petreanu L, Svoboda K (2011) *Long-range neuronal circuits underlying the interaction between sensory and motor cortex.* Neuron 72(1):111-23.

Soares MC, Oliveira RF, Ros AF, Grutter AS, Bshary R (2011) *Tactile stimulation lowers stress in fish.* Nat Commun 2:534.

Varela N, Avilla J, Anton S, Gemeno C (2011) *Synergism of pheromone and host plant volatile blends in the attraction of Grapholita molesta males.* Entomologia Experimentalis et Applicata 141 (2):114-122.

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Brendel W, Romo R, Machens CK (2011) *Demixed Principal Component Analysis.* Advances in Neural Information Processing Systems 24.

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Costa RM (2011). *A selectionist account of de novo action learning.* Curr Opin Neurobiol 21(4):579-86.

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## COMMENTS

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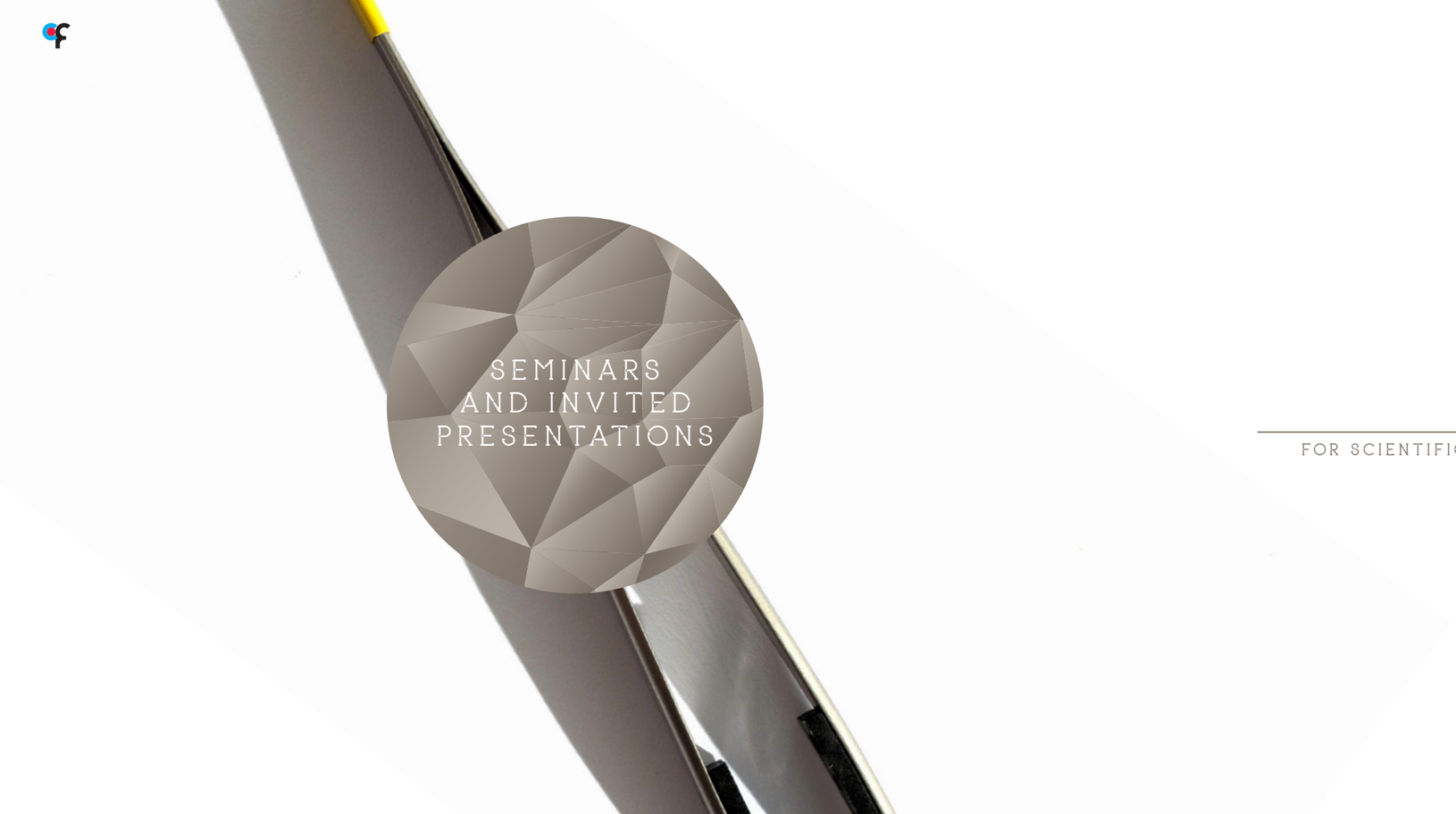



# TO BE A HUB

FOR SCIENTIFIC INTERACTION, ENGAGING OUR PEERS IN PRODUCTIVE EXCHANGE
RATHER THAN COMPETITION

## CNP SEMINARS 2011

| January 2011 |

**Noam Sobel**
Thu 13/01/2011
Department of Neurobiology, Weizmann Institute of Science, Israel
*Predicting odour perception and neural activity from odourant structure*

| February 2011 |

**Steve Kushner**
Thu 10/02/2011
Department of Psychiatry, University Medical Centre Rotterdam, Rotterdam, The Netherlands
*Selection of neuronal ensembles during fear learning*

| March 2011 |

**Jose Carmena**
Thu 17/03/2011
Helen Wills Neuroscience Institute, and Dept. of Electrical Engineering & Computer Sciences, University of California, Berkeley, USA
*Neural adaptations to a brain-machine interface*

| April 2011 |

**Mark E Walton**
Thu 14/04/2011
Department of Experimental Psychology, University of Oxford, UK
*Is it really worth it? Cost-benefit analyses within fronto-striatal-monoaminergic circuits*

**Gilles Laurent**
Thu 28/04/2011
Max Planck Institute for Brain Research, Frankfurt, Germany
*Adaptive regulation of activity in an olfactory system*

| May 2011 |

**Paul Glimcher**
Thu 05/05/2011
Centre for Neural Science, New York University, USA
*The Neuroeconomic Analysis of Decision-Making:*
*The Emerging 'Standard Model'*

**Jane Hurst**
Thu 12/05/2011
Institute of Integrative Biology, University of Liverpool, UK
*A walk on the wild side: what can we learn about scent communication from studies of wild mice?*

**Peter Mandik**
Thu 19/05/2011
Department of Philosophy, William Paterson University, Wayne, US
*Does the neuroscience of consciousness need to care about qualia?*

**Regina Sullivan**
Wed 25/05/2011
Emotional Brain Institute, Nathan Kline Institute and New York University School of Medicine, US
*Neurobiology of infant attachment: Lessons from an animal model*

| June 2011 |

**Ingo Willuhn**
Thu 02/06/2011
Departments of Psychiatry & Behavioural Sciences and Pharmacology, University of Washington, USA
*Progression of phasic dopamine signaling in limbic and sensorimotor regions of the striatum in a rodent model of drug addiction*

**Tiago Monteiro**
Fri 03/06/2011
The Behavioural Ecology Research Group, University of Oxford, UK
*Three different approaches to the study of decision-making, and their implementation in the European starling*

**Hanan Shteingart**
Mon 06/06/2011
Loewenstein Lab, The Hebrew University of Jerusalem, Israel
*Primacy in operant conditioning*

**Edward Kravitz**
Thu 09/06/2011
George Packer Berry Professor of Neurobiology, Harvard Medical School
*Genetic manipulations in the fruit fly fight club: love and war in a single gene and other stories*

| July 2011 |

**Yonatan Loewenstein**
Thu 07/07/2011
Department of Neurobiology, The Hebrew University, Israel
*The computational principles and neural mechanisms underlying choice preference*

| August 2011 |

**Artemy Kolchinsky**
Fri 05/08/2011
Centre for Complex Networks and Systems, Indiana University, USA
(I) *Prediction and Modularity in Dynamical Systems*
(II) *Spatial organisation of EEG cross-frequency coupling in a perceptual task*


Urban Legends
Princess
Organized
Pretty in pink
Teacher pleaser
Caring and kind to others!

| September 2011 |

**Tim Behrens**
Thu 01/09/2011
University of Oxford , UK
*Ventromedial prefrontal cortex and orbitofrontal cortex contributions to reward guided behaviour*

**Nicola Clayton**
Fri 02/09/2011
University of Cambridge, UK
*The Evolution of Shopping Lists*

**Andreas Schaefer**
Thu 08/09/2011
Max Planck Institute for Medical Research, Heidelberg, Germany
*Mechanisms of sensory processing: Inhibition and odour discrimination in mice*

**Frédéric Levy**
Thu 29/09/2011
Division Animal Physiology and Livestock Systems, PHASE, France
*Brain mechanisms involved in maternal motivation and recognition of the young in sheep*

| October 2011 |

**James Goodson**
Tue 11/10/2011
Centre for the Integrative Study of the Animal Behaviour, Indiana University, USA
*Neuroendocrine Mechanisms of Social Diversity in Birds*

**Edward Boyden**
Thu 27/10/2011
Synthetic Neurobiology Group, MIT, USA
*Optogenetics, And Other Neural Circuit Analysis Tools*

| November 2011 |

**Thomas Knopfel**
Thu 03/11/2011
RIKEN Brain Science Institute, Japan
*Enhanced genetically-encoded probes for voltage imaging*

**Julia Sliwa**
Fri 04/11/2011
CNRS, Centre de Neuroscience Cognitive, Lyon, France
*Rhesus monkeys' behavioural and neuronal responses to voices and faces of known individuals*

**Deborah Gordon**
Wed 23/11/2011
Department of Biology, Stanford University, USA
*The regulation of foraging activity in harvester ants*

| December 2011 |

**Terry Sejnowski**
Wed 07/12/2011
Computational Neurobiology Laboratory, Salk Lake Institute, USA
*Suspicious Coincidences in the Brain*

## INVITED PRESENTATIONS AT INTERNATIONAL MEETINGS AND INSTITUTIONS

**Megan Carey**
23 Mar 2011
LISBON AREA NEUROSCIENCE MEETING
*Endocannabinoid regulation of synaptic plasticity in the cerebellum*
Instituto de Medicina Molecular, Lisbon, Portugal.

27 May 2011
SOCIETY FOR PORTUGUESE NEUROSCIENCE MEETING
*The role of endocannabinoids in cerebellar plasticity and learning*
Instituto de Medicina Molecular, Lisbon, Portugal.

7 Nov 2011
EARLY CAREER SCIENTIST SYMPOSIUM
*The cerebellar circuit: from synapse to behaviour*
Howard Hughes Medical Institute International, Ashburn, VA, USA

**Rui M. Costa**
2011
SESSION CHAIR, PORTUGUESE SOCIETY FOR NEUROSCIENCE MEETING
*Generating and shaping novel actions repertoires*
Lisbon, Portugal

2011
FIRST SONGBIRD SATELLITE SYMPOSIUM
*Generating and shaping novel actions repertoires*
Washington, USA

2011
CRG
*Generating and shaping novel actions repertoires*
Barcelona, Spain

2011
JANELIA CONFERENCE
'THE NEURAL BASIS OF MOTOR CONTROL'
*Generating and shaping novel actions repertoires*
Ashburn, USA

2011
CRG
*Generating and shaping novel actions repertoires*
Barcelona, Spain

2011
RIKEN BSI
*Generating and shaping novel actions repertoires*
Barcelona, Wako, Japan

2011
DEVELOPMENT OF BRAIN AND MIND SYMPOSIUM
*Generating and shaping novel actions repertoires*
Kobe, Japan

2011
KEYNOTE
*Generating and shaping novel actions repertoires*
Portuguese Society for Educational Sciences, Guarda, Portugal

2011
ISPA
*Generating and shaping novel actions repertoires*
Lisbon, Portugal

2011
IMP
*Generating and shaping novel actions repertoires*
Vienna, Austria

2011
100TH ANNIVERSARY UNIVERSITY OF LISBON
*Generating and shaping novel actions repertoires*
Lisbon, Portugal

2011
*Generating and shaping novel actions repertoires*
College de France, Paris, France

2011
CSHL
*Generating and shaping novel actions repertoires*
Cold Spring Harbor, USA

2011
103RD TITISEE CONFERENCE
*Generating and shaping novel actions repertoires*
Titisee, Germany

2011
*Generating and shaping novel actions repertoires*
Janelia Farm Research Campus, Ashburn, USA

FMI, Basel, Switzerland
2011. Generating and shaping novel actions repertoires

**Inbal Israely**

13 Apr 2011
COLD SPRING HARBOR LABORATORY MEETING
*The dendritic branch as an integrative unit for protein synthesis dependent synaptic plasticity. Synapse: From Molecules to Circuits & Behaviour*
CSHL, NY, USA

**Christian Machens**

Jan 2011
*Disentangling the functional connectivity between optic-flow processing neurons*
University Tubingen, Germany

Feb 2011
WORKSHOP ON BIOINFORMATICS
*Information theory in the neurosciences*
Humboldt-University Berlin, Germany

Jun 2011
*Dynamics of an oculomotor integrator revealed by instantaneous optogenetic perturbations*
Institute for Molecular Pathology, Vienna, Austria

**Zach Mainen**

3 Apr 2011
*Task-dependent strategies for decision-making under uncertainty*
Columbia University, New York, USA

26 May 2011
SOCIÉTÉ DES NEUROSCIENCES 10E COLLOQUE
*Neural circuits for odour-guided decisions in the rat*
Marseille, France

19 Jun 2011
CAUSAL NEUROSCIENCE
*Targeting the serotonin system using optogenetics: Towards a post-pharmacological view*
FENS-IBRO-SfN School, Bertinoro, Italy

8 Jul 2011
WHAT MAKES US HUMAN? 2011 GABBA ANNUAL SYMPOSIUM
*Knowing what you know: Models and mechanisms for judgments of confidence*
Porto, Portugal

21 Oct 2011
"GENES, CIRCUITS, BEHAVIOUR" SYMPOSIUM
*Neural mechanisms for decision making in the rat: Uncertainty in brain and behaviour*
RIKEN Brain Science Institute, Tokyo, Japan

**Marta Moita**

20-23 Mar 2011
*Producing and Perceiving Complex Acoustic Signals: Songbirds and Mice as Model Systems Conference*
Janelia Farm, USA

23-27 Mar 2011
103RD INTERNATIONAL TITISEE CONFERENCE
*"Genetic analysis of neural circuits"*
Titisee, Germany


Apoiar sobre a barra para abrir
Apoiar sobre a barra para abrir

8-9 Dec 2011
*"Cutting edge in synapse research"*
NAIST, Japan

15 Dec 2011
RIKEN Brain Science Institute, Japan

4 Jan 2011
Tokyo University, Japan

**Joseph Paton**
2011
*A representation of time for learning in the striatum of behaving rats*
Paris, France

2011
PARALLEL DISTRIBUTED PROCESSING CONFERENCE
*A representation of time for learning in the striatum of behaving rats*
Princeton, NJ, USA

2011
DECISION MAKING IN NEURAL CIRCUITS CONFERENCE
*A representation of time for learning in the striatum of behaving rats*
Ashburn, VA, USA

2011
*A representation of time for learning in the striatum of behaving rats*
MIT, Boston, MA, USA

**Leoplodo Petreanu**
30 Nov 2011
*The structure and function of long-range cortical connections*
Oxford University

2 Dec 2011
*The structure and function of sensorimotor circuits*
Cardiff University, UK

**Alfonso Renart**
16 Jun 2011
*Temporal Correlations in Cortical Circuits*
Institut d'investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain

04 Abr 2011
*Temporal correlations in recurrent neural networks with balanced excitation and inhibition*
Banbury Centre, Cold Spring Harbor Laboratory, NY, USA

**Carlos Ribeiro**
1 Apr 2011
*The neuronal basis of nutrient choices*
Champalimaud Centre for the Unknwon, Lisbon, Portugal

26 April 2011
*The Molecular and Neuronal Control of Nutrient Choice in Drosophila*
ICVS, University of Minho, Braga, Portugal

10 May 2011
*The neuronal basis of nutrient choices*
IGC, Portugal

27 May 2011
XII MEETING OF THE PORTUGUESE SOCIETY FOR NEUROSCIENCE
*The Molecular and Neuronal Control of Nutrient Choice in Drosophila*
Lisbon, Portugal

22 Jun 2011
*The Molecular and Neuronal Control of Nutrient Choice in Drosophila*
Instituto de Medicina Molecular, University of Lisbon, Lisbon, Portugal

30 June 2011
E3 FORUM, EDUCATION, EMPLOYMENT, ENTRPRENEURSHIP, MIT PORTUGAL PROGRAMME
*Where did I go and how did I get there?*
Lisbon, Portugal

2 Sep 2011
THE FIRST JUNIOR EUROPEAN *DROSOPHILA* INVESTIGATOR MEETING
*The Behaviour and metabolism laboratory*
Leysin, Switzerland

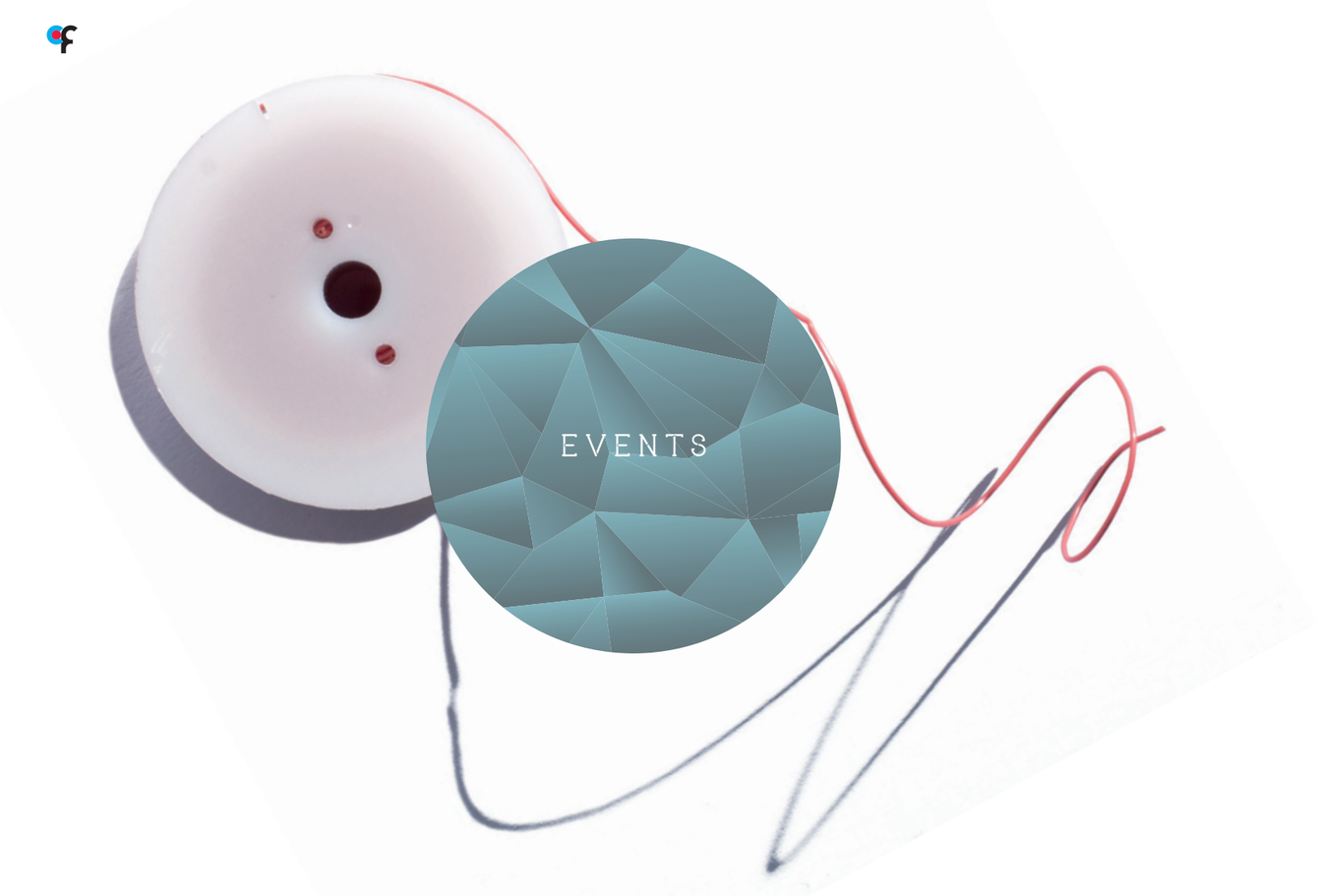
22 Sep 2011
22ND EUROPEAN *DROSOPHILA* RESEARCH CONFERENCE
*The Molecular and Neuronal Control of Nutrient Choice in Drosophila*
Lisbon, Portugal

1 Dec 2011
*The Molecular and Neuronal Control of Nutrient Choice in Drosophila*
Department of Zoology, Cambridge University, Cambridge, UK

**Maria Luísa Vasconcelos**
Oct 2011
*Search for neuronal circuits of innate responses in the fruit fly*
National Intitute of Medical Research, London, UK

**Wieland Brendel**
Oct 2011
MULTI-ELECTRODE WORKSHOP
*Demixed Principal Component Analysis*
INSERM, Lyon, France

**Ricardo Benjamim Leitão Gonçalves**
16 Nov 2011
*Metabolism and nutritional decision, present and future of a model*
ISAVE (Instituto Superior de Saúde do Alto Ave), Póvoa de Lanhoso, Portugal.




# TO FOSTER GOOD LIFE QUALITY

RECOGNISING THAT WELL-BEING AND PRODUCTIVITY GO HAND IN HAND

## CHAMPALIMAUD NEUROSCIENCE SYMPOSIUM

21-24 September, 2011

**Organisers:**
Megan Carey, Marta Moita, Zach Mainen.

**Sponsors:**
Blackrock Microsystems, Aralab, Merck Millipore, TSE Systems, Leica Microsystems, Tecniplast, Clever Sys, Fisher Scientific, Bayer, Lilico Biotechnology, Ultragene.

Surrounded by the spectacular views of the river Tagus and the distinct architecture of the Champalimaud Centre for the Unknown, hundreds of neuroscientists from across the world gathered on a cool Sunday evening in September. Among the clinks of wine glasses of old and new acquaintances meeting, the intricate notes of jazz music and the vibrant hues of sunset were setting the tone for the wide scope experience of the inaugural Champalimaud Neuroscience Symposium. This meeting exemplified the broad scientific interests of the CNP, featuring lectures by leading neuroscientists whose diverse specialties range from topics such as visual navigation in *Drosophila* to the neural mechanism of decision making.


*Over **400** scientists attended the symposium which included **27** distinguished speakers and two poster sessions.*


Fundação
Champalimaud
CHAMPALIMAUD
NEUROSCIENCE
SYMPOSIUM

**List of Speakers:**

Antonio Damasio, University of Southern California
*Feeling and sentience: Taking stock*

Haim Sompolinsky, Hebrew University
*Neural codes: The curses and blessings of high dimensions*

Gyorgy Buzsaki, Rutgers University
*Neural syntax: segmentation of information in the hippocampus*

Hannah Monyer, Heidelberg University
*GABAergic interneurons and their role in neuronal synchronization, learning and memory*

Judith Hirsch, University of Southern California
*Inhibitory circuits for visual processing in thalamus*

Hollis T. Cline, The Scripps Research Institute
*The balance of inhibition to excitation regulates visual responses and behaviour in vivo*

Sten Grillner, Karolinska Institute
*The computational logics of networks in motion - from ion channels to behaviour*

Silvia Arber, Biozentrum and Friedrich Miescher Institute
*Organisational principles of antagonistic motor circuits*

Tom Jessell, Howard Hughes Medical Institute, Columbia University
*Motor circuits and the sense of place*

Detlev Arendt, European Molecular Biology Laboratory
*Duplication and divergence of neural circuits in bilaterian brain evolution*

Michael Dickinson, University of Washington
*Visual navigation in Drosophila*

Daniel Wolpert, University of Cambridge
*Probabilistic models of human sensorimotor control*

Leslie B. Vosshall, The Rockefeller University
*Human sweat and insect repellents: the molecular biology of mosquito olfaction*

Ulrike Heberlein, University of California, San Francisco
*Social experiences affect ethanol intake in Drosophila through Neuropeptide F*

Lisa Stowers, The Scripps Research Institute
*Specialised odours that generate innate behaviour*

Takao Hensch, Harvard University
*Loss of cross-modal cortical activity by vision*

Yang Dan, University of California, Berkeley
*Dissection of neocortical microcircuit*

James J. DiCarlo, Massachusetts Institute of Technology
*What neuronal algorithms underlie visual object recognition?*

Michael N. Shadlen, University of Washington Medical School
*Believing and time: a neural mechanism for decision making*

Kelsey Martin, University of California, Los Angeles
*Synapse to nuclear transport of a transcriptional regulator during neuronal plasticity*

Alcino J. Silva, University of California, Los Angeles
*Molecular and cellular mechanisms of memory allocation in neuronal networks*

Carla J. Shatz, Stanford University
*Releasing the brake on synaptic plasticity*

Larry Abbott, Columbia University
*Functional consequences of different forms of spike-timing dependent plasticity*

Atsushi Miyawaki, RIKEN Brain Science Institute
*New fluorescent probes and new perspectives in bioscience*

Michael Hausser, University College London
*Dendritic computation*

Carl Petersen, École Polytechnique Fédérale de Lausanne
*Synaptic mechanisms of sensory perception*

Tobias Bonhoeffer, Max-Planck-Institute of Neurobiology
*How activity changes synapses in the mammalian brain*

*Join us for next year's symposium!*
***25-28 September, 2013!***

## 2011 CNP ANNUAL RETREAT

Each spring, the busy corridors of the CNP empty, as all CNP members travel together to a unique location where they dedicate five days to getting reacquainted with each other's research and to simply having a good time together. Even though the retreat boasts a busy schedule of talks, poster sessions and discussions, along-side these scientific events run group activities, parties and quiet pool-side relaxation. This balance between scientific and social interaction, lays the foundation to the collaborative spirit, solidarity and scientific excellence that are the core of the CNP.

A different location is chosen for CNP retreats each year. In 2011, the retreat was held at the serine Convento de São Paulo in the Aldeia da Serra region of Portugal. This remote and beautiful convent offered an ideal setting for introspection and reflection on the on-goings of the CNP.


From the introduction to the 2011 CNP retreat:
*"This is a pause in our work, but an important pause.*
*It is time to take stock of where we've been and where we are going. It is also a time to cement a special solidarity with our fellow "voyagers" in the CNP.*
*For in fact, we do share a kind of ship and we will count on each other to make our quest a successful one.*
*So this is a special time for both work and for play."*


# TO CONTINUOUSLY RENEW THE ORGANISATION ITSELF

NURTURING NEW SCIENTIFIC APPROACHES AND ORGANISATIONAL STRUCTURES

## INTERNATIONAL NEUROSCIENCE DOCTORATE PROGRAMME

**Programme Director:** Zach Mainen
**Programme Coordinator:** Alfonso Renart
**Administrative Assistant:** Alexandra Piedade

"Prism Goggles! Fly Tracking System! Snail Car!" Exclaim graduate students – Simone Lackner, Gonçalo Lopes, Tiago Marques and Gustavo Mello – when asked about their first year at the International Neuroscience Doctoral Programme (INDP). At the INDP, this opening year is wholly dedicated to providing students with a broad base of knowledge through formal lectures, critical reading of articles and hands-on experimentation. Students are taught how to approach research on all the levels which current neuroscience work requires. This includes understanding the equipment they use – students build computers, scanning microscopes, and sophisticated tracking systems, working with different model systems – *Drosophila*, zebrafish and human, performing data analysis – learning maths, computation and programming; all with the end goal of learning the basics of research – from hypothesis formulation, to experimental design and execution, to data analysis.

In order to accomplish this comprehensive educational endeavour, classes are organised into one or several week-long modules. Each module is dedicated to a different topic and is taught by field-experts, both in-house and international guest researchers. Module topics vary in focus and include, among others, cellular physiology, circuits, plasticity, experimental and computational approaches and techniques, molecular biology and genetic models. At the end of the year, students are required to write, in coordination with their advisor and thesis committee, a research proposal for their PhD work which they undertake in the following three years.

Despite their busy course and thesis work, INDP students are highly involved in the life of the CNP and organize many activities and events:

***Ar Event Series***
These are elaborate outreach events targeted at a general audience where scientific and science-related topics such as brain-machine interface and creativity are presented in original ways by a range of professionals including scientists, artists and inventors.

***PhD Student Seminar Series***
Students invite selected international researchers to present their work to the CNP community and visit CNP labs and faculty. In addition, speakers spend one full morning discussing significant issues in Neuroscience with students in an informal 'Nano-Course'.

***Annual Meeting for CNP***
*and Instituto Gulbenkian de Ciencia (IGC) Students*
This is a small internal annual meeting organised by PhD students of IGC and CNP. The major goal of this meeting is to create an open, inspiring and comfortable atmosphere for PhD students to discuss their research among peers.

*Student and Postdoc Joint Meetings with Foreign Institutions*
This is another initiative that aims to facilitate discussion among peers and interaction with other institutions. The first meeting, held at the Champalimaud Centre for the Unknown, joined students and post-doctoral fellows of the CNP and Centre de Recherche de l'Institut du Cerveau et de la Moelle Épinière (CRICM) of Paris, France. A second CNP-CRICM meeting is scheduled to be held at CRICM.

*Games, Interaction and Robotics (GIR) Club*
Here students experiment with interactive systems, figure out how to integrate interactive technology into experiments, or simply design cool games, simulations and reactive displays.

*Student Task Force*
This annually elected task force meets monthly to discuss student interests within the CNP, organisation of activities and general issues or problems.


KOPF INSTRUMENTS

## INDP STUDENTS

| 2011 Students |

**André Luzardo**
*BA, Psychobiology*
Universidade de São Paulo, Ribeirao Preto, Brazil

**Jacques Bourg**
*BS, Electrical Engineering*
INSA de Lyon , Institut National des Sciences Appliquées de Lyon, France

**Jens Bierfeld**
*Master in Biology*
University of Konstanz, Konstanz, Germany

**João Afonso**
Master in Clinical Psychology
Instituto Superior de Psicologia Aplicada, Lisboa, Portugal

**Joaquim Jacob**
*Master in Neuroscience*
Faculty of Medicine of the University of Lisbon, Lisbon, Portugal

**Ricardo Zacarias**
*Master in Evolutionary and Developmental Biology*
Faculdade de Ciências da Universidade de Lisboa, Lisbon, Portugal

**Roberto Medina**
*BA, Mathematics*
University of Illinois at Urbana-Champaign, Champaign, USA

**Silvana Araújo**
*Master in Psychopharmacology*
University of Nottingham, Nottingham, United Kingdom

**Sofia Soares**
*Master in Human Biology and Environment*
Faculty of Science - University of Lisbon, Lisbon, Portugal

**Luis Moreira**
*Master in Ecology*
University of Coimbra, Coimbra, Portugal

| 2010 Students |

**Bruno Miranda**
*The role of the entorhinal cortex in instrumental conditioning*
Laboratory of Steven W. Kennerley, University College of London, UK

**Ana Carolina de Sousa**
*Ant interaction networks: Task allocation in colonies in need of a new nest*
Laboratory of N. Franks, University of Bristol, UK

**Gustavo Mello**
*Influence of cortical input on time dependent striatal activity in rodents during interval timing*
Laboratory of J. Paton, CNP

**Gonçalo Lopes**
*Dissecting the Neural Basis of the Insect Path Integrator: A Comparative Approach*
Laboratories of J. Paton & A. Kampff, CNP

**Ivo Marcelo**
*Characterisation of memory trace networks in the lateral amygdala during consolidation*
Laboratory of S. Kushner, Erasmus MC: University Medical Centre Rotterdam, The Netherlands

**Raimundo Coelho Leong**
*Flexible decision-making in winner-take-all networks through activity--dependent positive feedback*
Laboratory of A. Renart, CNP

**Tiago Marques**
*A novel paradigm for studying feature-based attention in the mouse primary visual cortex using a calcium imaging brain-machine interface*
Laboratory of L. Petreanu, CNP

**Simone Lackner**
*Understanding the function of Hypocretin/Orexin expressing neurons in neural circuits controlling visual-evoked locomotor behaviour in larval zebrafish*
Laboratory of M. Orger, CNP

| 2009 Students |

**Ali Ozgur Argunsah**
*Hippocampal synaptic plasticity induced by natural spike trains*
Laboratory of I. Israely, CNP

**Andreia Cruz**
*Lessons from others: a study of the mechanisms underlying social learning*
Laboratory of M. Moita, CNP

**Anna Hobbiss**
*Clustered plasticity as a model for micro-rewiring*
Laboratory of I. Israely, CNP

**Diogo Peixoto**
*Dynamics of neural activity in LIP during decision-making*
Laboratory of W. Newsome, Stanford Univ., USA

**Elizabeth Rickenbacher**
*Social modulation of fear extinction*
Laboratory of M. Moita, CNP

**David Raposo**
*The integration of evidence across modalities in the brain*
Laboratory of A. Churchland, Cold Spring Harbor Laboratory, USA

**Niccolò Bonacchi**
*Context dependent modulation of value*
Laboratory of Z. Mainen, CNP

**Pedro Garcia da Silva**
*Neuromodulatory enhancement of odour representations in the rodent olfactory bulb*
Laboratory of F. Albeanu, Cold Spring Harbor Laboratory, USA

**Raquel Abreu**
*Somatostatin-expressing neurons of the PreBötzinger Complex underlying Central Sleep Apnea*
Laboratory of J. Feldman, UCLA, USA

**Sevinç Mutlu**
*Cortical dynamics of excitation and inhibition during passive and active perception*
Laboratory of Z. Mainen, CNP

**Thiago Gouvêa**
*Motivational state modulation of decision making: reward expectation, phasic dopamine and choice accuracy*
Laboratory of Z. Mainen, CNP

| 2008 Students |

**André Mendonça**
*Attentional modulation of odour discrimination in rodents*
Laboratory of Z. Mainen, CNP

**Ana Rita Fonseca**
*Neural Mechanisms of Action Inhibition and Generation*
Laboratory of Z. Mainen, CNP

**Clara Ferreira**
*The role of octopaminergic neurons in appetitive olfactory learning and memory in Drosophila Melanogaster*
Laboratory of G. Miesenböck, University of Oxford, United Kingdom

**Fernando Santos**
*Neuronal ensemble selection and competition during motor skill learning*
Laboratory of R. Costa, CNP

**João Marques**
*Understanding the Neural Mechanisms that Control Speed in Zebrafish Larvae*
Laboratory of M. Orger, CNP

**Ana Pereira**
*Sound discrimination in fear conditioning: an interaction between cortical and thalamic auditory structures*
Laboratory of M. Moita, CNP

**Ana Isabel Amaral**
*A Bayesian approach to audio hallucinatory perception using oddball paradigm*
Laboratory of D. Langers, Dep. of Otorhinolaryngology, University of Groningen, The Nederlands

**Scott Rennie**
*The neural basis of social decision making, Rodents playing an iterated stag hunt game*
Laboratory of M. Moita, CNP

**Ana Mafalda Vicente**
*Neural Mechanisms Underlying The Shift Between Goal-Directed and Habitual Actions*
Laboratory of R. Costa, CNP

**Dennis Herrmann**
*Functional Architecture of the Neural System Controlling Female Reproductive Behaviour in Drosophila Melanogaster*
Laboratory of L. Vasconcelos, CNP

| 2007 Students |

**Patrício Simões**
*The Influence of Phase Change on Learning and Memory in Desert Locusts*
Laboratory of J. Niven, Department of Zoology, University of Cambridge, UK

**Isabel Henriques**
*Hydrogen Sulphide Mechanisms in Acute Cerebral Ischemia*
Laboratory of J. Ferro, Universidade Autónoma de Madrid, Spain

**Rodrigo Abreu**
*Neuronal and endocrine mechanisms underlying cognitive appraisal and social modulation of behaviour in zebrafish (Danio rerio)*
Laboratory of R. Oliveira, Instituto Superior de Psicologia Aplicada, Portugal

**José Joaquim Fernandes**
*Neural correlates of hierarchical learning*
Laboratory of M. Botvinick, Neuroscience Institute, Princeton University, USA

**Íris Vilares**
*Uncertainty and decision making in the human brain: economics and motor control*
Laboratory of K. Koerding, Rehabilitation Institute of Chicago, Northwestern University, USA

**Patrícia Correia**
*Serotonin function in behaviour*
Laboratory of Z. Mainen, CNP

**Maria Inês Vicente**
*Neural mechanisms of uncertainty in brain function and behaviour*
Laboratory of Z. Mainen, CNP

**Pedro Ferreira**
*Circuit analysis of epigenetic changes during the consolidation of skills*
Laboratory of R. Costa, CNP

**Margarida Agrochão**
*Towards an ecological approach to vision: wireless recording from rat V1*
Laboratory of M. Meister, Department of Molecular Cellular Biology,
Harvard U. Uni. University, USA

**Mariana Cardoso**
*Testing the Role of Cerebral Blood Flow on Neuronal Activity, in Mice Olfactory Glomeruli*
Laboratory of A. Das, Department of Neuroscience,
Columbia University, College of Physicians and Surgeons, USA

## 2011 INDIVIDUAL COURSES

### SPRING COURSES IN NEUROSCIENCE
Held at the Champalimaud Neuroscience Programme (CNP)

**Introduction**
10-14 Jan
**Organisers:** Susana Lima (CNP), Marta Moita (CNP), Carlos Ribeiro (CNP)
**Teachers:** Susana Lima (CNP), Marta Moita (CNP), Carlos Ribeiro(CNP)

**Introduction: Evolution**
17-21 Jan
**Organisers:** Susana Lima (CNP), Marta Moita (CNP), Carlos Ribeiro (CNP), Maria Luísa Vasconcelos (CNP)
**Teachers:** Susana Lima (CNP), Marta Moita (CNP), Carlos Ribeiro (CNP), Maria Luísa Vasconcelos (CNP), Chris Braun (Department of Psychology Hunter College Biopsychology Programme City University of New York, USA)

**Cellular Physiology**
24-28 Jan
**Organisers:** Joshua Dudman (Howard Hughes Medical Institute, USA)
**Teachers:** Alex Reyes (Centre for Neural Science - New York University, USA)

**Circuits**
31 Jan - 4 Feb
**Organisers:** Michael Orger (CNP)
**Teachers:** Ruben Português (Department of Molecular and Cellular Biology, Harvard University, USA)

**Plasticity**
7-11 Feb
**Organisers:** Inbal Israeli (CNP)
**Teachers:** Steve Kushner (Erasmus MC University Medical Centre Rotterdam, The Netherlands)

**Learning**
14-18 Feb
**Organisers:** Megan Carey (CNP)
**Teachers:** Sam Sober (School of Biology Emory University Atlanta, USA)

**Metabolism**
28 Feb - 4 MaR
**Organisers:** Carlos Ribeiro (CNP)
**Teachers:** Matt Piper (University College London, UK)

**Sensory & Motor**
7-11 Mar
**Organisers:** Carlos Ribeiro (CNP), Eugenia Chiappe (Howard Hughes Medical Institute, USA), Michael Orger (CNP)
**Teachers:** Eugenia Chiappe (Howard Hughes Medical Institute, USA)

**Movement into Action**
14-18 Mar
**Organisers:** Rui M. Costa (CNP)
**Teachers:** José Carmena (Department of Electrical Engineering and Computer Sciences, University of California, Berkeley, USA), Joe Mcintyre (CNRS Laboratoire de Physiologie de la Perception et de l'Action - College de France, France)

**Experimental Approaches - Basic**
21-25 Mar
**Organisers:** Adam Kampff (CNP), Michael Orger (CNP), Florian Engert (Harvard University)
**Teachers:** Adam Kampff (CNP), Michael Orger (CNP)

**Experimental Techniques - Advanced**
28 Mar - 1 Apr
**Organisers:** Adam Kampff (CNP), Michael Orger (CNP), Florian Engert (Harvard University)
**Teachers:** Florin Albeanu (Cold Spring Harbor Laboratory, USA)

**Projects**
4-15 Apr
**Organisers:** Adam Douglass (Harvard University, USA), Janet Iwasa (Department of Teachers: Cell Biology - Harvard Medical School, USA)

**Computational Approaches**
26-29 Apr
**Organisers:** Christian Machens (CNP), Alfonso Renart (CNP)
**Teachers:** Sophie Deneve (Départment d'Etudes Cognitives (DEC) at the Ecole Normale Supérieure), John Hertz (Niels Bohr Institute, Denmark)

**Vision to Decision**
9-13 May
**Organisers:** Joe Paton (CNP)
**Teachers:** Gabe Murphy (Howard Hughes Medical Institute, USA) Virginia Flanigan (Ludwig-Maximilians-Universität - Department of Neurology, Germany), Brian Lau (Dept of Neuroscience Columbia University, USA), Kenway Louie (Centre for Neural Science, New York University, USA) David Freedman (Department of Neurobiology, The University of Chicago, USA)

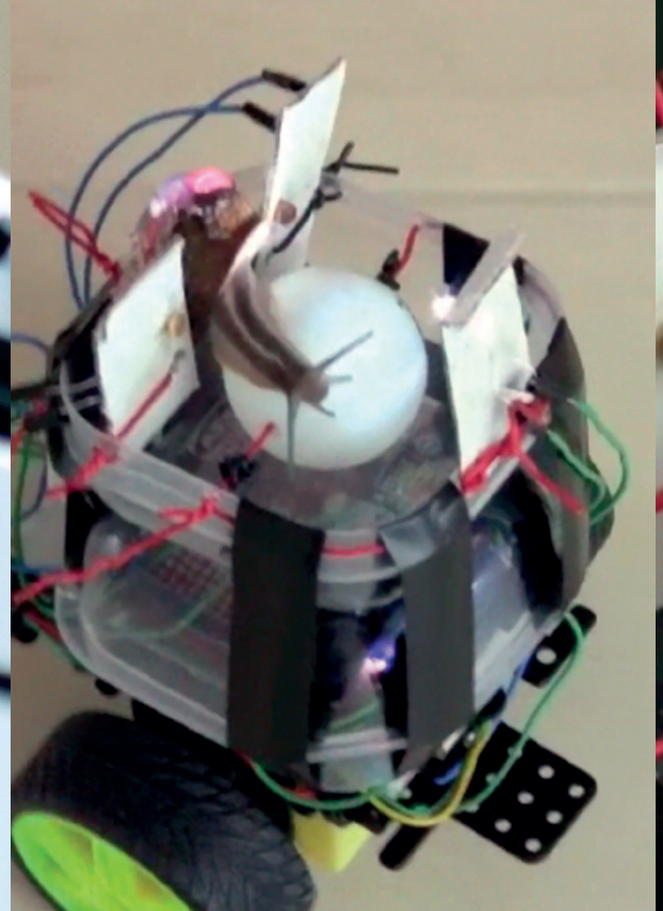
**Consciousness**
16-20 May
**Organisers:** Zach Mainen (CNP)
**Teachers:** Peter Mandik (Department of Philosophy William Paterson University of New Jersey, USA), Brian L. Keeley (Pitzer College, USA)

**Social Interactions**
23-27 May
**Organisers:** Marta Moita (CNP), Susana Lima (CNP)
**Teachers:** Regina Sullivan (Department of Zoology, University of Oklahom, USA)

**Extroduction**
30 May - 3 Jun
**Organisers:** Élio Sucena (IGC)

### AUTUMN COURSES IN INTEGRATIVE BIOLOGY
Held at the Instituto Gulbenkian de Ciência (IGC)

**History of Biological Concepts**
3-7 Oct
**Organisers:** Thiago Carvalho (IGC)
**Teachers:** Pietro Corsi (Faculty of History, University of Oxford, UK), Jonathan Howard (Department of Cell Genetics, Institute for Genetics, University of Cologne, Germany), Thiago Carvalho (IGC), Chrirsten Mirth (IGC), Lars Jansen (IGC), José Pereira Leal (IGC), Joe Paton (CNP)



Self-operated snail mobile.
*As part of their first year courses, 2011 INDP students constructed a vehicle that was self-operated by snails through antenna movements.*
*(image frames taken from the project video, courtesy of Tiago Marques)*

### Molecular and Structural Biology

10-14 Oct
**Organisers:** Alekos Athanasiadis (IGC)
**Teachers:** Niels Gehring (Institute for Genetics, University of Cologne, Germany), Guillermo Montoya (Spanish National Cancer Research Centre, Spain), Manwlis Matzapetakis (Instituto de Tecnologia Química e Biológica, Portugal), Claudio Soares (Instituto de Tecnologia Química e Biológica, Portugal), Bruno Viktor (Instituto de Tecnologia Química e Biológica, Portugal)

### Inside the Cell

17-21 Oct
**Organisers:** Lars Jansen (IGC)
**Teachers:** Niels Gehring (Institute for Genetics, University of Cologne, Germany), Bjoern Schumacher( CECAD Cologne at the Institute for Genetics, University of Cologne, Germany), Geneviève Almouzni (Nuclear Dynamics and Genome Plasticity Unit, Curie Institute, France), Andrew Holland (Ludwig Institute for Cancer Research, USA), Rob Wolthuis ( The Netherlands Cancer Institute, The Netherlands)

### Cells to Organisms I

24-28 Oct
**Organisers:** Thiago Carvalho (IGC)
**Teachers:** Mathieu Molet (Université Pierre et Marie Curie, France), Kevin Foster (Department of Zoology, Oxford University, UK), Pierre Golstein (Centre d'Immunologie de Marseille-Luminy, France), Etienne Danchin (Directeur de Recherche CNRS Head of the Laboratoire Evolution et Diversité Biologique Univ. Paul Sabatier, France)

### Cells to Organisms II - Limb Development

31 Oct - 4 Nov
**Organisers:** Diogo Castro (IGC), Joaquin Léon (IGC)
**Teachers:** Malcolm Logan (National Institute for Medical Research, UK), Juan Hurlé (University of Extremadura, Spain), James Sharpe (EMBL - Centre for Genomic Regulation, Spain), Diogo Castro (IGC), Joaquin Léon (IGC), Florence Janody (IGC), Solveig Thorsteinsdottir (FCUL)

### Statistics

7-11 Nov
**Organisers:** Jorge Carneiro (IGC)
**Teachers:** Jorge Carneiro (IGC)

### Genetic Models

14-18 Nov
**Organisers:** Vitor Barbosa (IGC)
**Teachers:** Jesús Aguirre (Dep. de Biología Celular y Desarrollo, Inst. de Fisiología Celular, Univ. Nacional Autónoma de México, México), Fernando Roch (University of Toulouse, France), Karen Liu (King's College London, UK), Miodrag Grbic (University of Western Ontario, Canada), Thiago Carvalho (IGC), Filipa Alves (IGC), Sara Carvalho (IGC), Ana Borges (IGC), Clara Reis (IGC), Moises Mallo (IGC), Elena Baena (IGC), Ana Mena (IGC)

### Evolution

21-25 Nov
**Organisers:** Isabel Gordo (IGC)
**Teachers:** Brian Charlesworth (School of Biological Sciences, University of Edimburgh, UK), Olivier Tenaillon (Faculté de Médecine Xavier Bichat, Universite de Paris VII, France), Michael Turelli (University of California, Davis, USA), Henrique Teotónio (IGC), Gabriela Gomes (IGC)

### Evolution, Development and Ecology

28 Nov - 2 Dec
**Organisers:** Patricia Beldade (IGC), Élio Sucena (IGC), Christen Mirth (IGC)
**Teachers:** Atanasios Pavlopoulos (University of Cambridge, UK), Christian Braendle (Université de Nice, France), Johannes Jaeger (EMBL - Centre for Genomic Regulation, Spain), Patricia Beldade (IGC), Élio Sucena (IGC), Christen Mirth (IGC)

### Instrumentation

5-10 Dec
**Organisers:** Nuno Moreno (IGC)
**Teachers:** Andrew Riddell (Head of Flow Cytometry Core Facility, EMBL, Germany), Jan Willem Brost (JWB, The Netherlands), Nuno Moreno (IGC), Emilio Gualda (IGC), Gabriel Martins (IGC), Pedro Almada (IGC), Jorg Becker (IGC), José Rino (IMM)

### Neurobiology

12-19 Dec
**Organisers:** Michael Orger (CNP), Maria Luísa Vasconcelos (CNP)
**Teachers:** Rui Costa (CNP), Zach Mainen (CNP), Michael Orger (CNP), Alfonso Renart (CNP), Adam Kampff (CNP), Inbal Israeli (CNP), Carlos Ribeiro (CNP), Susana Lima (CNP), Maria Luísa Vasconcelos (CNP), Joe Paton (CNP), Magor Lorincz (postdoctoral fellow, CNP), Florian A. Dehmelt (PhD student, CNP)


# TO SHARE OUR KNOWLEDGE

NOT ONLY WITHIN THE SCIENTIFIC COMMUNITY BUT WITH THE COMMUNITY AT LARGE

## AR | RESPIRE CONNOSCO

Drawing on the enthusiasm of the Champalimaud Neuroscience Programme community and spearheaded by students, a series of science communication events called Ar was established. Ar is Portuguese for air, representing how pervasive and fundamental science is in our daily lives.

Ar events explore fundamental scientific themes by intertwining work from leading thinkers, both local and international. On each event scientists and non-scientist, such as plastic artists, chefs, mind readers, group facilitators, cyborgs and others, engage the public to think, interact and debate their ideas. Presentations are entertaining and dynamic and include cutting edge interactive games and open discussion. Each event has drawn more than 400 people to the Champalimaud Foundation Auditorium and has received wide acclaim in important local publications.

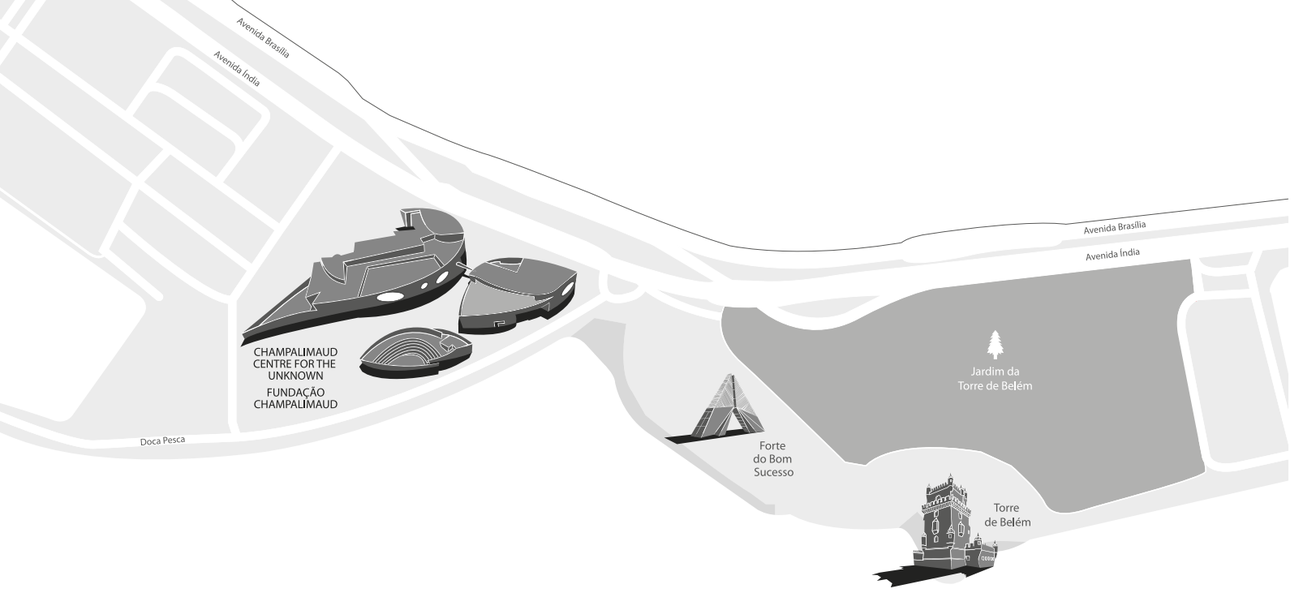
Supporting these regular events, the same group of students has implemented a range of online resources, including streaming and hosted multimedia content, a webzine, a newsletter and social networking that links the actual events with a range of relevant established sources from scholarly blogs to TED talks and much more.

A ciência está no **Ar**...
Respire connosco

**Organisers:**

TS Gouvea, BAC Afonso, C Afonso, N Bonacchi, W Brendel, V. M. Corrales, PA Correia, GMP Costa, FA Dehmelt , EEJ Dewitt, AR Fonseca, AF Hobbiss, S Lackner, GC Lopes, TG Marques, SPS Matias, AG Mendonça, SV Meyler, C Monroy, CEL Ramos, SM Rennie, SLS Soares, R Venturini, A Vicente, E Vinnik, AR Kampff, ZF Mainen

From Ar Event on Emergence (23/11/2011):
*"You are not alone in the universe. While leading your busy life you are constantly interacting with other human beings and your environment in diverse ways. Every other human being is doing the same. If we could step aside and look at the tapestry of all this activity at the same time, what patterns would emerge?"*

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EVERYONE IN CNP
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Administration.