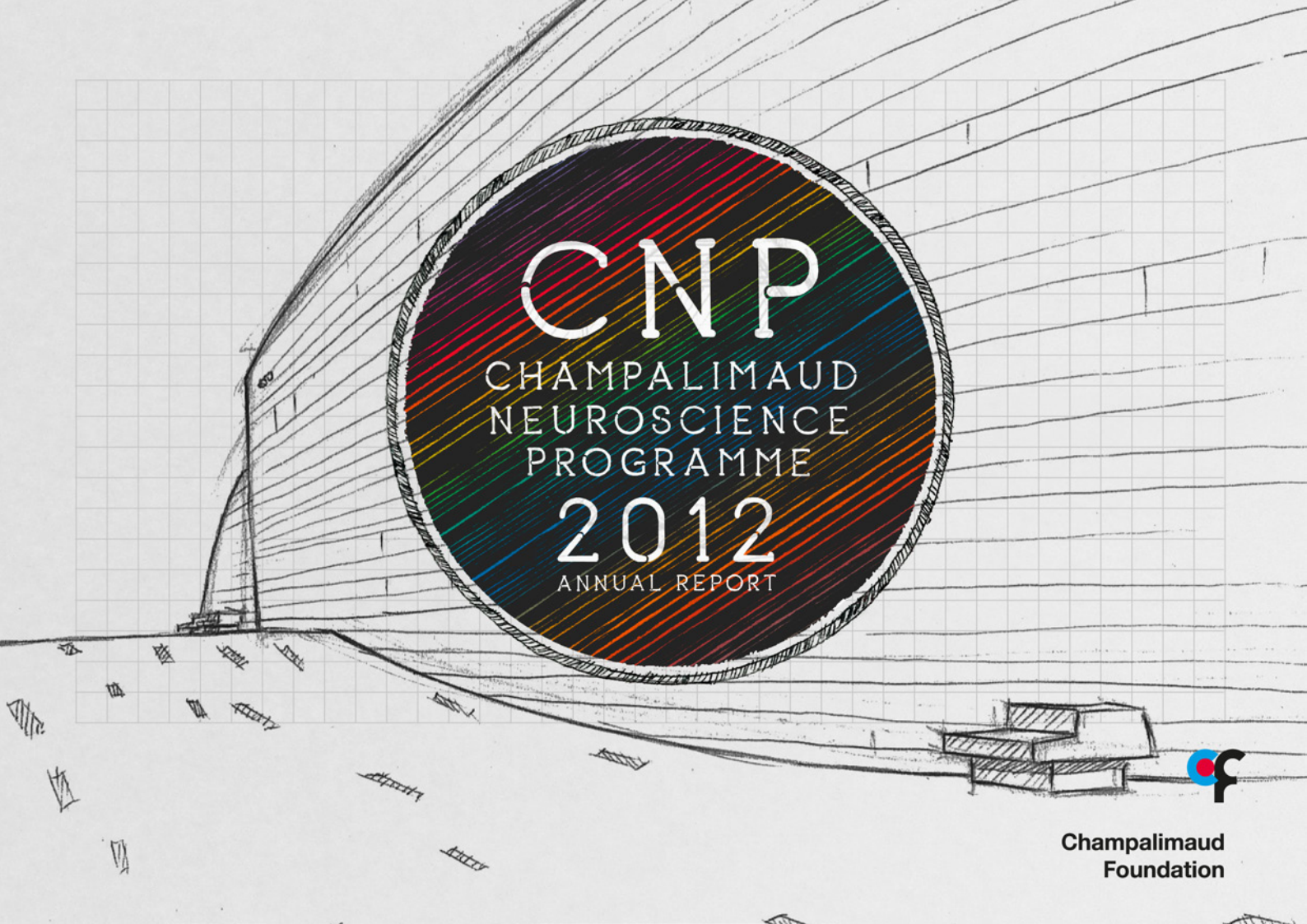


Champalimaud
Foundation

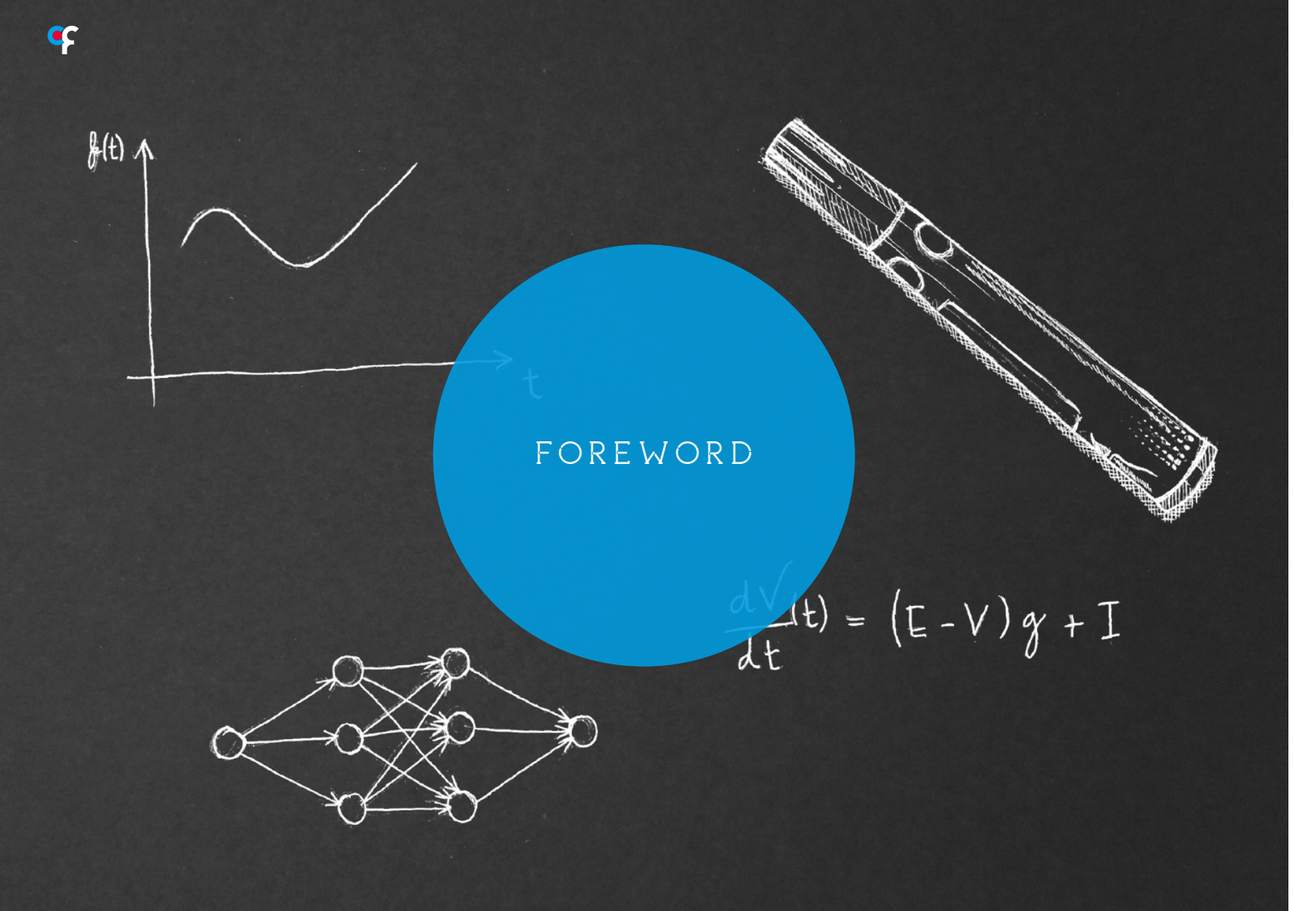
CNP

CHAMPALIMAUD
NEUROSCIENCE
PROGRAMME

2012

ANNUAL REPORT

Champalimaud
Foundation



MEETING THE CHALLENGES

FOLLOWING OUR VISION

WORDS FROM THE DIRECTOR

The symbol of the Champalimaud Neuroscience Programme (CNP) retreat of 2012, our fifth, was the seagull.

The seagull was chosen because it is one of our new neighbours. The gull alighting on a Roman column represents our arrival at this Champalimaud Centre for the Unknown. After 5 years of incubating and over one year of being split in two, we are united at this fabulous facility on the banks of the Tejo. The seagull has landed.

As I pondered upon this beautiful image, I started to wonder what the seagull represents to us.

As with many animals, the seagull has a certain anthropomorphised reputation in human culture. Gulls are seen as ruthless scavengers reputed to make a meal out of almost anything they can, alive or dead, plant or animal, swimming or hopping or flying. They are rather fearless and will take food right out of a person's hand. In Native American mythology, the seagull is an important figure, mythologised for its endurance. The gull is also especially known in this mythology as a symbol for opportunism. Opportunism literally means taking advantage of opportunities.

Of all the species, humans, like seagulls, are amongst the most successful and adaptable. Yet, all too often, in striving for a scientific or a personal goal, we also select a path to get there and we fail to see how to proceed when that path is blocked. What separates the gulls from other species of birds, faring far less well with the overabundance of people and buildings in their habits, is their ability to work with what they are given to achieve their aims.

If we were to create our own CNP mythology I think the seagull could be our totem. The seagull would represent being adaptable, resourceful and pragmatic. It would represent seizing hold of what is available to make reaching a goal possible. It would represent not getting stuck on a preconceived plan or failing due to unforeseen obstacles. And it would represent doing so in a way that adheres to the larger principles while being willing to deviate from typical behaviour.

In science and life, we strive to be like the seagull. We endeavour not to mistake the path for the goal. Be observant for the affordances that our experiments or our life throws up. Make plans, but don't set them in stone. Keep principle and goals, but don't stop revising our plans when new circumstances arise.

We have arrived at the end of another very full year, a year replete with plans, meetings, experiments and conversations, a year of accomplishments and also setbacks, large and small. As the seagull, we persevere in meeting the challenges and sticking to our vision. We aspire to show our endurance in work and in life.

Zach Mainen
Director, Champalimaud Neuroscience Programme

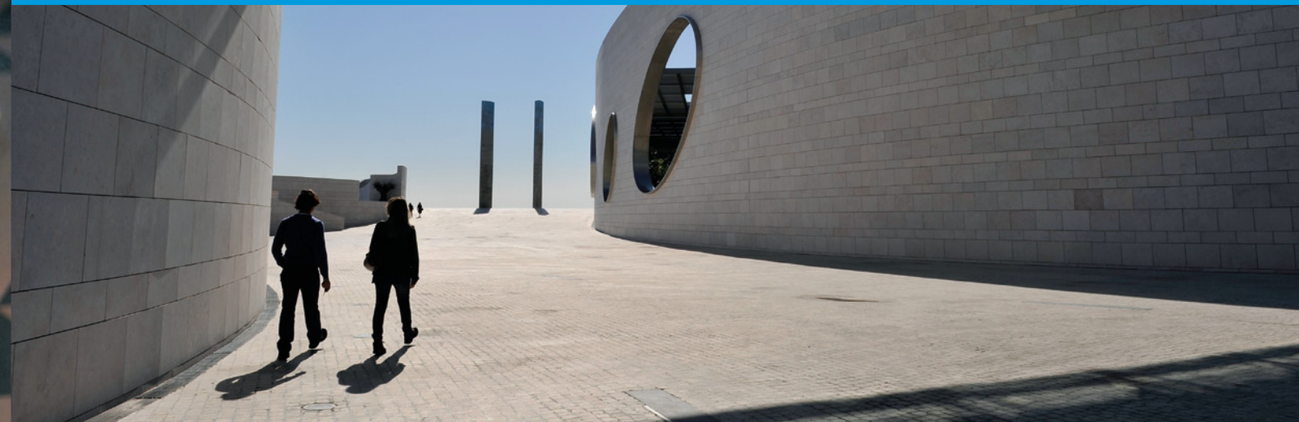
Design: Gil Costa

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

LEONOR BELEZA (PRESIDENT)

JOÃO SILVEIRA BOTELHO

ANTÓNIO HORTA-OSÓRIO

General Council

DANIEL PROENÇA DE CARVALHO (CHAIRMAN)

FERNANDO HENRIQUE CARDOSO

SIMONE VEIL

ANÍBAL CAVACO SILVA (EMERITUS)

ANTÓNIO ALMEIDA SANTOS

ANTÓNIO COUTINHO

ANTÓNIO DAMÁSIO

ANTÓNIO TRAVASSOS

CARLOS EUGÉNIO CORRÊA DA SILVA

JOÃO RAPOSO MAGALHÃES

ANTÓNIO BORGES

PEDRO D'ABREU LOUREIRO

Scientific Committee

JAMES WATSON (CHAIRMAN)

ALAN ASHWORTH

MARK BEAR

MARIA BLASCO

RONALD BLASBERG

BARRY DICKSON

PAUL MARKS

J. ANTHONY MOVSHON

KEITH PETERS

MARTIN RAFF

SUSUMU TONEGAWA

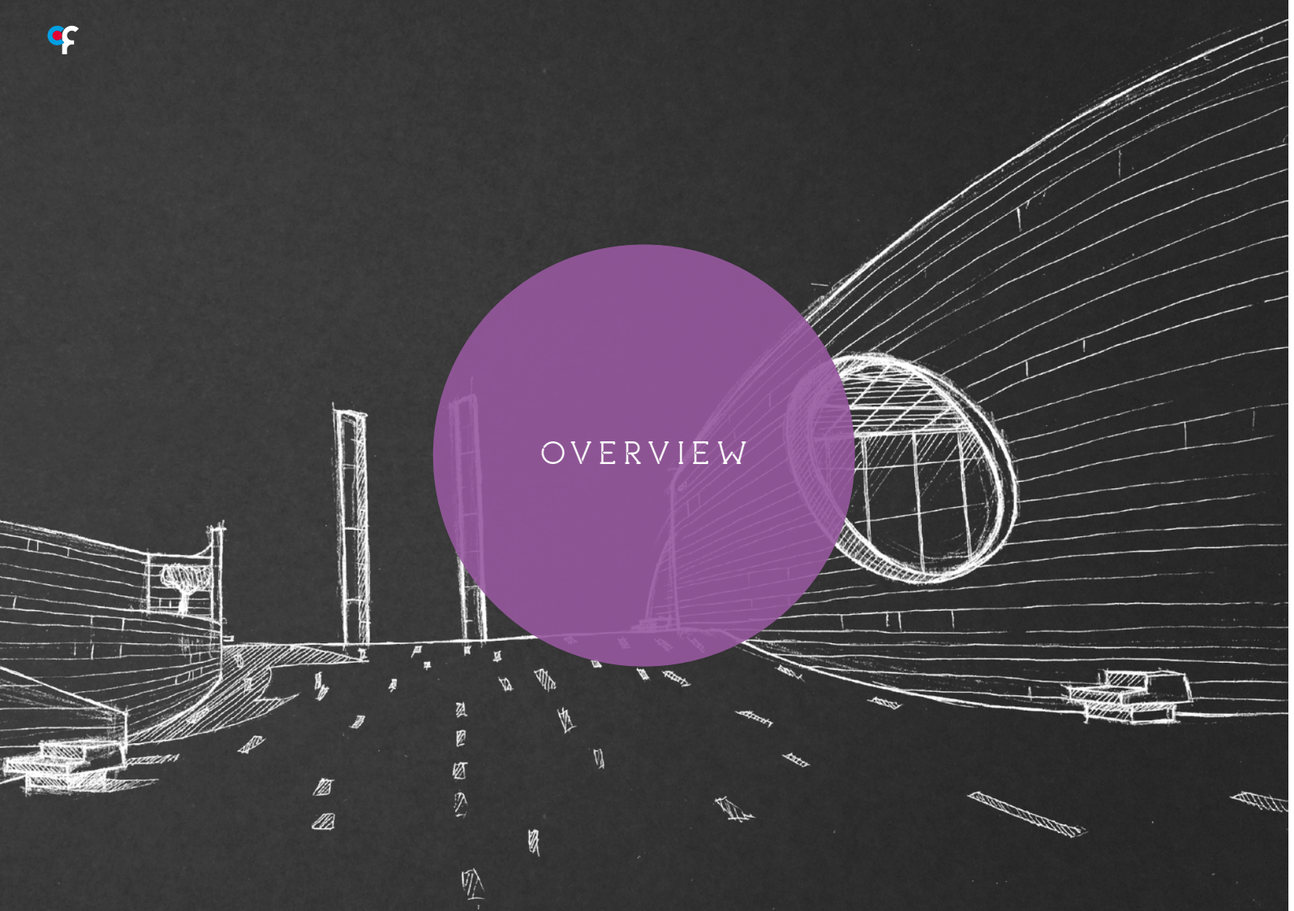
CHAMPALIMAUD CENTRE FOR THE UNKNOWN

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



OVERVIEW

THE CHAMPALIMAUD NEUROSCIENCE PROGRAMME

AIMS TO UNRAVEL THE NEURAL BASIS OF BEHAVIOUR

THE CHAMPALIMAUD NEUROSCIENCE PROGRAMME

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 process 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

ZACHARY MAINEN
CNP Director

RUI COSTA
Deputy Director

ALFONSO RENART
INDP Director

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 London
London, UK

2012 SAB members

CLAUDE DESPLAN
Department of Biology
New York University
New York, USA

THOMAS JESSELL
Department of Neuroscience and Department
of Biochemistry and Molecular Biophysics
Columbia University
New York, USA

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

Maria 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 Azaruja;

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 Carlos Ribeiro and Inbal Israely join the CNP.

CCU

Zach Mainen

2010

Zach Mainen appointed CNP Director;

Investigators 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 Inauguration

2011

Investigators Christian Machens, Leopoldo Petreanu, Alfonso Renart, Adam Kampff and Maria 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 Champalimaud Neuroscience Symposium

2012

Investigator Eugenia Chiappe joins the CNP;

Vivarium opens;

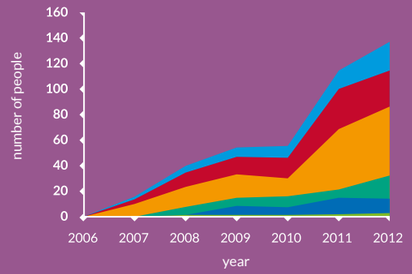
29 March
CNP awarded The Scientist "Best Places to Work: Postdocs, 2012" award.

"Best Places to Work: Postdocs, 2012" award

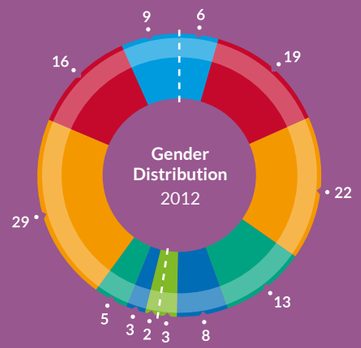
GROWTH AND DIVERSITY

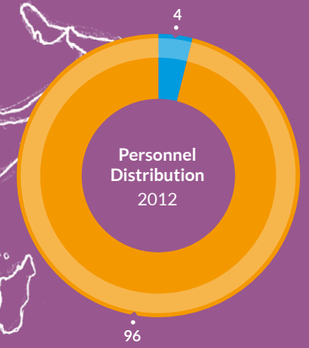
Since its establishment in 2007 until December 2012, the CNP grew to include 135 members.

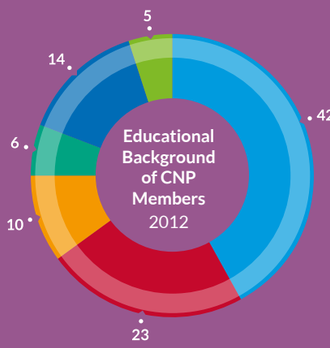
CNP Growth
2007-2012



male | **47%** female | **53%**







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

Results presented in %

- Non-Scientific
- Scientific

- Biology
- Exact Sciences
- Neuroscience
- Psychology
- Medical Sciences
- Other

TO FORGE NEW LINKS

BETWEEN NERVOUS SYSTEM FUNCTION AND BEHAVIOUR

NEURAL CIRCUITS AND BEHAVIOUR

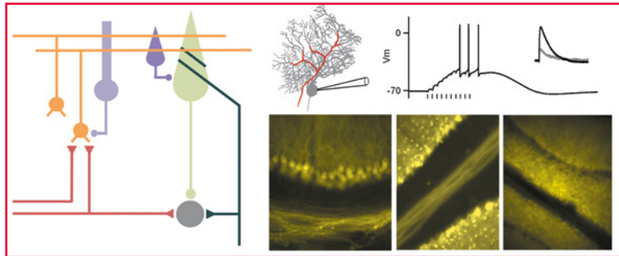
Research Groups

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 trans genes 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**.

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

LAB MEMBERS

Catarina Albergaria
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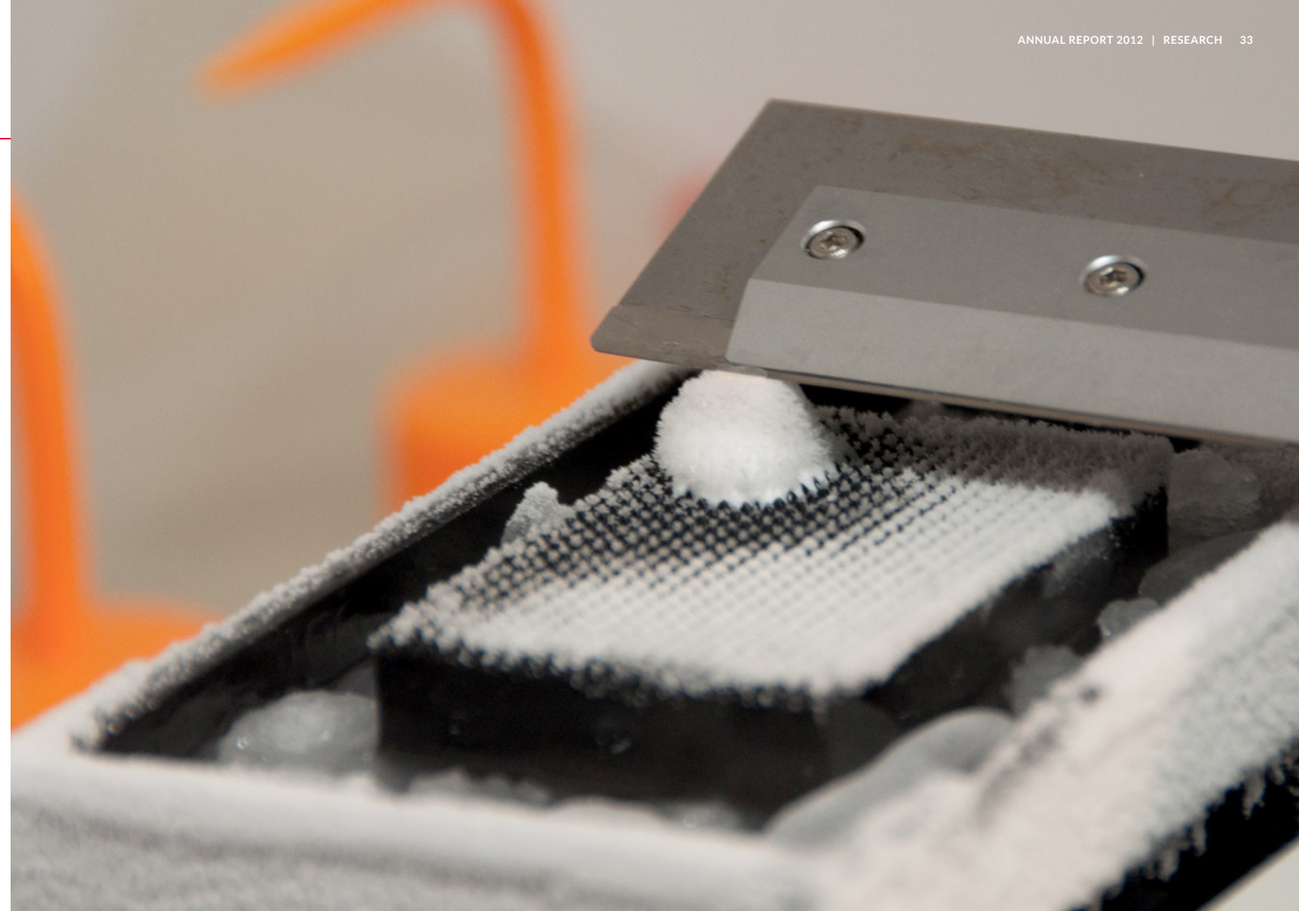
Ana Sofia Machado
MIT-Portugal PhD Student, FCT Fellow

Sofia Araújo
IMM MSc Student

Dana Darmohray
Research Assistant

Carla Matos
Research Technician

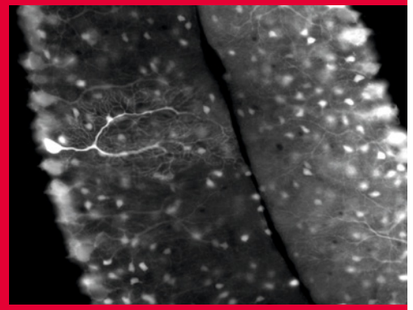
Claire Monroy
Research Technician



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.



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.

SENSORIMOTOR INTEGRATION

Research Groups

EUGENIA CHIAPPE
Principal Investigator

We are interested in the relationship between the dynamics of neural networks and animal behaviour. Our research focuses on the integrative processes by which the brain corresponds ongoing sensory signals with proceeding motor actions. Our goal is to identify patterns of neural activity representing computational principles occurring during sensorimotor tasks in small networks. In addition, we aim to describe the mechanisms by which these neural circuit computations emerge from the biophysical properties of neurons and synapses.

With only about 100,000 neurons, the brain of *Drosophila melanogaster* produces rather sophisticated orientation behaviours. The balance between brain numerical simplicity and behavioural complexity makes *Drosophila* an attractive experimental system to investigate how visually guided behaviours are implemented by small neural networks. We use novel methods that allow us to record the activity of neurons in a behaving fly during locomotion.

KEY PUBLICATIONS

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* equal contribution

LAB MEMBERS

Francisco Semedo
Lab Manager

Michael Mende
Lab Manager
and Research Assistant

Tomás Cruz
IST MSc Student

FUNDING

CHAMPALIMAUD FOUNDATION

Development of behavioural paradigms to study sensorimotor integration

We are currently developing “freely moving” and “tethered” behavioural paradigms in virtual reality-like worlds designed to probe the computational capacities of the fly’s brain during visually guided orientation behaviours. These shall form a platform for studying:

a) how the fly uses its own movements and the generated visual motion cues to explore an environment;
b) how its brain incorporates sensory signals to correct locomotion during orientation towards objects;
c) how do past experiences inform ongoing behaviour.

FUNDING

CHAMPALIMAUD FOUNDATION

Identification of neurons and circuits involved in sensorimotor processing

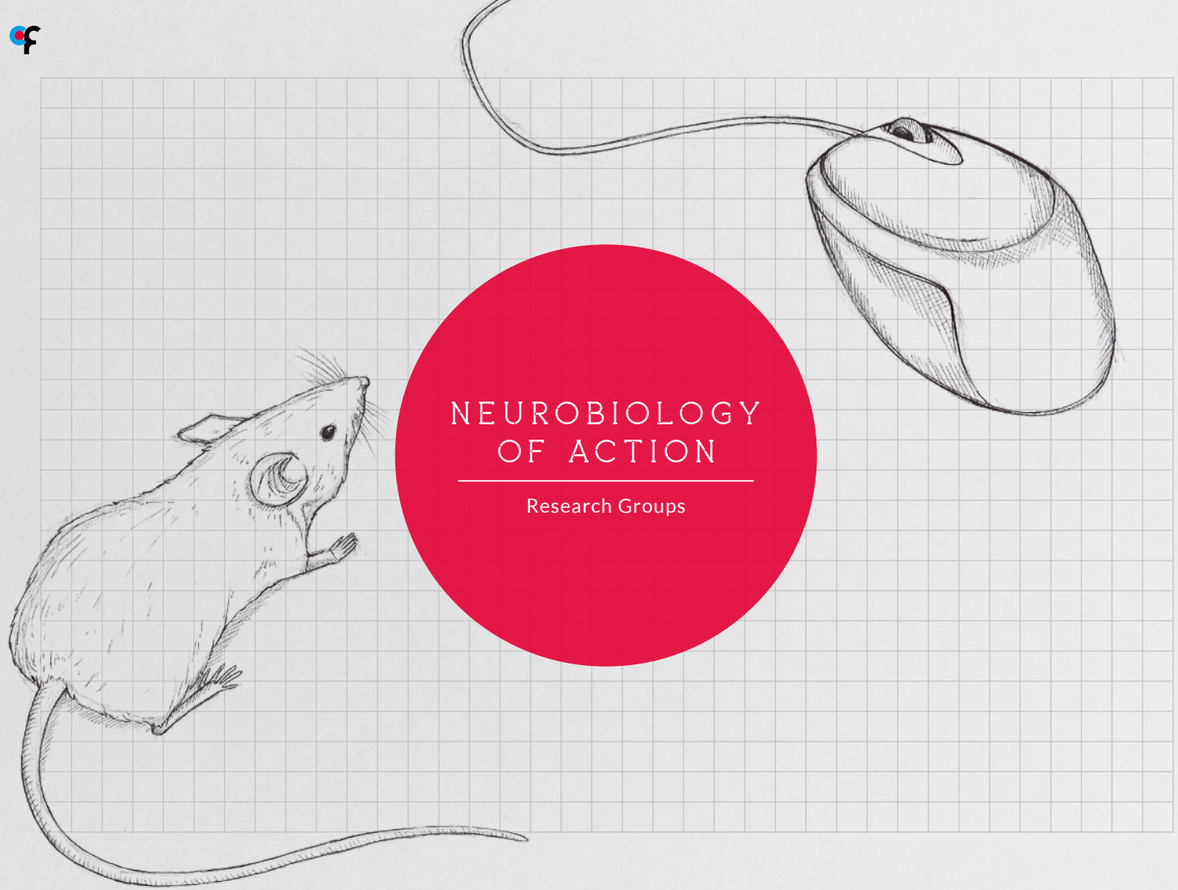
The aim of this project is to understand how components in the circuit are linked and how the activity patterns of neurons arise from their synaptic connectivity. We identify neuronal components of a network using behavioural, physiological and anatomical methods. We then map connectivity among candidate neurons by combining chemical, optical and electrical techniques. Importantly, in the brain of the fruitfly it is possible to systematically identify the same class of neurons across different individuals. This allows investigating variability in synaptic connectivity and circuit function across different flies.

FUNDING

CHAMPALIMAUD FOUNDATION

Probing neural processing during sensorimotor tasks

In simultaneous with head-fixed, tethered locomotion, we use electrophysiological and imaging techniques to monitor the activity dynamics of populations of genetically- or anatomically-defined groups of neurons. We apply quantitative analytical tools to correlate neural population activity with the behaviours described above, and to make predictions about the contribution of different groups of neurons to such behaviours. We examine the roles of different groups of neurons in the circuit by precise manipulations of their activity with genetic and optical techniques. These experiments are aimed at defining the functional logic of the circuitry in the context of a specific behaviour. By comparing different visual-motor tasks, our research attempts to identify common principles of visual-motor transformations.



NEUROBIOLOGY OF ACTION

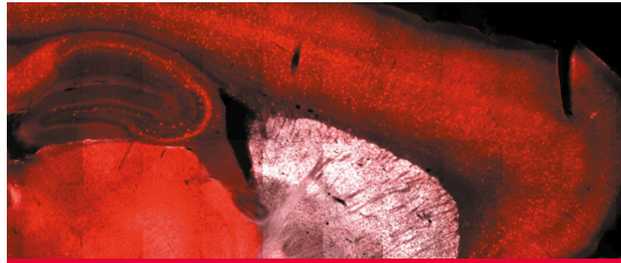
Research Groups

RUI M. COSTA
Principal Investigator

To study actions is to study the way we do things, which is different than studying how we remember stimuli, or facts and events. Some actions are innate or prewired. Others are learned anew throughout life, likely through a process of trial and feedback. We currently focus on understanding the processes mediating the latter.

Our overall goal is to understand how changes in molecular networks in the brain modify neural circuits to allow the generation of novel actions and their shaping by experience. To achieve this, we subdivided our experiments into different subgoals to study action generation, action shaping and automatisation and action goals.

KEY PUBLICATIONS



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* equal contribution

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Postdoctoral Researcher

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Postdoctoral Researcher, FCT fellow

Fatuel Aguilar, PhD
Postdoctoral Researcher, FCT fellow

Vitor Paixão, PhD
Postdoctoral Researcher

Rodrigo Oliveira, PhD
Postdoctoral Researcher

Cátia Feliciano, PhD
Postdoctoral Researcher

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Lauren McElvain, PhD
Postdoctoral Researcher

Ana Fernandes, PhD
Postdoctoral Researcher

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Clinical Research Fellow

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Clinical Research Fellow

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Clinical Research Fellow

Matthew Child
Consultant

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Sevinç Mutlu
2009 INDP PhD student, FCT fellow

Eduardo Dias-Ferreira
PDBEB-Coimbra PhD Student, FCT fellow

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PFMA-Gulbenkian PhD student

Ana Castro, MD
PFMA-Gulbenkian PhD student

Mariana Correia
Research Technician

Ana Maria Vaz
Research Technician

FUNDING

EUROPEAN RESEARCH COUNCIL (ERC); MARIE CURIE INTEGRATION GRANT; 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.

NEURONAL STRUCTURE AND FUNCTION

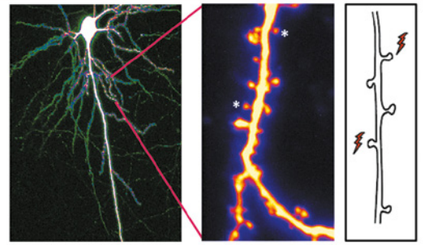
Research Groups

INBAL ISRAELY

Principal Investigator

We are interested in understanding how activity can lead to specific structural changes in neurons which 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



Govindarajan A*, Israely I*, Huang SY, Tonegawa S (2011) *The dendritic branch is the preferred integrative unit for protein synthesis-dependent LTP.* **Neuron 69 (1):132-146.**

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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

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FUNDING

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

Dendritic compartmentalisation of protein synthesis-dependent synaptic plasticity

Neural connectivity may be shaped by activity, leading co-active synapses to become clustered on the same dendritic branch. Recent evidence provides support for such functional organisation of synapses *in vitro* and *in vivo*. We aim to determine whether the physical clustering of synapses also occurs and by which mechanism may this be affected. We examine whether endogenous activity shapes the distribution of spines within dendrites of hippocampus, in order to determine whether clustering can be induced with activity. As protein synthesis dependent plasticity at individual spines can facilitate long lasting changes at neighbouring spines, this may provide such a mechanism. Additionally, we probe if competition for proteins during synaptic plasticity also shapes the organisation of inputs. Using 2-photon imaging and glutamate uncaging, we examine how activity at spines leads to structural changes, and whether such changes give rise to computational units.

In order to determine whether experience leads to spine clustering, we are investigating the endogenous distribution of spines in the hippocampus at various developmental stages. We compare animals that are reared in an enriched environment (to provide activity) versus a deprived one. Thus far, spine distribution in naïve slice cultures at the early time point of post-natal day 7-9, is not different from random. We will next uncage glutamate to determine whether clustering can be induced.

FUNDING

BIAL FOUNDATION,;
FUNDAÇÃO PARA A CIÊNCIA
E A TECNOLOGIA (FCT);
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 signalling 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 investigated the structural correlates of protein synthesis dependent long-term depression (LTD) mediated by metabotropic glutamate receptors (mGluRs) through two-photon imaging of dendritic spines on hippocampal pyramidal neurons. We find that induction of mGluR-LTD leads to robust and long lasting spine shrinkage and elimination. These effects depend on group I mGluRs, require protein synthesis, and activity. These findings are being prepared for publication in 2013.

FUNDING

FUNDAÇÃO PARA A CIÊNCIA E A TECNOLOGIA (FCT); 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 investigate how such complex trains of activity interact across multiple synapses within a dendritic branch. We use this information to model neuronal information processing in order to develop an understanding of the learning rules which govern synaptic weight changes.

The ability to deliver patterns of information with narrow time frames at single spines is a crucial first step which precedes delivery of complex patterns of activity at synapses. Thus far, we have validated an uncaging paradigm for the induction of spike timing dependent plasticity at synapses in slice cultures. Also, we have recorded activity from CA3 neurons *in vivo* in freely behaving mice. These data will be used to design *in vitro* uncaging paradigms that mimic naturalistic activity.

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 are developing 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.

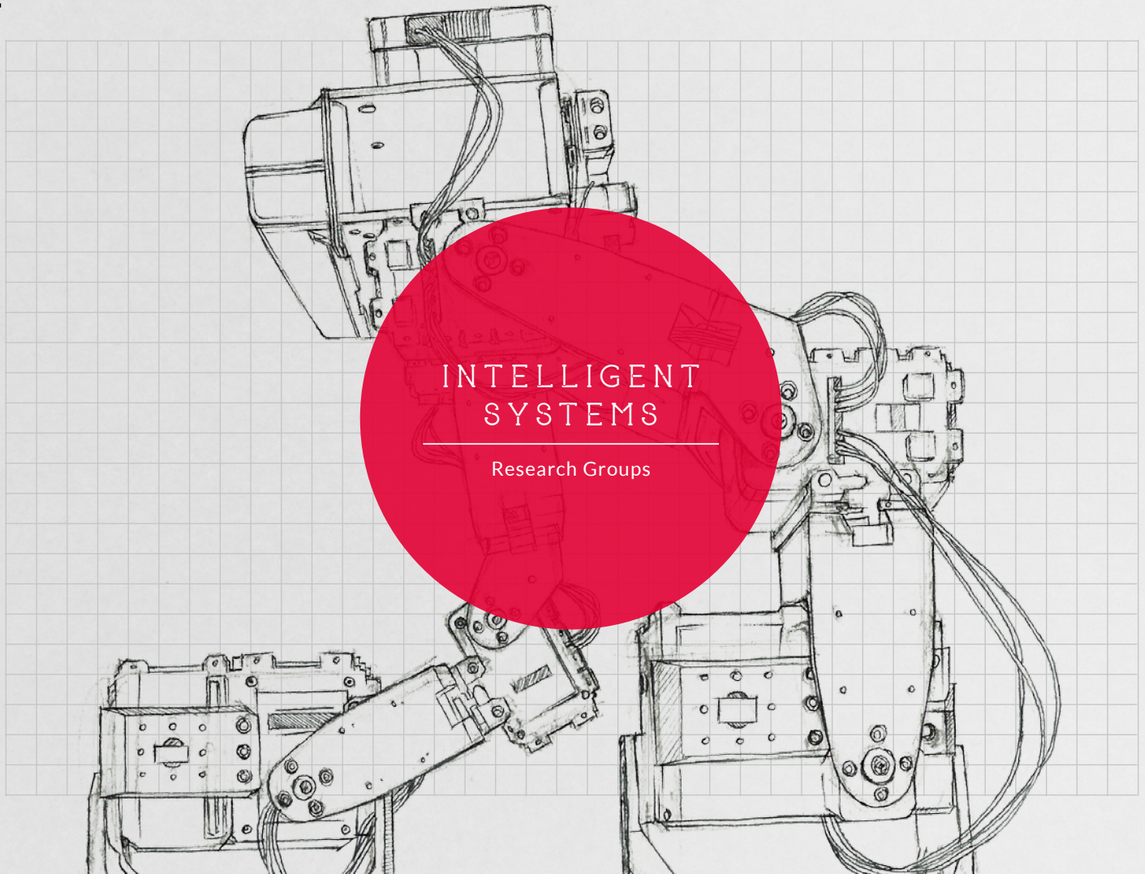
Thus far, we have developed an automated, multi-level, region based segmentation method to detect dendritic spines from two-photon laser scanning microscopy images. Identified structures in two-photon images of dendritic spines are used to train the segmentation algorithm. This is the first step towards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

FUNDING

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

Activity-dependent regulation of local translation in neuronal dendrites

Enduring changes in neurons require the synthesis of new proteins, however the regulation of this important biological process following synaptic activity is poorly understood. The goal of this project is to examine the mechanisms by which synaptic activity engages the local dendritic translational machinery, and to determine the parameters over which newly made proteins are available to influence plasticity. We aim to develop reporters of protein synthesis and its neuronal targets, in order to understand the role of activity-dependent translation within dendrites. Following the induction of activity at single synapses, we will determine how new protein production is triggered, where new proteins are available relative to activated synapses, and for how long such proteins can influence plasticity. Additionally, we will investigate how activity-dependent translation might be altered in animal models of mental retardation in which there is an aberrant increase of protein translation.



INTELLIGENT SYSTEMS

Research Groups

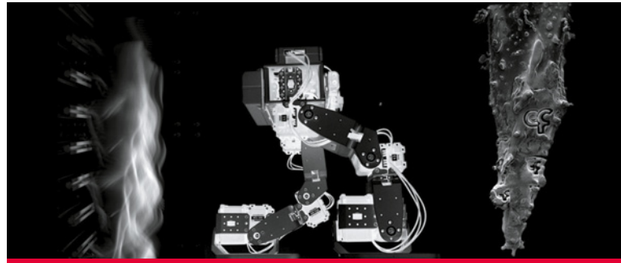
ADAM KAMPFF
Principal Investigator

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 environment? 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.

KEY PUBLICATIONS



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Orger M*, Kampff AR*, Severi K, Bollmann J, Engert F (2008) *Control of visually guided behaviour by distinct populations of spinal projection neurons.* **Nat Neurosci 11 (3):327-33.**

Vislay-Meltzer RL, Kampff AR, Engert F (2006) *Spatiotemporal specificity of neuronal activity directs the modification of receptive fields in the developing retinotectal system.* **Neuron 50 (1):101-14.**

* equal contribution

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Summer 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 programmable 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.

FUNDING

BIAL FOUNDATION; CHAMPALIMAUD FOUNDATION

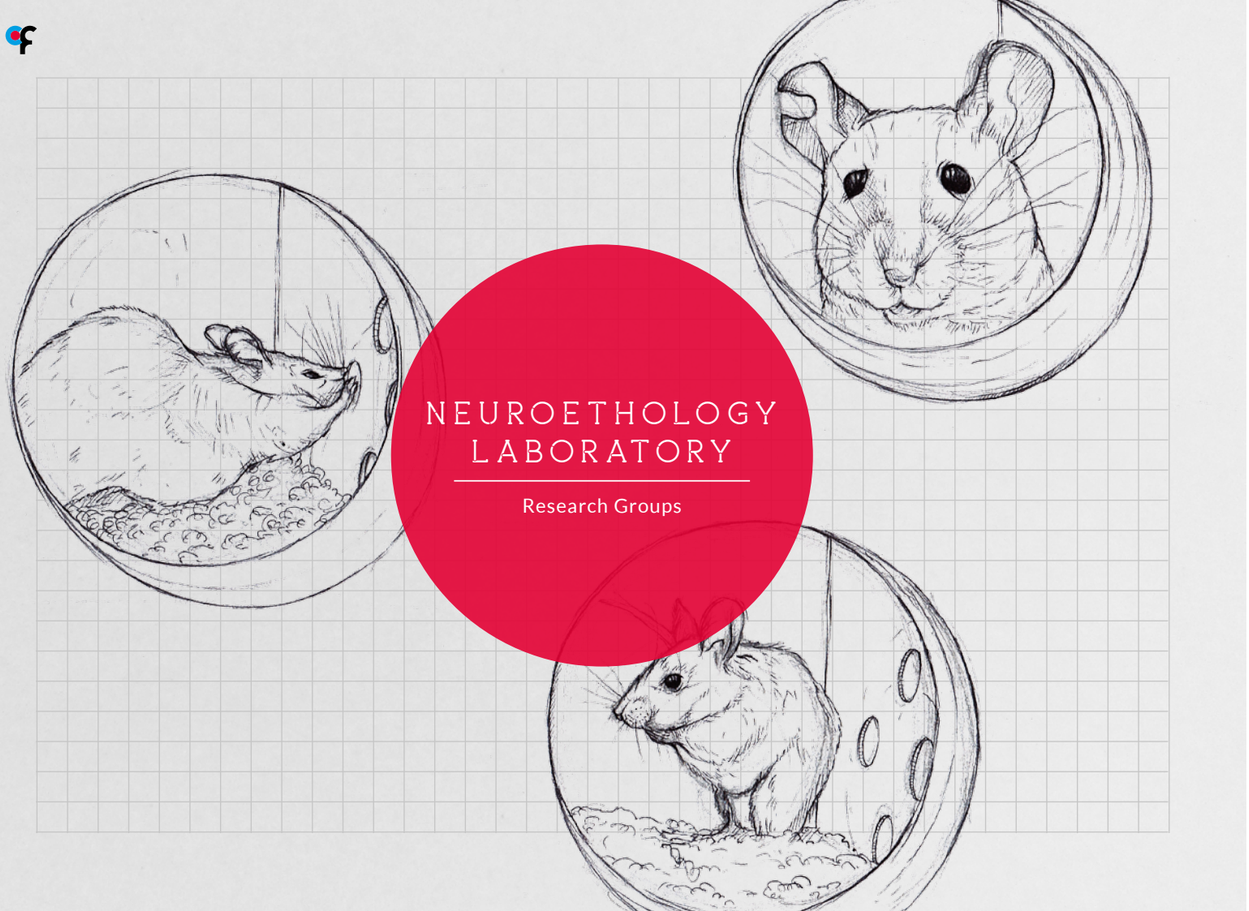
COLLABORATORS

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 Signal to Noise Ration (SNR), and increase selectivity for dense signals. We used material processing techniques to make "nano-structural" 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.



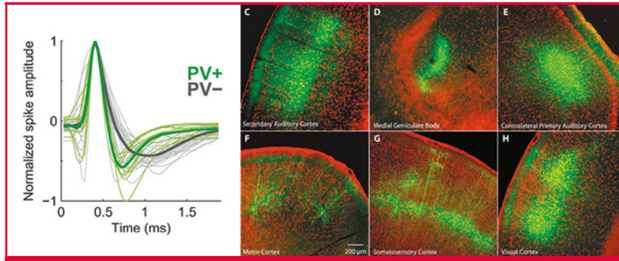
NEUROETHOLOGY LABORATORY

Research Groups

SUSANA LIMA
Principal Investigator

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 test the hypothesis that mate choice has an impact on the regulation of sexual behaviour.

KEY PUBLICATIONS



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Lima SQ and Miesenbock G (2005) *Remote control of fly behaviour through genetically targeted photostimulation of neurons*. **Cell 121 (1):141-52**.

Ng M, Roorda RD, Lima SQ, Zemelman BV, Morcillo P, Miesenbock G (2002) *Transmission of olfactory information between three populations of neurons in the antennal lobe of the fly*. **Neuron 36:463-74**.

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FUNDING

MARIE CURIE REINTEGRATION GRANT; EUROPEAN; BIAL FOUNDATION; CHAMPALIMAUD FOUNDATION

Neuronal mechanisms for mate choice in mice

Once receptive, females need to choose their mate, a process that involves acquiring information about available mates and which is dependent on prior experience. We have set up a behavioural paradigm to study assortative mate choice in the laboratory, and our results indicate that mate choice is set during early life. We are currently exploring novel avenues to understand how early experience affects neuronal circuits that might be involved in mate choice. Candidate brain areas that might be involved include the Islands of Calleja in the olfactory tubercle, a region that has been implicated in the rewarding aspects of olfactory stimuli.

1. Mate choice in *Mus musculus* is relative and dependent on the estrous state. Zinck and Lima, Submitted;
2. Early experience participates in setting the rules of assortative mate choice in the mouse *Mus musculus musculus*. Zinck and Lima, In Prep.

FUNDING

BIAL FOUNDATION; CHAMPALIMAUD FOUNDATION

Neuronal mechanisms underlying sex hormone-dependent switching of sexual receptivity

Female sexual receptivity changes across the reproductive cycle, being maximal during the fertile phase. This represents an interesting state-dependent behavioural output, where the interaction of sexual hormones and the physiology of neuronal circuits alters the way a female treats the same male stimulus. We are interested in understanding the role of the ventromedial nucleus of the hypothalamus (VMH) in the control of this receptivity switch. To this end, we are performing electrophysiological recordings of this area in naturally cycling female mice exposed to male stimuli.

FUNDING

CHAMPALIMAUD FOUNDATION

Female sexual behaviour: neuronal pathways for arousal termination

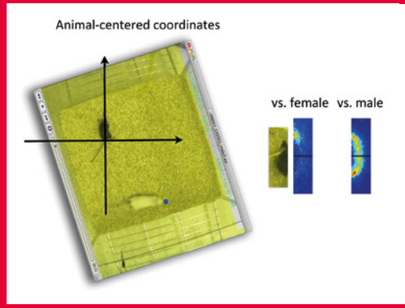
Like all behaviours, sexual arousal has a beginning and an end. Sensory genital stimulation received by the female during copulation (sensed by mechanoreceptors present in the cervix and clitoris) is relayed to the brain and is important for the rewarding effects of copulation and for its termination. 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 uses this information to inhibit further sexual arousal.

FUNDING

CHAMPALIMAUD FOUNDATION

Imprinting in mice

Sexual selection is an important evolutionary agent that has repercussions in the morphology, behaviour, mating system and life history evolution of species, and it may even influence speciation as well as extinction. With this project we aim at clarifying some of the pre-zygotic divergence mechanisms that could be behind the low genetic flow across two very similar subspecies: *Mus musculus musculus* and *Mus musculus domesticus*. Because olfaction is the major communication highway in newborn rodents we will explore



SNAPSHOT OF A SOCIAL INTERACTION BETWEEN THE TEST ANIMAL (FEMALE) AND STIMULUS ANIMAL (MALE OR FEMALE).
The position of the animals was automatically detected and the test animal became the 0,0 position with the x axis aligned to the nose-tail and the y axis perpendicular to this. The nose of the stimulus animal was detected, and transformed in x, y coordinates relative to the test animal. This allows us to know the type of interaction between the two animals. This can then be transformed into a heat map that reflects the relative positions of both animals across the full session. With this type of analysis we learned that, when the stimulus animal is a female, the predominant type of interaction is nose-nose contact. In contrast, when the stimulus animal is a male, the male investigates the full body of the female. We are using this type of behavioural analysis to correlate with neural activity recorded at different nuclei of the hypothalamus.

the possibility that an early olfactory experience might play an important role in choosing a sexual partner later in life. Hence, using both behavioural testing and immunohistochemistry techniques in mice we will initiate the study to unravel the neuronal circuitry behind this early life learning.

COLLABORATORS

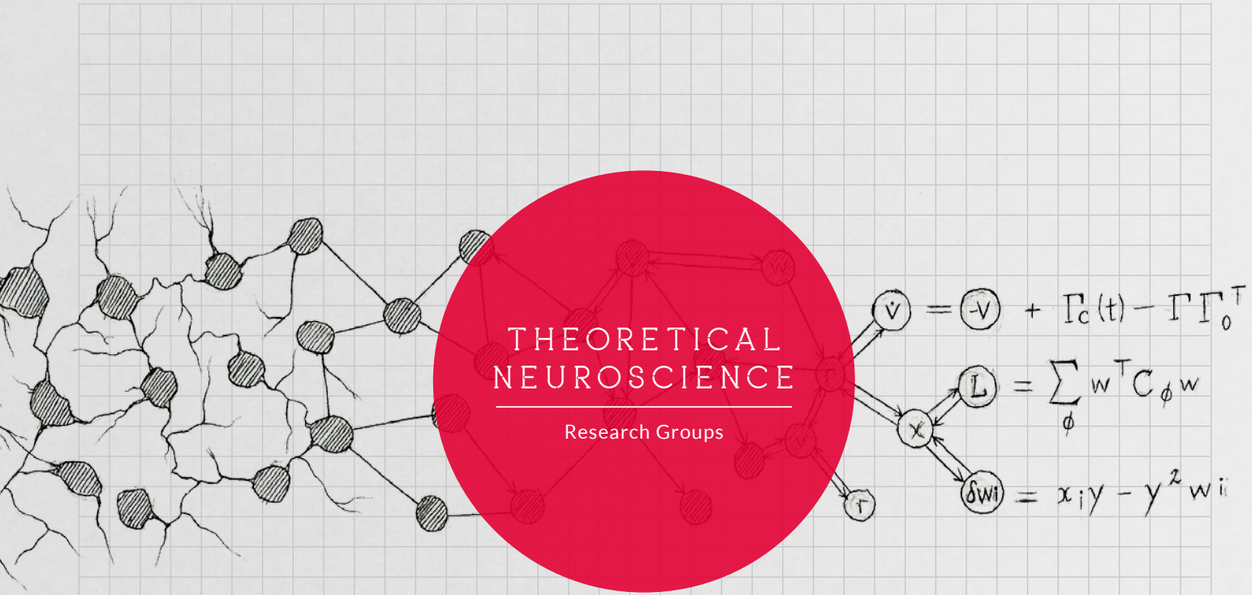
ZACH MAINEN (CNP)

5HT and male sexual behaviour

5HT has been implicated in a variety of behavioural phenomena, from sleep, to feeding, but also sexual behaviour. Using optogenetic tools which give us high temporal precision for neuronal manipulation we are investigating the impact of 5HT release in male sexual behaviour.

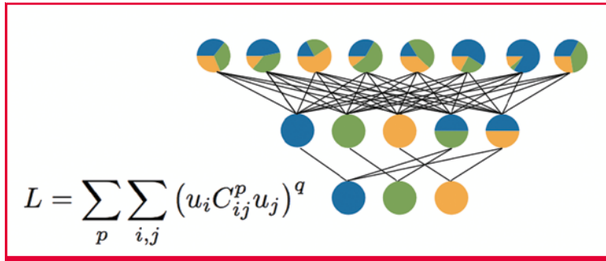
ADDITIONAL COLLABORATORS

MARTA MOITA (CNP):
Social Transmission of Fear



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.



KEY PUBLICATIONS

Weber F, Machens CK, Borst A (2012) *Disentangling the functional consequences of the connectivity between optic-flow processing neurons.* **Nat Neurosci 15:441-448.**

Machens CK, Romo R, Brody CD (2010) *Functional, but not anatomical, separation of "what" and "when" in prefrontal cortex.* **J Neurosci 30 (1):350-360.**

Wohrer A, Romo R, Machens CK (2010) *Linear readout from a neural population with partial correlation data.* **Adv Neural Inf Process Syst 23.**

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Bruno Ceña
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Postdoctoral Researcher

David Barrett, PhD
Postdoctoral Researcher

FUNDING

ECOLE NORMALE SUPERIEURE, PARIS, FRANCE

COLLABORATORS

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(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

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 Prefrontal Cortex (PFC) of monkeys and rodents during Two Alternate Forced Choice (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.

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.

FUNDING

ECOLE NORMALE SUPERIEURE, PARIS, FRANCE

Control of cerebral energy metabolism

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.

FUNDING

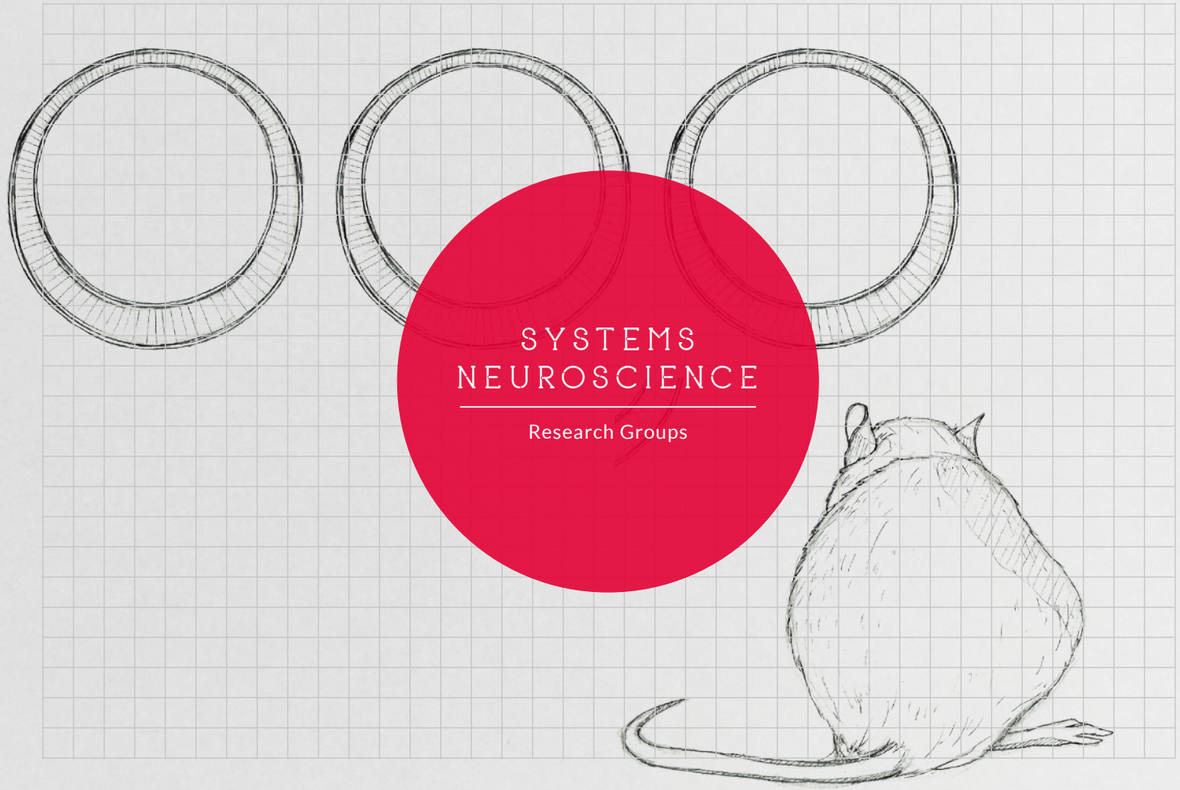
ECOLE NORMALE SUPERIEURE, PARIS, FRANCE

COLLABORATORS

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

Dynamics of an oculomotor integrator revealed by instantaneous optogenetic perturbations

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: Gonçalves P, Arrenberg A, Baier H, Machens CK (2012). Dynamics of an oculomotor integrator revealed by instantaneous optogenetic perturbations.



SYSTEMS NEUROSCIENCE

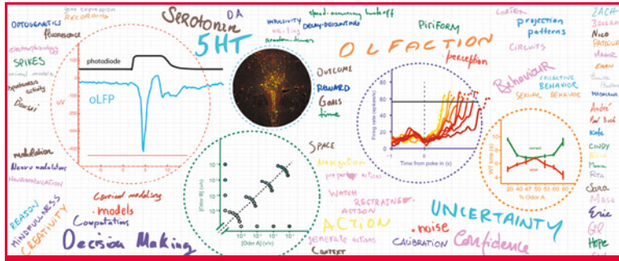
Research Groups

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 to 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



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FUNDING

EUROPEAN RESEARCH COUNCIL (ERC)

COLLABORATORS

SUSANA VALENTE, SUSANA LIMA (CNP)

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 are using optogenetic methods that target 5-HT neurons, gaining access to record and perturb this system optically with high temporal and genetic specificity. We are combining 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. Recently, we developed a new methodology that allows us to calibrate expression levels of ChR2 and placement of fiberoptic delivery in the DRN *in vivo* as well as a bulk imaging system to detect 5-HT neuron activity using genetically-encoded calcium sensors in behaving animals. With respect to sensory function, we have found that 5-HT stimulation inhibits spontaneous and odour-evoked activity in the piriform cortex and also decreases behavioural sensitivity to nociceptive stimuli (manuscript in preparation). In the motor system, we have examined the effect of 5-HT stimulation on locomotion in the home cage and open field and performed detailed characterisation of the effects on mice performing a water-reinforced nose poke and an impulse control (waiting) task. Preliminary results suggest inhibitory effects on these behaviours. We have also begun testing the impact of 5-HT activation in the context of sexual behaviour, in which we hypothesised an enhancement of satiety. Finally, we have begun to implement methods for expressing ChR2 and other reporters in a pathway and cell-type specific or an activity-dependent manner.

FUNDING

HUMAN FRONTIERS SCIENCE PROGRAMME (HFSP)

COLLABORATORS

ALEX POUGET (University of Geneva)

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. In recent work, we demonstrated large differences in speed-accuracy trade-offs (SATs) between odour detection and categorisation, (manuscript submitted).

We developed a computational model of these tasks, which can be fit to the data, and which has allowed us to formalise the hypothesis that SAT is problem-specific and suggesting that the locus of performance-limiting noise is a critical variable (manuscript in preparation). The model postulates, that categorisation decisions are limited by trial-to-trial variability in the decision boundary, a prediction that was independently verified by conditional trial analysis (manuscript in preparation). Finally, we began the development of a task for testing probabilistic inference using spatial contextual cues on an olfactory sensory identification problem.

FUNDING

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

COLLABORATORS

HANAN SHTEINGART, YONATAN LOWENSTEIN (Hebrew University)

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. Recently, we documented neural correlates of action timing in the premotor and medial prefrontal cortices, documenting two classes of waiting-time predictive neurons (manuscript submitted). We established a head-fixed version of the waiting-time task and we began testing optogenetic interventions in these contexts. We also developed two new tasks, including a grid maze task in which we can manipulate the availability of potential action options.

FUNDING

CHAMPALIMAUD FOUNDATION

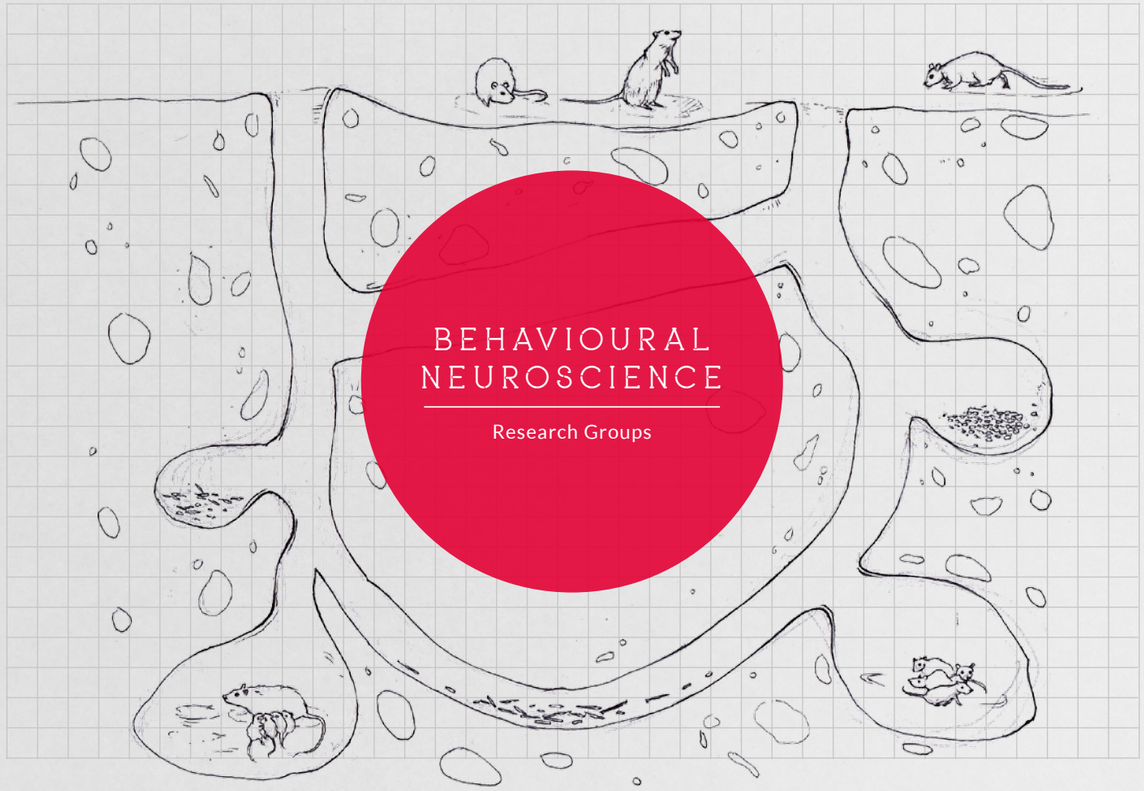
COLLABORATORS

ALEX POUGET (University of Geneva)

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 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. An important issue we wish to address is how confidence is "calibrated" such that subjects have an accurate estimate of their performance. These experiments will give us further insights into the nature of the neural processes underlying confidence estimation. Recently, in rats, we found that inactivation of the rat orbitofrontal cortex impairs confidence reporting but

not choice behaviour suggesting that confidence-related neural activity in the OFC is causally related to confidence judgments (manuscript under review). We used chronic multi-electrode recordings to assay neural ensemble function in the olfactory tubercule of rats performing a confidence reporting task together with a reward value manipulation (study in progress). In humans, we tested confidence reporting tasks similar to those we deployed in rats under several different psychophysical paradigms. We aim to use manipulations to test whether there are task-general as well as task-specific mechanisms for confidence calibration.



BEHAVIOURAL NEUROSCIENCE

Research Groups

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 animal respond to the distress of con-specifics. We chose fear learning since 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

CHAMPALIMAUD FOUNDATION

COLLABORATORS

ALFONSO RENART
(Champalimaud Neuroscience Programme)

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 memory and in the case of long intervals they rely on episodic memory between the two stimuli, where in the case of a short interval rats rely on working memory.

We have successfully set-up a single-unit recording system to record the activity of populations of simultaneously recorded neurons in medial prefrontal cortex. As we are recording neural activity during a single training and testing session, maximising the number of simultaneously recorded cells is crucial. We have now recorded about 30 single-units and another 30 multi-units from 3 rats. Currently we are running more experiments and analysing existing data.

FUNDING

CHAMPALIMAUD FOUNDATION

Cooperation in social dilemmas in rats

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 underlying the decision to cooperate or defect.

To this end we are using the Stag Hunt game, a coordination game in which the best thing to do is the same as the other subject, and where the choice of cooperating entails a higher risk than defecting.

We have established a Stag Hunt game for rats using an automated double T-maze. First, we established that rats learn to coordinate in order to maximise food rewards, that they are not just following the other rat and that they prefer the safer choice to the risky choice. We have started to run this game as a simultaneous choice game between to freely choosing agents.

FUNDING

CHAMPALIMAUD FOUNDATION
BIAL FOUNDATION

COLLABORATORS

SUSANA LIMA
(CNP)

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 are investigating the sensory cues that mediate this process, how these are perceived by the brain and how they come to trigger freezing. In addition, as vicarious freezing requires prior experience with shock, we are studying how prior self-experience with the aversive stimulus contributes to this process.

Having discovered that rats freeze to the silence that result from freezing by a con-specific, we have focused on developing tools to study the neural mechanisms underlying this process. We are optimising the use of optogenetics which allows for temporally

precise manipulation of neural activity. In addition, we found that footshock or contextual fear learning are not sufficient to drive vicarious freezing. It seems that learning to associate one's own freezing with shock may be important for normal vicarious freezing.

COLLABORATORS

REGINA SULLIVAN
(New York University, USA)

Social buffering of fear

Social interactions can decrease anxiety and fear in a variety of circumstances, 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.

In parallel, we have started to examine the effects of social buffering in the context of maternal behaviour. In essence we are testing whether the presence of pups promotes a switch in the defensive behaviours of mothers from passive to active. This would ensure a proper defensive reaction which would protect the pups form potential threats.

Previously we found that social buffering has long lasting effects on fear. Currently we are testing the role of oxytocin in the central nucleus of the amygdala (CeA), a major output station that controls several defence responses. Preliminary data suggests that blocking oxytocin in CeA blocks the immediate and long lasting effect of social buffering on freezing. In addition, we have successfully developed a protocol to study the regulation of fear in dams by the presence of pups.

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.

Rats are trained in a double T-maze, where they nose-poke to access rewarded arms. The focal rat can choose to reward a conspecific or not, depending on the arm where it nose-pokes. Rats showed a clear preference for the cooperation side (providing food to the recipient rat). Detailed characterisation of the behaviour in the maze showed that cooperation trials are shorter, possibly benefiting the cooperator. Finally, focal rats seem to gaze more to the recipient rat in cooperative trials.

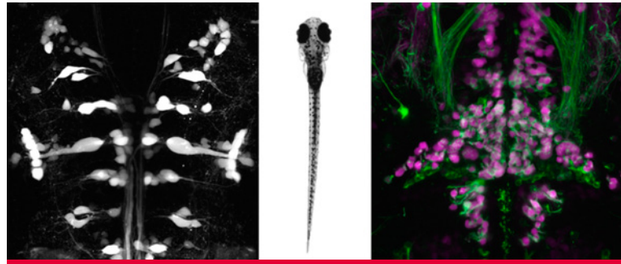
VISION TO ACTION

Research Groups

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 the zebrafish as a model organism because it allows us to visualize and manipulate activity in neural circuits throughout a vertebrate brain. As early as one week post-fertilization, zebrafish display a rich repertoire of innate visual behaviours, following moving patterns, avoiding predators and tracking and capturing live prey. With no skull and transparent skin, the entire volume of the brain can be imaged non-invasively in one field of view, and many neurons are individually identifiable from fish to fish. 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.

KEY PUBLICATIONS



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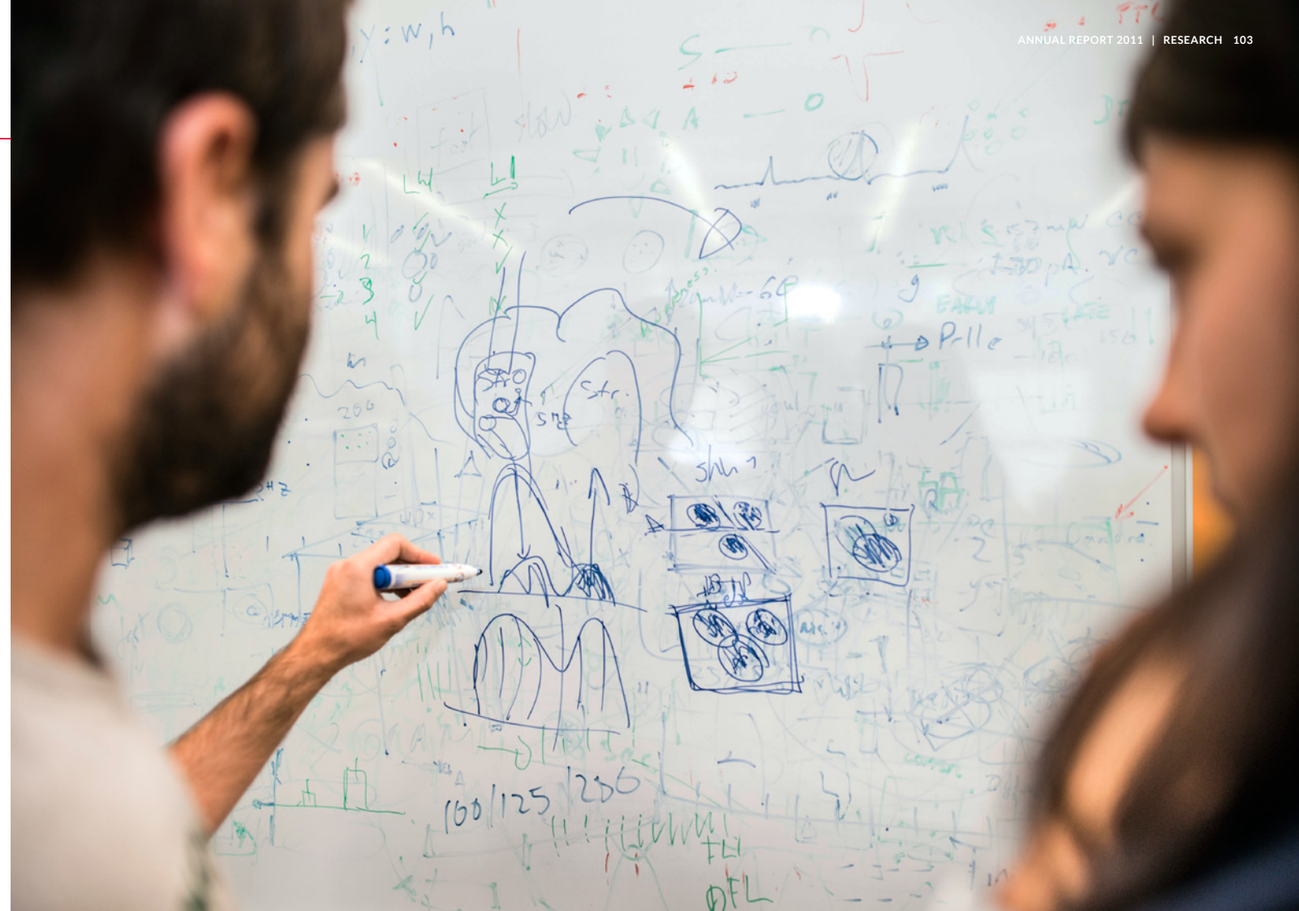

FUNDING

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.

FUNDING

MARIE CURIE CAREER INTEGRATION GRANT

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.

COLLABORATORS

RUBEN PORTUGUES;
FLORIAN ENGERT
(Department of Molecular and Cellular Biology, Harvard University, USA)

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. Presentation of different stimuli, such as monocular, or binocularly conflicting gratings allows us to determine what sensory or motor signals are represented at each point. These experiments represent the first comprehensive analysis of the neural circuit underlying a sensorimotor behaviour in a vertebrate brain.

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:

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 dynamics of population activity in the optic tectum and other visual areas, when the fish is presented with competing visual targets.

Using optogenetics and laser ablations we will interfere with defined circuit components, to determine the link between circuit computations and behaviour.

FUNDING
CHAMPALIMAUD FOUNDATION

How zebrafish respond to changes in illumination

Larval zebrafish show several 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 can be combined with different reporter lines to optogenetically activate or silence these populations, and record activity in freely swimming fish using GFP-Aequorin.

FUNDING
CHAMPALIMAUD FOUNDATION

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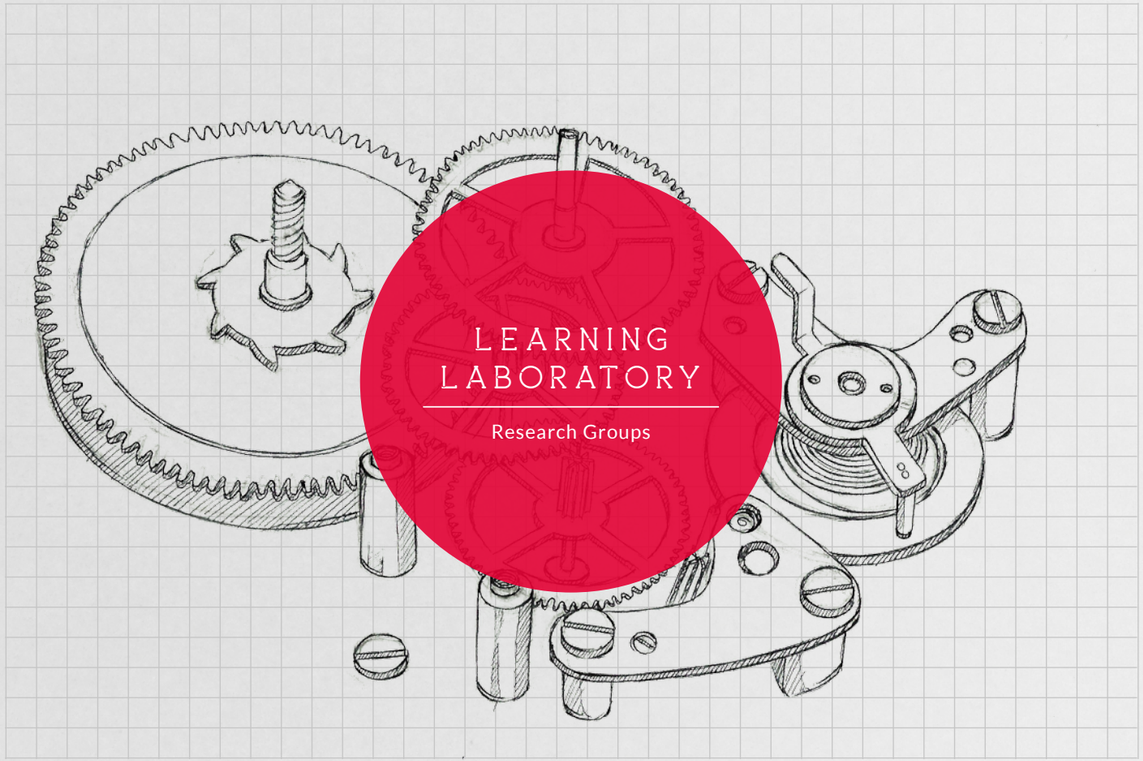
REX A. KERR;
DOUGLAS S. KIM
(HHMI Janelia Farm Research Campus, Ashburn, Virginia, USA);

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 signalling 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 characterizing 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.



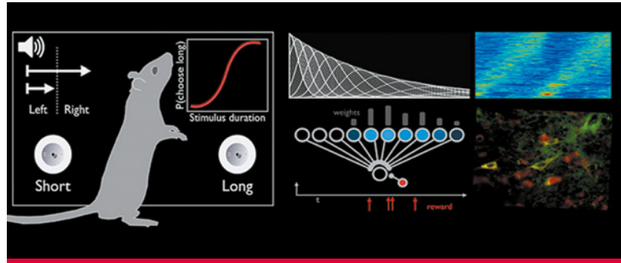
LEARNING LABORATORY

Research Groups

JOE PATON
Principal Investigator

Learning to adaptively respond to cues in the environment that predict behaviourally relevant events is critical for survival. However, in the natural world, where animals are exposed to a myriad of 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, lack of randomness in the time of occurrence of cues 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 time. We aim to reveal neural mechanisms for time by observing and manipulating neurophysiology in behaving rodents performing tasks that lead them to estimate intervals.

KEY PUBLICATIONS



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FUNDING

HHMI JANELIA FARM VISITING SCIENTIST PROGRAMME

COLLABORATORS

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(Janelia Farm Research Campus, USA)

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.

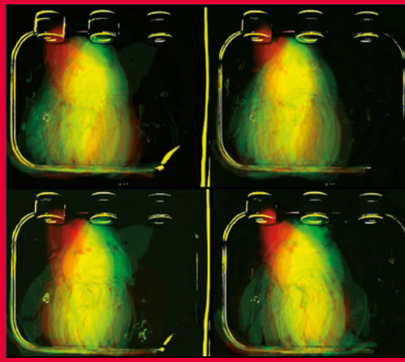
We have finalised the design of the electronics and are currently testing the hardware and developing software for use in all of our experimental paradigms.

FUNDING

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

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.We have moved forward significantly in this project by training mice on a two alternative forced choice temporal discrimination task, as well as by acquiring and expanding a transgenic rat line that will allow us to optogenetically manipulate midbrain dopamine neurons



TIME: AN EMBODIED PROCESS?
Images from four sessions of a rat trained to make perceptual decisions about stimulus duration. Stimuli lasting longer/shorter than a fixed standard time (1.5 seconds) indicate reward availability on the leftward/rightward option. Trials where the animal chose left (long)/right (short) are colored red/green. The frames reflect the moment before stimulus offset. Trials where the animal has progressed more/less through a behavioral sequence at stimulus offset will result in a long/short choice, suggesting animals may use ongoing behavior to time.

during timing behaviour. In addition, mice have been trained in a reward probability matching task to allow us to quantitatively test hypotheses about the role of dopamine in value-based decision-making.

FUNDING

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

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 framework 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 have submitted a manuscript reporting on these experiments (Mello, G. M., Soares, S., and Paton, J. J.. A re-scalable population code for time in the striatum). We have trained more rats and plan to begin simultaneous recordings in cortex and the basal ganglia to better understand how the neural signals we have already recorded are constructed.

FUNDING

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

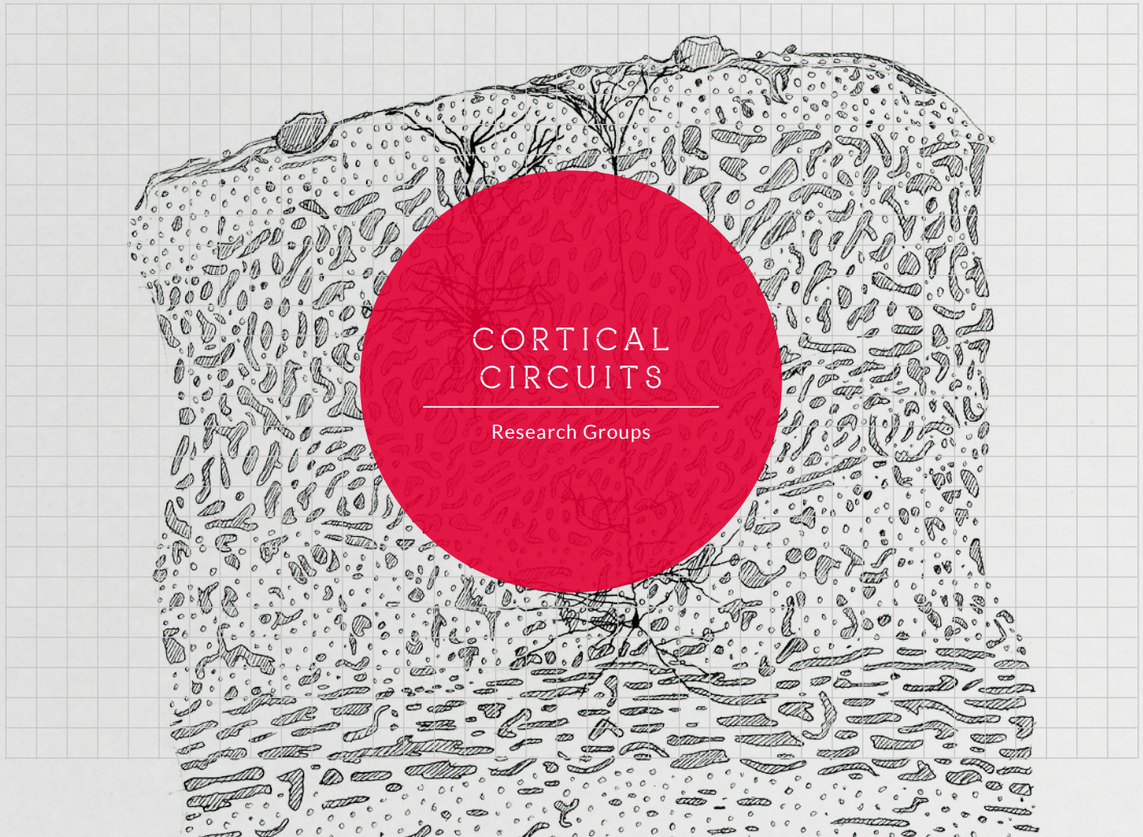
Neurometric - Psychometric comparison of interval timing performance

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.

We are testing hypotheses about how time is encoded in neural populations generated by the experiments described above, by recording neural activity in the same brain area (striatum) during this two alternative forced choice temporal discrimination task. Recording studies are ongoing. In addition, we have begun to train transgenic rats that will allow us to optogenetically manipulate dopamine neurons, that have been implicated in action production, learning, and timing, during this task.

ADDITIONAL COLLABORATIONS

ADAM KAMPFF, CNP:
learning how to interact with a dynamic environment: the role of motor cortex.



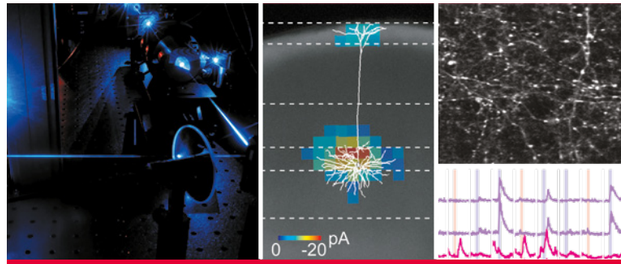
CORTICAL CIRCUITS

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 the 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.

KEY PUBLICATIONS



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* equal contribution

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Francisco Semedo
Lab Manager

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.

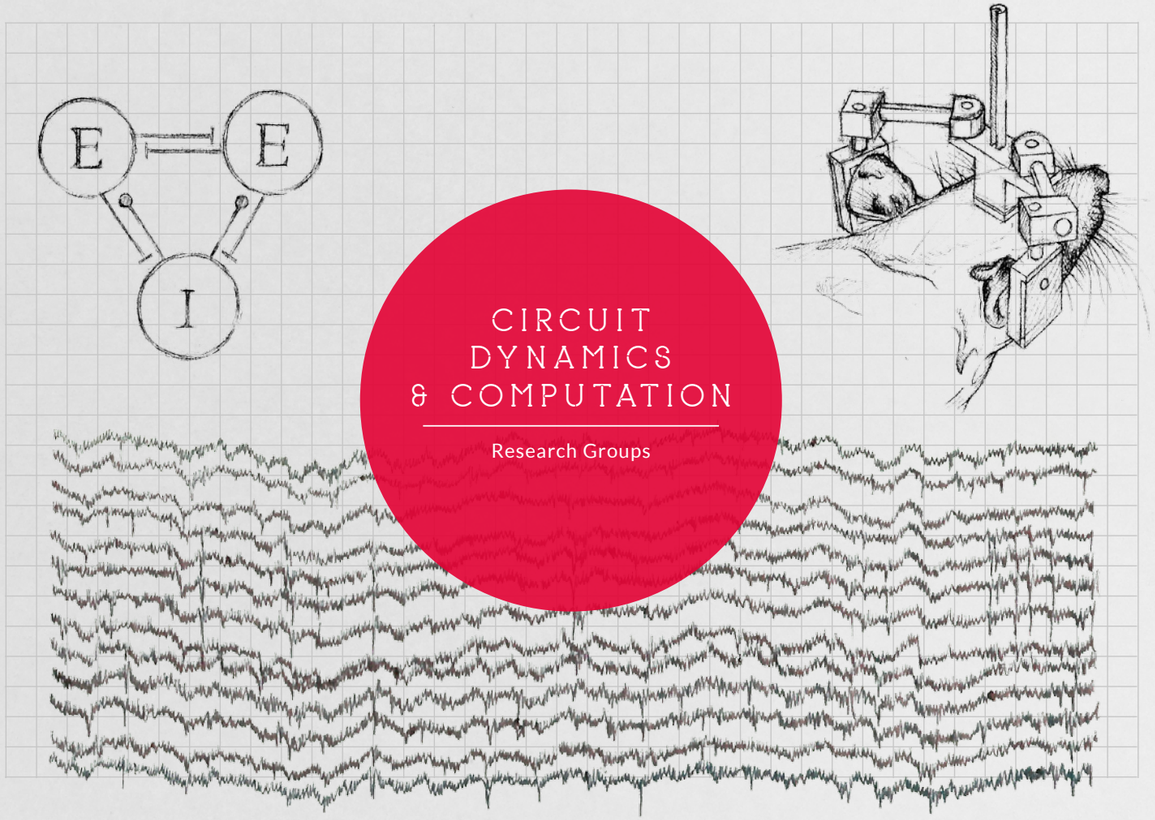
FUNDING

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. Recording 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.



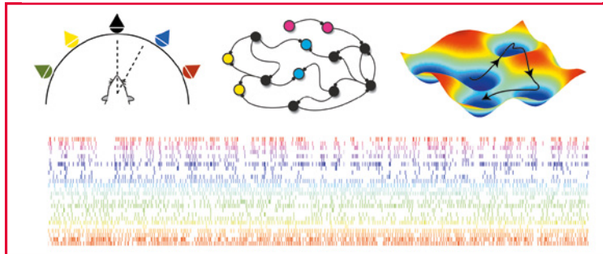
CIRCUIT DYNAMICS & COMPUTATION

Research Groups

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 evolves around two lines of research: sensory perception in the auditory modality, 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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* equal contribution

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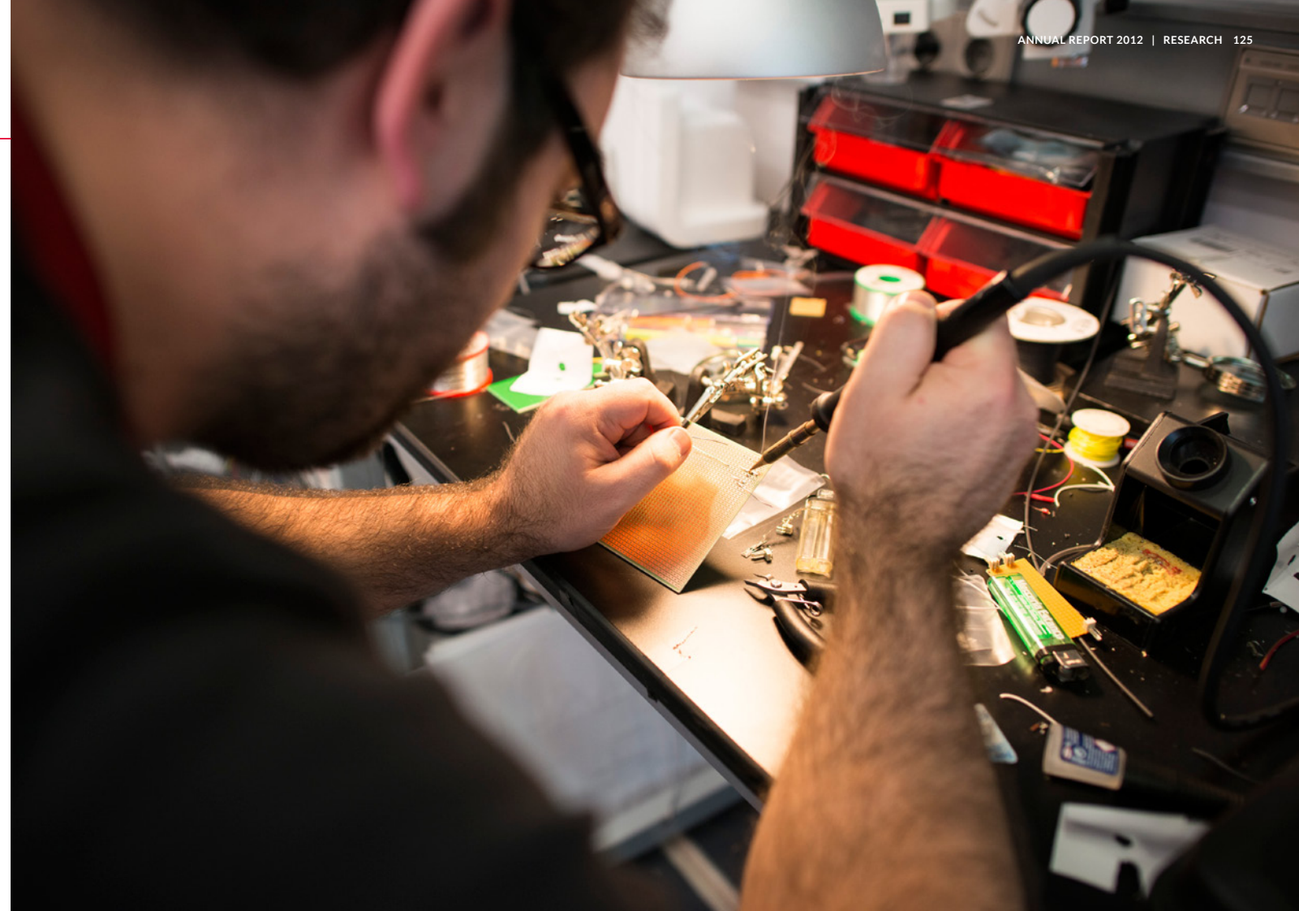
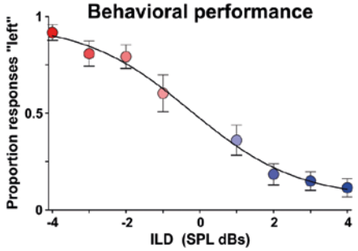


FUNDING

FP7-PEOPLE: MARIE CURIE CAREER INTEGRATION GRANT;
FP7-COOPORATION;
CHAMPALIMAUD FOUNDATION

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 localization 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 feedback influences in perception.



Behavioural performance in a sound discrimination task in which the inter-aural level difference (ILD) is used to generate a lateralised percept.

FUNDING

INTERNATIONAL HUMAN FRONTIERS SCIENCE PROGRAMME YOUNG INVESTIGATOR AWARD

COLLABORATORS

PAUL CHADDERTON
(Imperial College 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

Behaviour is the ultimate phenotypic output of organisms, arising from an interplay between an animal's brain, its body and the external world. 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 and mating 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 need of the fly.

KEY PUBLICATIONS

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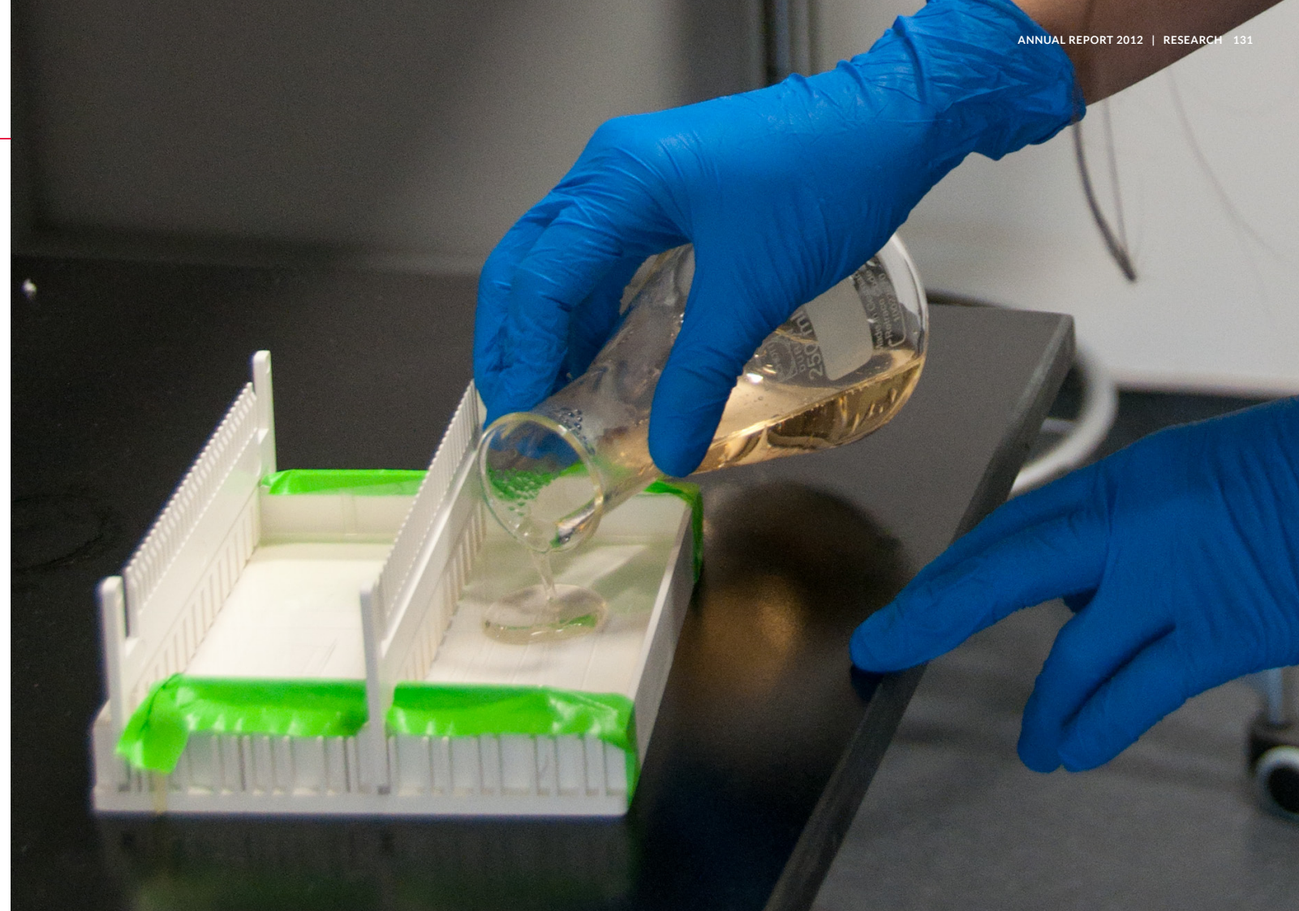


FUNDING

CHAMPALIMAUD FOUNDATION

COLLABORATORS

MATTHEW PIPER;
LINDA PARTRIDGE
(Institute of Healthy Ageing,
University College London, UK)

What are the exact nutritional variables affecting nutritional decisions?

Animals choose which macronutrient to eat according to their current internal nutrient status and optimise the protein to carbohydrate ratio in their diet to maximise their evolutionary fitness in terms of lifetime egg production. One of the cornerstones of our work is the use of an ethologically relevant behavioural paradigm to study nutrient homeostasis. For this we use yeast as nutritional source complementing the carbohydrate sucrose. In the field it is well accepted that yeast is mainly used by flies as a protein and, therefore, amino acid source. While yeast is likely to be the protein source for flies in the wild the use of yeast has many experimental disadvantages ranging from the poorly controlled nutrient content, the fact that it is not possible to independently manipulate specific nutrients, to variations in the nutrient quality of the used yeast batch, which introduces experimental variability in experiments. Together with the laboratories of Dr. Matthew Piper and Prof. Linda Partridge at UCL we have been using chemically defined diets to dissect the contribution of specific nutritional components on nutrient homeostasis as well as specific life history traits.

FUNDING

HUMAN FRONTIERS SCIENCE
PROGRAMME (HFSP);
CHAMPALIMAUD FOUNDATION

COLLABORATORS

ALDO FAISAL
(Imperial College London, UK);
MICHAEL DICKINSON
(University of Washington, USA)

What are the behavioural strategies used by the animal to find, identify and decide which nutrients to eat?

At all life stages *Drosophila* make sophisticated cost-benefit analysis involving the use of limited energy stores to find optimal

feeding sites, where flies eat, mate, and lay eggs. In this HFSP funded collaborative project with the laboratories of Prof. Michael Dickinson at University of Washington and Dr. Aldo Faisal at Imperial College London, we use foraging behaviours as vehicles to enable high-throughput discovery of the neuronal and genetic factors of cost-benefit decision making in fruit flies. We use food choice experiments, in which an animal navigates to different food sources of varied composition, to provide a framework within which we can quantitatively assess feeding reward against the cost of imposed environmental constraints and the animal's internal state. We aim to combine these experiments with genetic manipulations of specific neuronal circuits to assess the role these circuits play in behavioural decision making.

FUNDING

FUNDAÇÃO PARA A CIÊNCIA
E A TECNOLOGIA (FCT);
BIAL FOUNDATION;
CHAMPALIAMAUD FOUNDATION

What are the molecular and cellular mechanisms used by the brain to identify what type of nutrients the animal needs and to change its behaviour to allow it to find and eat food containing the required nutrients?

At the centre of developing and deploying optimal strategies for nutrient uptake and utilisation lies the ability of the central nervous system to detect the availability of nutrients and to use this information to induce changes in the behaviour as well as metabolism of the animal. 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 neuronal whole-genome RNAi screens we

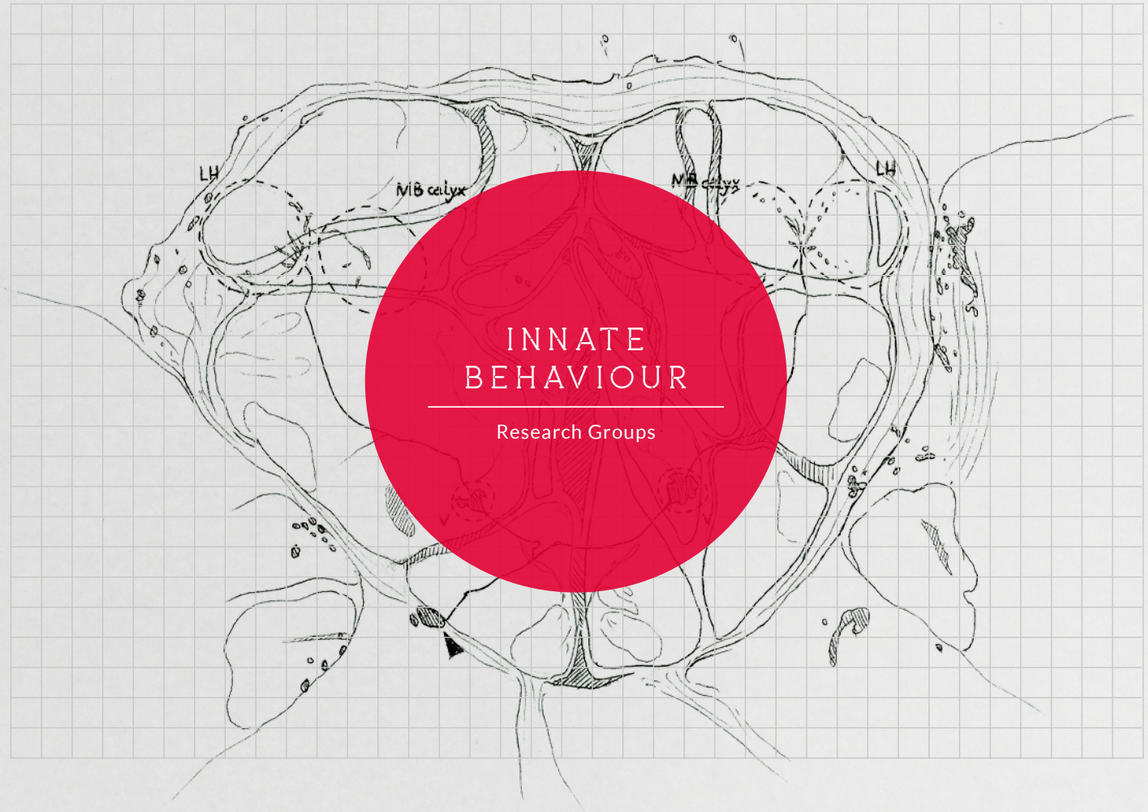
are investigating novel molecular mechanisms mediating nutrient homeostasis. Taken together these studies are providing us with an entry point for studying nutrient balancing and value-based decision making at the molecular level.

FUNDING

HUMAN FRONTIERS SCIENCE PROGRAMME (HFSP);
FP7 – PEOPLE (MARIE CURIE INITIAL TRAINING NETWORK GRANT: FLIACT);
CHAMPALIMAUD FOUNDATION

Which are the neuronal networks involved in nutrient homeostasis and what are the changes happening in them when the internal metabolic and mating state of the animal changes?

Currently only the neuronal population described by us to mediate the mating status of the fly is known to modulate nutrient homeostasis. To understand nutritional decision making it is essential that we identify and characterise further neuronal components controlling this important homeostatic behaviour. 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 identified neuronal substrates to understand how these neuronal populations act to guide feeding decisions. Being able to identify restricted sets of neurons is giving us the unique opportunity to make in depth analyses of the function of these neurons using activity imaging and electrophysiology as well as to characterise the molecular and cellular mechanisms acting in these neurons to mediate nutrient decisions.



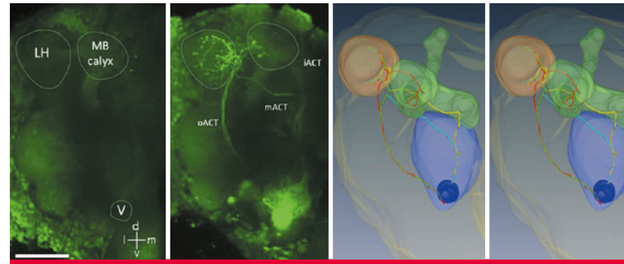
INNATE BEHAVIOUR

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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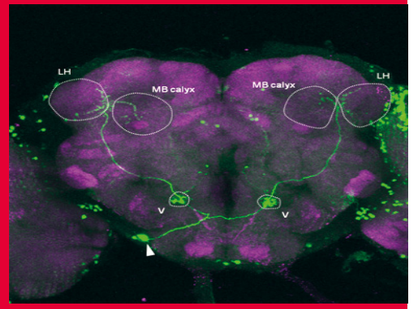
FUNDING

EUROPEAN COMMISSION FP7 - MARIE CURIE RE-INTEGRATION GRANT

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 have performed an intersecctional approach to pinpoint which of the apterous neurons are important for female receptivity. We found that removing the inhibition in cholinergic neurons rescues the phenotype. We have started setting up to further manipulate specifically the apterous neurons that are cholinergic. We have initiated a high throughput inactivation screen of Janelia Farm lines for female fertility.



SINGLE CELL PHOTOACTIVATION reveals a bilateral projection neuron that connects the v glomeruli to lateral horn and Mushroom body.

FUNDING

FUNDAÇÃO PARA A CIÊNCIA E TECNOLOGIA (FCT)

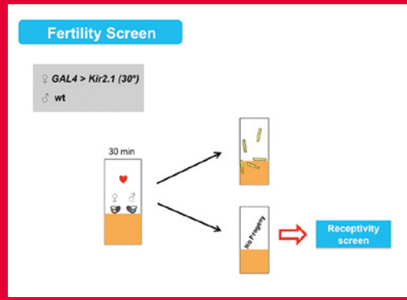
Across species stress odour response

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.

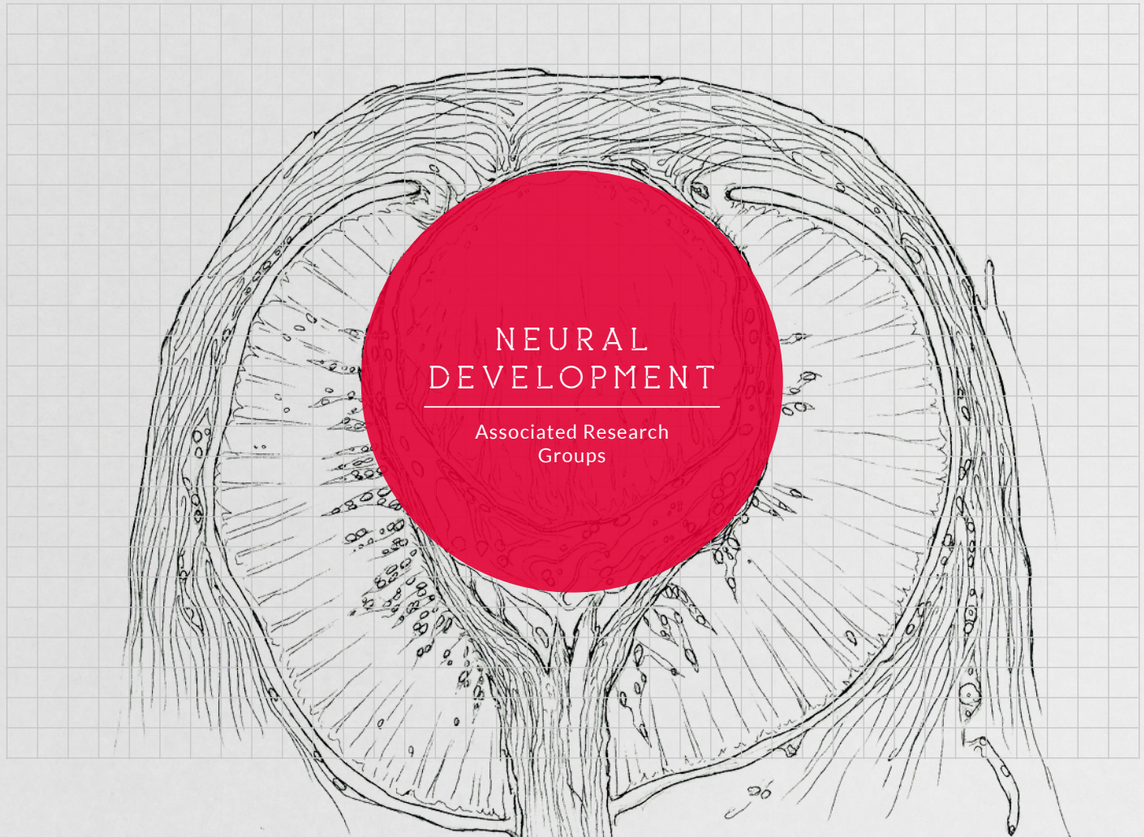
COLLABORATORS

ILONA KADOW (Max-Planck Institute of Neurobiology, Germany)

We identified an atypical projection neuron (PN) that connects CO2 sensory input bilaterally to the MB calyx. The group of Ilona Kadow as shown that the mushroom body (MB), the fly's learning and memory centre, is essential for CO2 avoidance behaviour exclusively in the context of starvation. Together we have submitted a manuscript. We began characterising third order neurons.



SCHEMATIC OF THE APPROACH TO SCREENING 1050 LINES.
We started with a fertility screen and will select the lines with a phenotype for a receptivity screen.



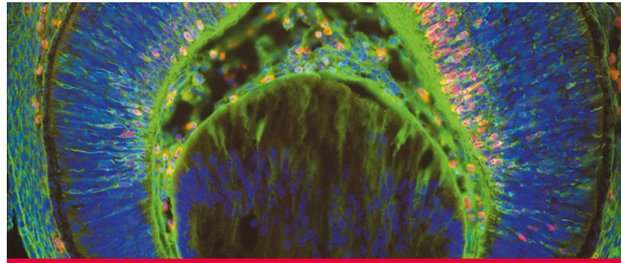
NEURAL DEVELOPMENT

Associated Research Groups

DOMINGOS HENRIQUE
Principal Investigator

Generation of tissues and organs during embryonic development relies on complex cell fate decision processes that establish the multitude of cellular types present in the body. Our work aims to provide a deeper understanding of how cell fate decisions are controlled at the single-cell level, while at the same time revealing how cell-cell communication functions to coordinate the proper assembly of tissues and organs. In the developing nervous system, our research allowed us to unravel how neuronal differentiation is controlled by the timing of Notch activity. We have also investigated how the pluripotent state is regulated in embryonic stem (ES) cells. By monitoring the activity of the pluripotency gene Nanog, combined with mathematical modelling, our work uncovered the existence of significant stochastic gene expression noise in individual ES cells, which we propose allow these cells to explore the pluripotent decision space. This research shall contribute to design more rational strategies to direct the *in vitro* and *in vivo* production of specific cell types, required to develop cell-replacement therapies in humans, aimed at regenerating damaged tissues and organs.

KEY PUBLICATIONS



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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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FUNDING

FUNDAÇÃO PARA A CIÊNCIA E TECNOLOGIA (FCT)

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 signalling plays a central role. Our work focuses 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.

FUNDING

FUNDAÇÃO PARA A CIÊNCIA E TECNOLOGIA (FCT)

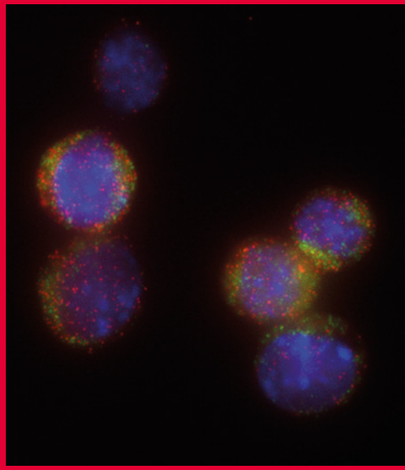
COLLABORATORS

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

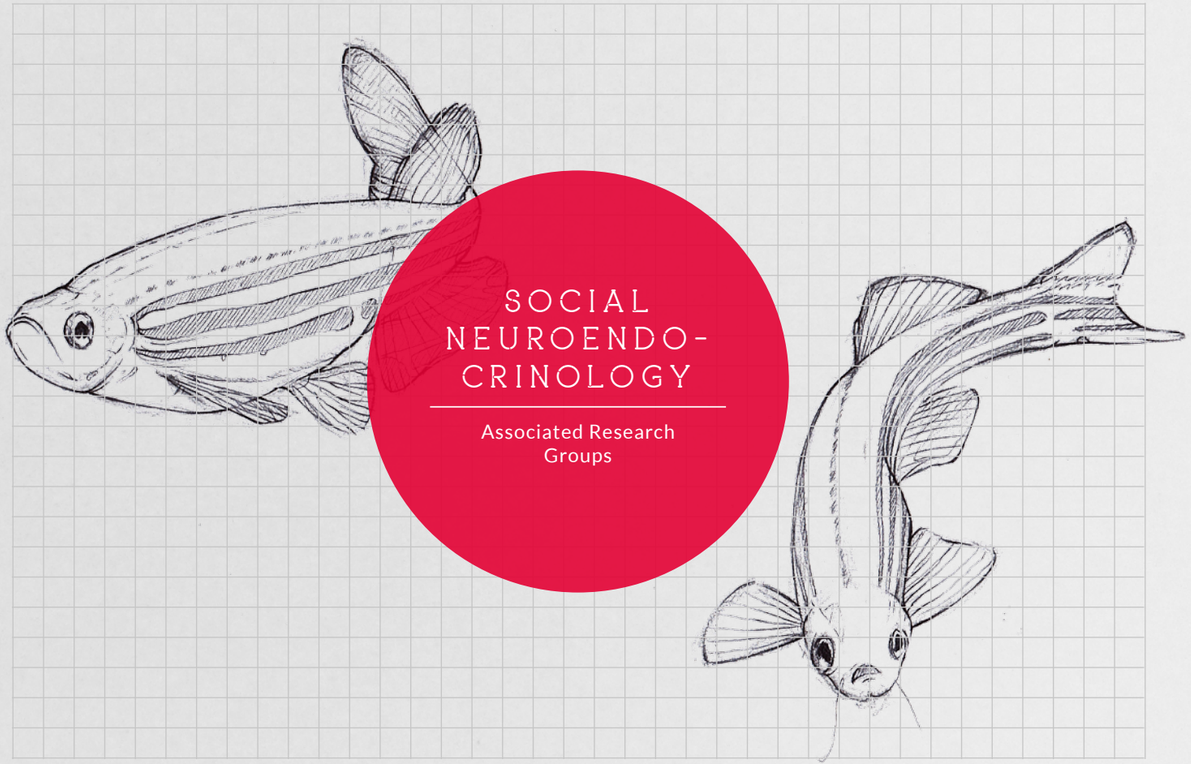
The key role of the dynamic nanog expression in pluripotent stem cells

Pluripotency in Embryonic stem (ES) cells is controlled by a dedicated gene regulatory network, above 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.



SINGLE-MOLECULE FISH RNA IN MOUSE EMBRYONIC STEM CELLS.
Expression of the embryonic stem cell RNA Nanog (red) and the RNA of a GFP-based fluorescent reporter (green) (nuclei in blue). Each dot represents a single RNA molecule.



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**.

Gonçalves DM, Saraiva JL, Teles M, Teodósio R, Canário AVM, Oliveira RF (2010) *Brain aromatase mRNA expression in two populations of the peacock blenny Salaria pavo with divergent mating systems*. **Horm Behav 57:155-161**.

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**.

LAB MEMBERS

Leonor Galhardo, PhD
Postdoctoral Fellow

Sílvia Costa, PhD
Postdoctoral Fellow

Ana Faustino
PhD Student

José Simões
PhD Student

Magda Teles
PhD Student

Rodrigo Abreu
2007 INDP PhD Student

COLLABORATORS

JORG BECKER
(Instituto Gulbenkian de Ciência, Oeiras, Portugal);
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 signalling 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 mediates the effects of prior 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.

COLLABORATORS

KOICHI KAWAKAMI
(Natl. Inst. Genetics, Japan)

Social learning in zebrafish

Social information can be collected 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.

COLLABORATORS

GEERT FLICK
(Nijmegen Univ. Netherlands)

Cognitive appraisal and cognitive bias in zebrafish

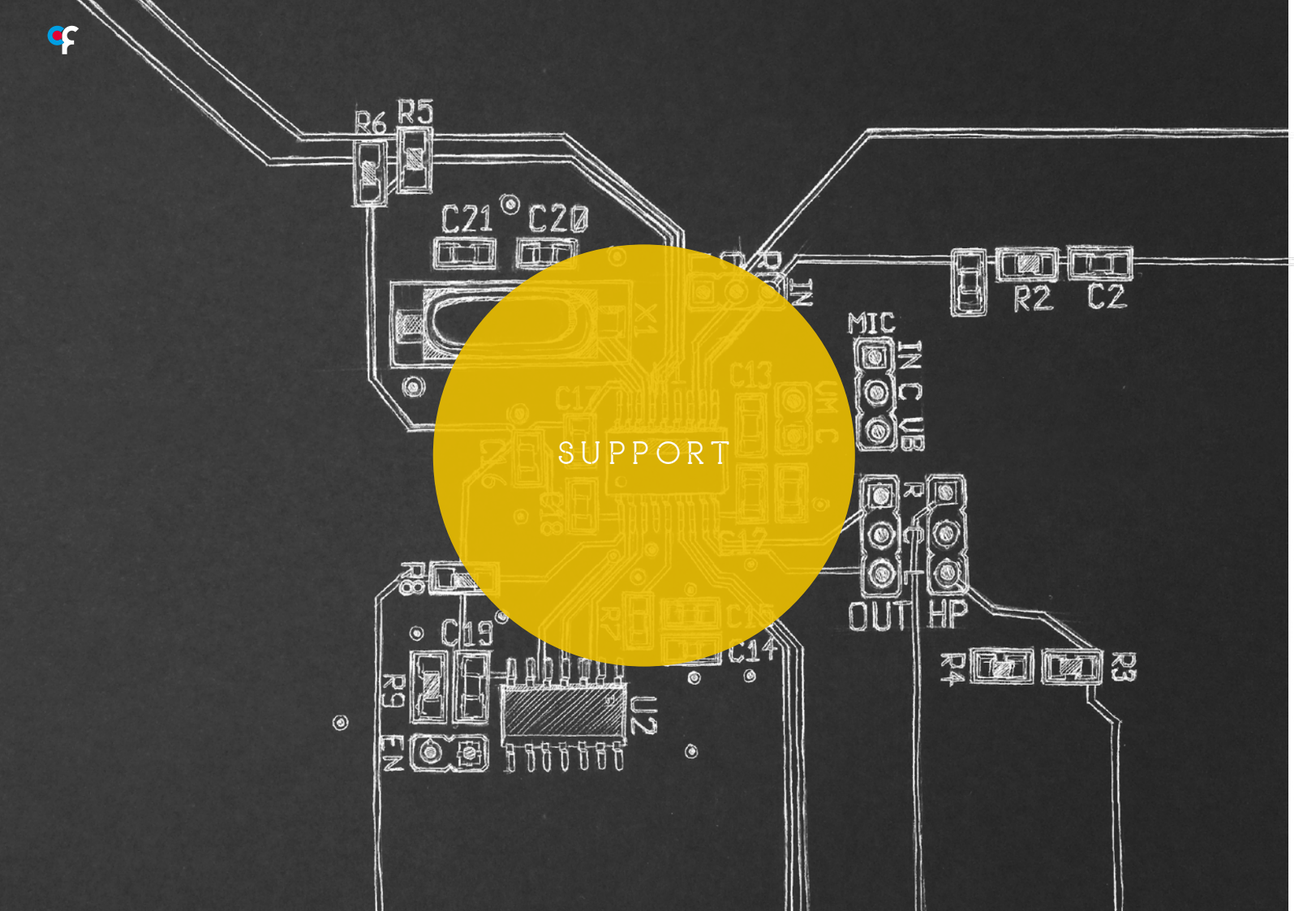
A central concept in social cognition is that what trigger a response to a stimulus are not only its intrinsic characteristics but rather the evaluation of what that stimulus or event means to that organism at that moment in time. Therefore, the exactly same event may elicit different responses, depending 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

DAVID GONÇALVES
(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 expressing 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

ADMINSTRATIVE SUPPORT

ALEXANDRA PIEDADE
Meetings and Courses

ANTÓNIO COELHO
Grants Manager

PHILIPP TSOLAKIS
Financial Manager / Controller

RAQUEL GONCALVES
Purchasing and Ordering

TERESA CARONA
Project Manager

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.

SCIENTIFIC AND TECHNOLOGICAL PLATFORMS

TÂNIA VINAGRE, PhD
Platforms Director

The mission of the Champalimaud Platforms is to assist the research and clinical community in achieving their experimental objectives, by providing key services and expertise targeted to increase the impact of the research being pursued at the Champalimaud Centre for the Unknown (CCU).

During 2012, the Champalimaud Platforms ran their daily operations at the Champalimaud Centre for the Unknown providing services for a fee at user's specific request. In 2012, Platforms performed 1 billing event in each semester.

During the first half of 2012 the Platforms also hosted a technology discussion forum called Technology Club. The main goal of this initiative was to share expertise and brainstorm how to implement interesting technologies that could have a high-impact on research at CCU.

GLASS WASH AND MEDIA PREPARATION PLATFORM

MARIA VITO
Platform Manager

Glass wash and media preparation are core functions, essential in any research institution. The Glass Wash & Media Preparation Platform (GWMP) supports laboratories and clinical units at the CCU by providing cleaning and sterilising services to labware such as glass and plastic instruments and by preparing high quality tissue culture and bacteriological media required for standard research protocols. This Platform is responsible for implementing and enforcing Biosafety and Waste disposal procedures.

During 2012 the GWMP Platform provided sterilisation services and a variety of media and solutions for the majority CNP groups, and well as for several clinical units and the Pharmacy in the Champalimaud Clinical Centre.

During this year, the GWMP Platform participated in the following projects:

Fractioning of HMDP Kits for 99mTc-labeling - The role of temperature and age of fractions
In this work for the Nuclear Medicine Service, the GWMP Platform was responsible for designing and implementing the proper bacteriological and sterility controls in the biosafety cameras and refrigerators used for performing the project's activities.

68-Gallium-DOTANOC - Utilisation of 68-Gallium for the evaluation of neuroendocrine tumors
In this project, the GWMP Platform collaborated with the Nuclear Medicine Service by preparing and decontaminating all glassware and preparing standardised solutions.

HISTOLOGY PLATFORM

ANA SANTOS
Platform Manager

LEO MADRUGA
Research Technician

The Histology Platform (HP) aids in the study of the microscopic anatomy of tissues and cells by sectioning of samples in very thin sections and staining them, using specific reagents, allowing identification of different structures, cells and microorganisms. The Histology Platform provides standard and custom histological services, support and training to researchers and to clinicians for diagnostic histopathology.

In 2012 the Histology Platform provided services to 10 CNP research groups, preparing about 370 samples for microscopic analysis. Besides the sectioning services, in 2012, the HP started performing histochemistry and immunohistochemistry procedures.

During this year the HP also started working with the Champalimaud Clinical Centre regarding pathological analysis of human samples. From July to December the HP technicians dealt with 217 samples.

VECTOR PRODUCTION PLATFORM

TATIANA
VASSILEVSKAIA, PhD
Platform Manager

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

In 2012 the VP Platform was responsible for:

Routine production of AAVs, which in 2012 totalled 18 batches;

Acquisition of virus-related plasmids from Addgene;

Establishing a comprehensive database of common CNP viruses stocks at the common CNP, in collaboration with the Scientific Software Development Platform;

Setting-up the production and concentration of an anterograde trans-synaptic viral tracer-H129 (Herpes simplex type-1);

Developing the production of highly efficient retrograde gene transfer (HiRet) vector;

Preparing for the production of delta G Rabies, which will initiate in early 2013.

FLY FACILITY

ISABEL
CAMPOS, PhD
Unit Manager

LILIANA COSTA
Research Technician

The core purpose of the CCU Fly Facility is to provide state of the art conditions for breeding, maintenance and manipulation of the fly *Drosophila Melanogaster*. The Fly Facility is available to all CCU researchers that use *Drosophila* as a model system in their experiments. This facility is maintained by dedicated, fulltime, expert staff that support state-of-the-art equipment and services.

During the year 2012, the Fly Facility provided several core services to both internal and external users.

As part of a collaboration with the Instituto Gulbenkian de Ciência (IGC), the facility produced fly food for all 12 IGC campus *Drosophila* groups, besides the 3 in-house fly groups – adding to more than 100 users on total. Fly food started being produced at the CCU in February 2012 and by the end of the year more than 10,000 liters of food had been cooked – enough to fill a 4x5m pond with 0.5m depth!

Besides food production, during 2012 the fly facility was also responsible for:

Maintenance and database management of common fly stocks for internal laboratories - almost 2000 stocks are kept in duplicate by the platform staff;

Fly stock ordering and quarantine - more than 600 stocks quarantined in 2012;

Maintenance of all rooms and state-of-the-art equipment, such as breeding and behaviour chambers and fly-pushing and dissection stations.

OPTICAL IMAGING & MICROSCOPY PLATFORM

JOSÉ RINO, PhD
Microscopy and Image Processing Expert

The Optical Imaging & Microscopy Platform provides access to a variety of cutting-edge light microscopes and image analysis software.

During 2012, the Optical Imaging & Microscopy Platform started providing specialised training and customised services to investigators and clinicians.

SCIENTIFIC HARDWARE PLATFORM

MATTHIEU PASQUET
Platform 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 at 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 DEVELOPMENT PLATFORM

JOSÉ CRUZ, PhD
Platform Manager

RICARDO RIBEIRO
Software Developer

The mission of the Scientific Software Development Platform is to provide engineering expertise and high-quality software support, in order to increase efficiency by controlling costs and reducing redundant efforts.

In 2012 the Platform offered services in several different domains, particularly:

Customised Scientific Software: video analysis and tracking software were developed in collaboration with laboratories;

Web Applications: rollout of the new CNP Website, CNP News, Retreat, Symposium and Shuffle Dating;

Processes Management Support: development of Customer Relation Management (CRM) and Databases to streamline the resources management;

Expert Consulting: in software engineering for research groups;

Teaching: INDP PhD Programme training.

VIVARIUM

NIKOL TSCHAEPE
Manager

RUI COSTA
Attending Veterinarian

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 specialized 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 scientific research.

TRANSGENIC & REDERIVATION UNIT

RUBINA CALDEIRA

JOANA ALMEIDA

The chief mission of the Transgenic & Rederivation Unit is to provide support to the research work of neuroscience investigators (and in the future the oncology programme). 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 an accepted method for cleaning animals from infectious agents. The rederivation process is 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. This year the unit hosted a workshop on microinjection techniques for both internal and external researchers.

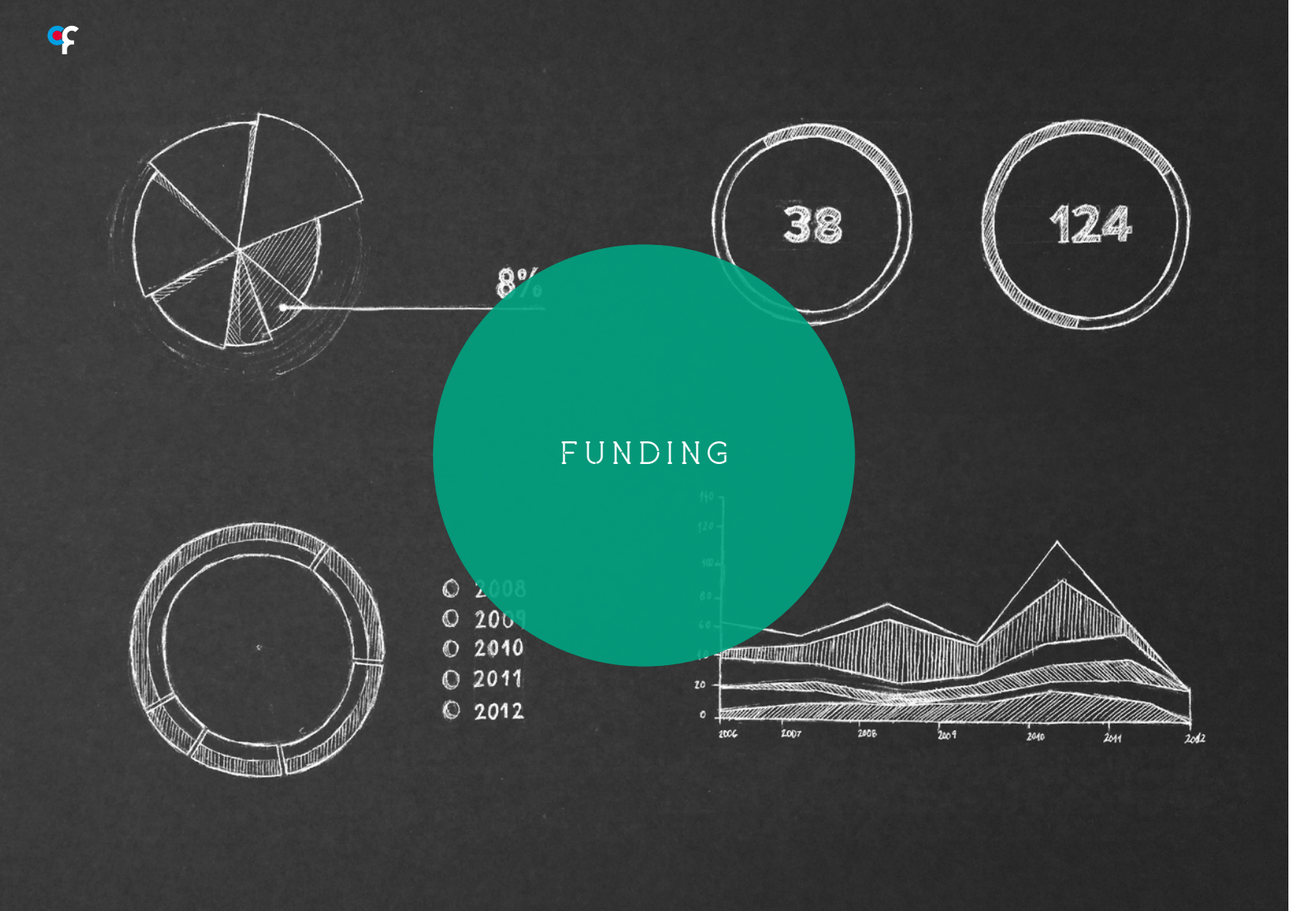
In addition to the services provided, the unit strives to stay at the forefront of new technologies and the development of new tools.

AQUATIC UNIT

ANA CERTAL, PhD

The primary function of the Aquatics Unit is to house, breed and maintain wild-type, mutant and transgenic fish in accordance with the health and welfare standards. The unit provides state-of-the-art research support services dedicated to the fish as a research model.

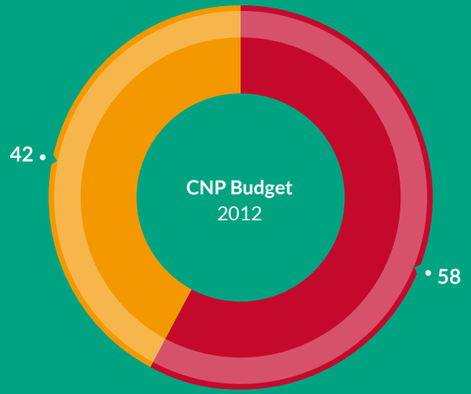
The Aquatics Unit provides the husbandry for zebrafish, which emerged in the last decade as one of the key vertebrate model in biomedical, developmental and behavioural studies. Zebrafish are particularly valuable research tools because they develop rapidly, have transparent bodies and can be easily 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 FACILITATE THE QUEST OF SCIENTISTS

TO UNDERSTAND HOW NEURAL CIRCUITS GENERATE BEHAVIOUR

AS OF DECEMBER 2012, **80** ACTIVE GRANTS AND FELLOWSHIPS WERE RUNNING AT THE CNP, CONSTITUTING NEARLY HALF OF THE CNP YEARLY BUDGET:



Results presented in %

- Internal Funding
- External Funding

THESE EXTERNAL FUNDS WERE AWARDED BY THE FOLLOWING AGENCIES AND ORGANISATIONS:

Results presented in %

- Fundação para a Ciência e a Tecnologia
- Human Frontier Science Program
- FP7-Ideas (European Research Council)
- Fundação Bial
- FP7-People (Marie Curie)
- FP7-Cooperation
- Howard Hughes Medical Institute
- Other (Austrian Academy of Science, Wellcome Trust, European Molecular Biology Organisation, more)

- RESEARCH GRANTS -

HOWARD HUGHES MEDICAL INSTITUTE INTERNATIONAL

Early Career Scientist Award
2012-2017
AWARDED TO MEGAN CAREY

Early Career Scientist Award
2012-2017
AWARDED TO RUI COSTA

FP7-COOPERATION
European Union

BrainFlight
2012-2014
AWARDED TO AN INTERNATIONAL GROUP OF INVESTIGATORS, INCLUDING RUI COSTA

NeuroSeeker
Investigation of local and global cortical circuits with advanced neural probes for high-resolution electrophysiological monitoring and optogenetic stimulation
2013-2017 (officially announced in 2012)
AWARDED TO AN INTERNATIONAL GROUP OF INVESTIGATORS, INCLUDING ADAM KAMPFF, LEOPOLDO PETREANU AND ALFONSO RENART

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

FP7-PEOPLE (MARIE CURIE)
European Union

Marie Curie Career Integration Grant
Sound Localisation by Neural Populations in the Rat Auditory Cortex
2013-2017 (officially announced in 2012)
AWARDED TO ALFONSO RENART

Marie Curie Career Integration Grant
The rules of connectivity of genetically-defined long-range projections
2013-2016 (Officially announced in 2012)
AWARDED TO LEOPOLDO PETREANU

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
Neural circuits underlying visually guided behaviour
2011-2015
AWARDED TO MICHAEL ORGER

Marie Curie Initial Training Network Grant
FLiACT - Systems neuroscience of Drosophila: from genes to circuits to behaviour
2012-2016
AWARDED TO CARLOS RIBEIRO

FUNDAÇÃO BIAL
Portugal

Bial Science Research Grant
Embodied cognition: the neural basis of time encoding in the brain?
2013-2016 (Officially announced in 2012)
AWARDED TO JOE PATON

Bial Science Research Grant
Spatial Attention
2013-2016 (officially announced in 2012)
AWARDED TO MICHAEL ORGER

Bial Science Research Grant
Interfacing Technology with the Brain: Novel materials for implantable neural devices
2013-2016 (officially announced in 2012)
AWARDED TO ADAM KAMPFF

Bial Science Research Grant
Defining the functional architecture of motion vision sensitive visual-motor circuit
2013-2016 (officially announced in 2012)
AWARDED TO EUGENIA CHIAPPE

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

Bial Science Research Grant
Effects of Conditional Foxp2 Deletion on Motor-Sequence Learning
2013-2015 (announced in 2012)
AWARDED TO RUI COSTA AND CATHERINE FRENCH

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
2011-2014
AWARDED TO CARLOS RIBEIRO

FUNDAÇÃO PARA A CIÊNCIA E A TECNOLOGIA (FCT)
Portugal

Research Project Grant
PZLOC (Peixe-zebra Locomoção)
2013-2015 (officially announced in 2012)
AWARDED TO MICHAEL ORGER

Research Project Grant
Decision confidence
2013-2015 (officially announced in 2012)
AWARDED TO ZACHARY MAINEN

Research Project Grant
Dopaminergic Neurotransmission
2012-2014
AWARDED TO RUI COSTA

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

Research Project Grant
Unravelling 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
Identifying and characterising the molecular mechanisms at the basis of nutritional decisions
2012-2015
AWARDED TO CARLOS RIBEIRO

INTERNATIONAL HUMAN FRONTIER SCIENCE PROGRAMME ORGANISATION (HFSPO)
International

HFSP Young Investigator Award
The dynamical basis of working memory in the prefrontal cortex
2012-2015
AWARDED TO ALFONSO RENART

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

HFSP Young Investigator Award
Value-based decision making in Drosophila foraging:
genes, computations and behaviour
2012-2015
AWARDED TO CARLOS RIBEIRO

- FELLOWSHIPS -

AUSTRIAN ACADEMY OF SCIENCE

DOC-fFORTE fellowship
Understanding the function of Hypocretin/Orexin expressing neurons in neural circuits controlling locomotor behaviour of larval zebrafish
2012-2015
AWARDED TO SIMONE LACKNER

CONSEJO NACIONAL DE CIENCIA Y TECNOLOGÍA

Estancias posdoctorales y sabáticas en el extranjero para la consolidación de grupos de investigación
Bi-direccionalidad estructural dependiente de la actividad sináptica en espinas dendríticas individuales: efecto de LTD mediado por receptores metabotrópicos de glutamato
2011-2012
AWARDED TO YAZMÍN CORTÉS

EUROPEAN MOLECULAR BIOLOGY ORGANISATION

Long - Term fellowship
Elucidating the molecular basis of food choice behaviour
2012-2014
AWARDED TO RICARDO GONÇALVES

FP7-PEOPLE (MARIE CURIE)
European Union

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

FUNDAÇÃO PARA A CIÊNCIA E A TECNOLOGIA (FCT)
Portugal

Postdoctoral Fellowship
2010-2013
AWARDED TO HOPE JOHNSON

Postdoctoral Fellowship
2012-2015
AWARDED TO PAVEL ITSKOV

Postdoctoral Fellowship
2009-2012
AWARDED TO MASAYOSHI MURAKAMI

Postdoctoral Fellowship
2012-2015
AWARDED TO CLAUDIA FEIERSTEIN

Postdoctoral Fellowship
2012-2015
AWARDED TO KENSAKU NOMOTO

Postdoctoral Fellowship
2012-2015
AWARDED TO MÁRCIA ARANHA

Postdoctoral Fellowship
2012-2015
AWARDED TO NÉLIA VARELA

Postdoctoral Fellowship
2012-2015
AWARDED TO ZITA SANTOS

Postdoctoral Fellowship
2008-2012
AWARDED TO CRISTINA AFONSO

Postdoctoral Fellowship
2011-2013
AWARDED TO FATUEL TECUAPELTA

PhD Fellowship
2012-2015
AWARDED TO JOÃO AFONSO

PhD Fellowship
2012-2015
AWARDED TO SILVANA ARAÚJO

PhD Fellowship
2012-2015
AWARDED TO JOAQUIM JACOB

PhD Fellowship
2012-2015
AWARDED TO RICARDO SILVA ZACARIAS

PhD Fellowship
2012-2015
AWARDED TO JENS BIERFELD

PhD Fellowship
2012-2015
AWARDED TO JACQUES BOURG

PhD Fellowship
2012-2015
AWARDED TO ROBERTO MEDINA

PhD Fellowship
2012-2015
AWARDED TO ANDRÉ LUZARDO

PhD Fellowship
2012-2015
AWARDED TO SOFIA SOARES

PhD Fellowship
2012-2015
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
2012-2015
AWARDED TO SAMANTHA HERBERT

PhD Fellowship
2012-2015
AWARDED TO CATARINA ALBERGARIA

INTERNATIONAL HUMAN FRONTIER SCIENCE PROGRAMME 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

HFSP Long Term Fellowship
Neural mechanisms underlying the encoding of contextual information in olfactory cortex
2012-2015
AWARDED TO CINDY POO

HFSP Long Term Fellowship
Covariations between population neuronal activity and choice: a sensory or cognitive origin?
2012-2015
AWARDED TO JOSE LUIS PARDO-VAZQUEZ

SWISS NATIONAL SCIENCE FOUNDATION

2012-2013
AWARDED TO SABINE RENNINGER

WELLCOME TRUST

UK

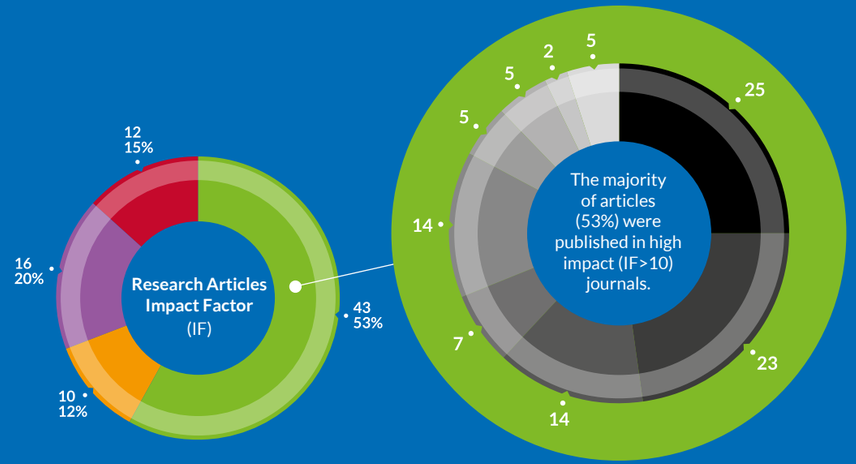
Postdoctoral Fellowship
The neural basis of goal-directed behaviour
2011-2015
AWARDED TO THOMAS AKAM

ADVANCING SCIENTIFIC KNOWLEDGE

WHILE ADVANCING THE SCIENTIFIC PROCESS ITSELF

A TOTAL OF **81** 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.

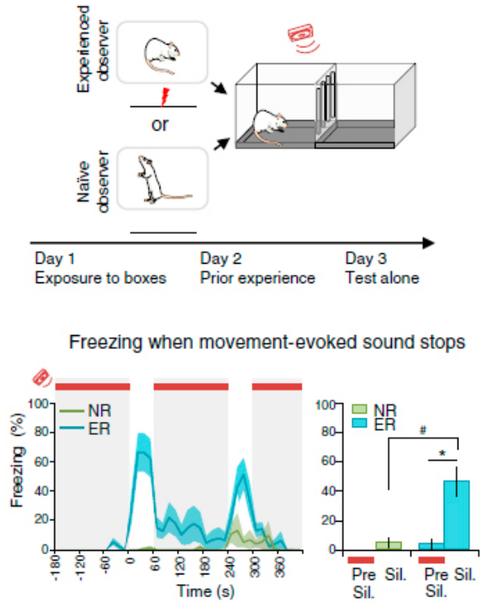


IF>10
5>IF>10
1>IF>5
IF undetermined

Results presented in %

Neuron
Nature
Nature Neuroscience
Nature Methods
Current Biology
Science
PloS Biology
Cell
Molecular Psychiatry

PI HIGHLIGHTS

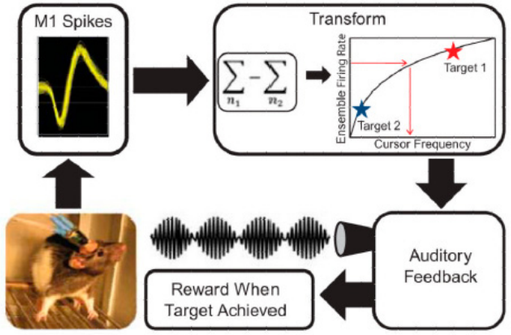


THE SOUND OF SILENCE

In this study, a new form of social communication between rats was discovered - Silence. Unexpectidly, not the sights, nor vocalisations, nor smell exchanges between cage-mates communicated the existence of a threat, it was the sound of silence resulting from the cessation of movement.

Figure adapted from: Pereira AG, Cruz A, Lima SQ, Moita MA (2012). Silence resulting from the cessation of movement signals danger. Curr. Biol. 22 (16): R627-R628.

PI HIGHLIGHTS

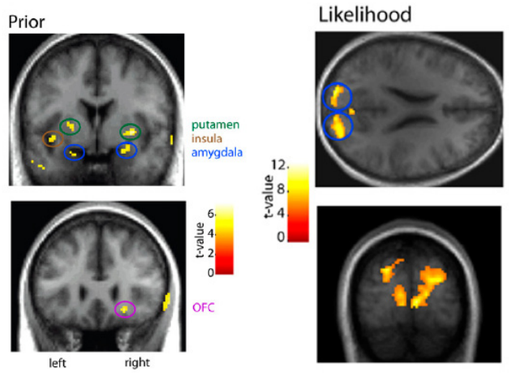


MICE OVER MATTER – HOW DO MICE LEARN TO CONTROL COMPUTERS WITH THEIR MINDS?

This study shows that mice can learn how to control the pitch of a sound emitted by a computer by thinking about it. It also shows that the learning of this new ability depends on functional connectivity between motor cortex and the striatum.

Figure adapted from: Koralek AC, Jin X, Long JD 2nd, Costa RM, Carmena JM (2012). Corticostriatal plasticity is necessary for learning intentional neuroprosthetic skills. Nature. 483(7389): 331-335.

INDP STUDENTS HIGHLIGHTS

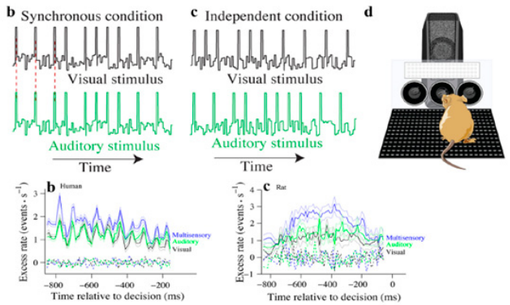


ARE YOU UNCERTAIN, OR ARE YOU UNCERTAIN?

When going through experiences, uncertainty can stem from two different sources: the past (prior experience) and the present (likelihood). In this study, it was discovered that these different types of uncertainty are generated in different brain regions, and that graded activation of both leads to optimal decision making.

Figure adapted from: Vilares I, Howard JD, Fernandes HL, Gottfried JA, Kording KP (2012). Differential representations of prior and likelihood uncertainty in the human brain. Curr. Biol. 22(18):1641-1648.

INDP STUDENTS HIGHLIGHTS



MULTISENSORY ENHANCEMENT – THROW ANOTHER ONE INTO THE MIX, IT CAN ONLY MAKE IT BETTER!

This study demonstrates that pinning down abstract features of a stimulus (in this case, rate) is easier when the feature is displayed to two different sensory modalities simultaneously (in this case, visual and auditory). Surprisingly, performance is enhanced even when the information is out of synch between the two modalities. As long as the two are played at the same time performance is better - in humans as well as in rats.

Figure adapted from: Raposo D, Sheppard JP, Schrater PR, Churchland AK (2012). Multisensory decision-making in rats and humans. J. Neurosci. 32 (11): 3726-3735.

PEER-REVIEWED RESEARCH ARTICLES

Afonso C, Paixão VB, Costa RM (2012). *Chronic Toxoplasma Infection Modifies the Structure and the Risk of Host Behaviour.* PLoS One 7(3): e32489.

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.

Akam T, Oren I, Mantoan L, Ferenczi E, Kullmann DM (2012). *Oscillatory dynamics in the hippocampus support dentate gyrus–CA3 coupling. Nat Neurosci.* 15(5):763-8.

Akam TE, Kullmann DM (2012). *Efficient "Communication through Coherence" Requires Oscillations Structured to Minimize Interference between Signals.* PLoS Comput Biol. 8(11):e1002760.

Akerboom J, Chen T-W, Wardill TJ, Tian L, Marvin JS, Mutlu S, Calderón NC, Esposti F, Borghuis BG, Sun XR, Gordus A, Orger MB, Portugues R, Engert F, Macklin JJ, Filosa A, Aggarwal A, Kerr R, Takagi R, Kracun S, Shigetomi E, Khakh BS, Baier H, Lagnado L, Wang S S-H, Bargmann CI, Kimmel BE, Jayaraman V, Svoboda K, Kim DS, Schreiter ER, Looger LL (2012). *Optimization of a GCaMP Calcium Indicator for Neural Activity Imaging.* J. Neurosci. 32(40): 13819-13840.

Aquino T, Abranches E, Nunes A (2012). *Stochastic single-gene autoregulation.* Phys. Rev. Lett. 85 (5): E85.

Bianco IH, Ma LH, Schoppik D, Robson DN, Orger MB, Beck JC, Li JM, Schier AF, Engert F, Baker R (2012). *The tangential nucleus controls a gravito-inertial vestibulo-ocular Reflex.* Curr. Biol. 22(14):1285-95.

Cardoso MM, Sirotin YB, Lima B, Glushenkova E, Das A (2012). *The neuroimaging signal is a linear sum of neurally distinct stimulus- and task-related components.* Nat. Neurosci. 15(9):1298-306.

Felsen G, Mainen ZF (2012). *Midbrain contributions to sensorimotor decision making. J Neurophys.* 108(1):135-47.

Hilario M, Holloway T, Jin X, Costa RM (2012). *Different dorsal striatum circuits mediate action discrimination and action generalization.* Europ. J. Neurosci. 35(7): 1105-1114.

Itskov PM, Vinnik E, Honey C, Schnupp J, Diamond ME (2012). *Sound sensitivity of neurons in rat hippocampus during performance of a sound-guided task.* J. Neurophysiol. 107 (7): 1822-1834.

Jacob V*,Petreanu L*, Wright N,Svoboda K and Fox K (2012). *Regular spiking and intrinsic bursting pyramidal cells show orthogonal forms of experience-dependent plasticity in layer V of barrel cortex.* Neuron 73 (2): 391-404.

Koralek AC, Jin X, Long JD 2nd, Costa RM, Carmena JM (2012). *Corticostriatal plasticity is necessary for learning intentional neuroprosthetic skills.* Nature. 483(7389): 331-335.

Miura K, Mainen ZF, Uchida N (2012). *Odour Representations in Olfactory Cortex: Distributed Rate Coding and Decorrelated Population Activity.* Neuron 74(6):1087-98.

Oliveira-Maia AJ, de Araujo IE, Monteiro C, Workman V, Galhardo V, Nicolelis MAL (2012). *The insular cortex controls food preferences independently of taste receptor signaling.* Front Syst Neurosci 6 (5).

Pereira AG, Cruz A, Lima SQ, Moita MA (2012). *Silence resulting from the cessation of movement signals danger.* Curr. Biol. 22 (16): R627-R628.

Pereira CS, Santos AJ, Bejerano-Sagie M, Correia PB, Marques JC, Xavier KB (2012). *Phosphoenolpyruvate phosphotransferase system regulates detection and processing of the quorum sensing signal autoinducer-2.* Mol Microbiol. 84 (1): 93-104.

Petreanu L, Gutnisky DA , Huber D, Xu N, O'Connor DH, Tian L, Looger L and Svoboda K (2012). *Activity in motor-sensory projections reveals distributed coding in somatosensation.* Nature 489(7415):299-303.

Raposo D, Sheppard JP, Schrater PR, Churchland AK (2012). *Multisensory decision-making in rats and humans.* J. Neurosci. 32 (11): 3726-3735.

Renart A, van Rossum MC (2012). *Transmission of population-coded information.* Neural Comput. 24(2):391-407.

Rousseau CV, Dugué GP, Dumoulin A, Mugnaini E, Dieudonné S, Diana MA. (2012). *Mixed inhibitory synaptic balance correlates with glutamatergic synaptic phenotype in cerebellar unipolar brush cells.* J. Neurosci. 32 (13), 4632-44.

Simões PM, Ott SR, Niven JE (2012). *A long-latency aversive learning mechanism enables locusts to avoid odours associated with the consequences of ingesting toxic food.* J. Exp. Biol. 215(Pt 10):1711-1719.

Vilares I, Howard JD, Fernandes HL, Gottfried JA, Kording KP (2012). *Differential Representations of Prior and Likelihood Uncertainty in the Human Brain.* Curr. Biol. 22(18):1641-1648.

Vinnik E, Itskov PM, Balaban E (2012). *6- And γ-band EEG power predicts illusory auditory continuity perception.* J Neurophys. 108(10):2717-24.

Weber F, Machens CK, Borst A. (2012). *Disentangling the functional consequences of the connectivity between optic-flow processing neurons.* Nat. Neurosci. 15(3):441-448.

SPECIAL CONFERENCE PUBLICATIONS

Bourdoukan R, Barrett D, Machens CK, Deneve S (2012). *Learning optimal spike-based representations. In: Advances in Neural Information Processing Systems 25.*

REVIEW ARTICLES

Feierstein CE (2012). *Linking adult olfactory neurogenesis to social behaviour.* Front. Neurosci. 6 (173): 1 -13.

Kepecs A, Mainen ZF. (2012). *A computational framework for the study of confidence in humans and animals.* Philos. Trans. R. Soc. Lond., B, Biol. Sci. 367 (1594), 1322-1337.

Paton JJ, Louie K (2012). *Reward and punishment illuminated. Nat.* Neurosci. 15 (6), 807-809.

Wohrer A, Humphries MD, Machens CK. (2012). *Population-wide distributions of neural activity during perceptual decision-making.* Prog Neurobiol. 103(2013): 156-193.

COMMENTS

Dias-Ferreira E, Costa RM (2012). *Neuroscience: The symphony of choice.* Nature. 484(7392): 42-43.

Machens CK (2012). *Neuroscience. Building the human brain.* Science. 338(6111):1156-1157.

Silva JA, Costa RM (2012). *Bursting for exploration.* Nature neurosci. 15(9): 1178-1179.

Vicente AM, Costa RM (2012). *Looking at the trees in the central forest: a new pallidal-striatal cell type.* Neuron. 74(6): 967-969.

* equal contribution

TO BE A HUB FOR SCIENTIFIC INTERACTION

ENGAGING OUR PEERS IN PRODUCTIVE EXCHANGE RATHER THAN COMPETITION

CHAMPALIMAUD NEUROSCIENCE SYMPOSIUM

30 September - 3 October 2012

Organisers:
Marta Moita and Maria Luísa Vasconcelos

Sponsors:
Thorlabs, Clever Sys, PhenoWorld, Go Natural, Zeiss, Fisher Scientific, Nature Communications, Tebu-Bio, Olympus, Ultragene, Aralab, Alfagene

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 Champalimaud Neuroscience Symposium. This meeting exemplified the broad scientific interests of the CNP. The programme, which included 21 distinguished speakers and two poster sessions, covered a broad range of areas within neuroscience, from cognitive science to synaptic plasticity. With this symposium we aimed to promote the exchange of ideas between researchers approaching brain function from different angles.

List of Speakers:

Eve E. Marder (Brandeis University, USA)
Post Connectome Analyses of Circuit Dynamics: Variability, Modulation and Compensation in a Rhythmic Neuronal Circuit

Alexander Borst (Max Planck Institute of Neurobiology, Germany)
Genetic Dissection of the Fly Visual Course Control System

Joseph R. Fetcho (Cornell University, USA)
An orderly plan underlies the construction of motor circuits in hindbrain and spinal cord.

Cori Bargmann (Rockefeller University, USA)
Using fixed circuits to build flexible behaviours

Karel Svoboda (Howard Hughes Medical Institute, USA)
Neural coding underlying active object localization

David W. Tank (Princeton University, USA)
Neural Circuit Dynamics in Mice Navigating in Virtual Reality

Erin M. Schuman (Max Planck Institute for Brain Research , Germany)
Local Translation in Neurons

Bernardo L. Sabatini (Harvard Medical School, USA)
Dopaminergic neurons inhibit striatal output via non-canonical release of GABA

Markus Meister (Harvard University, USA)
Neural computations in the retina

Eric I. Knudsen (Stanford University School of Medicine, USA)
Neural Mechanisms of Attention in Birds

Adrienne Fairhall (University of Washington, USA)
Gain control in single neurons and networks

Gero Miesenböck (University of Oxford, UK)
The neural basis of a perceptual decision in Drosophila

Daniel Robert (University of Bristol, UK)
The mechanics of auditory frequency analysis in insects

Allison Doupe (University of California, San Fransisco, USA)
Basal ganglia circuits, social context, and plasticity

Rui M. Costa (Champalimaud Neuroscience Programme, Portugal)
Generating and shaping novel action repertoires

Atsushi Iriki (RIKEN Brain Science Institute, Japan)
Triadic (ecological, neural, cognitive) niche construction as a scenario of human brain evolution

Eero P. Simoncelli (New York University, USA)
Encoding of visual information in neural populations

Pieter R. Roelfsema (Netherlands Institute for Neuroscience, The Netherlands)
Neuronal mechanisms for perceptual grouping

Elizabeth S. Spelke (Harvard University, USA)
Origins of knowledge of geometry

Richard Morris (University of Edinburgh, UK)
The place of novelty and familiarity in cellular and systems consolidation

Zachary Mainen (Champalimaud Neuroscience Programme, Portugal)
The neural dynamics of waiting and giving up in the rat premotor cortex

CNP SEMINARS 2012

| February 2012 |

André A. Fenton
Thu 16/2/2012
New York University, New York, NY, USA
Rethinking Schizophrenia: Preemptive Cognitive Experience

Bartlett Mel
Tue 21/2/2012
Laboratory for Neural Computation, University of Southern California

| March 2012 |

Roland Strauss
Thu 8/3/2012
Howard Hughes Medical Institute, Janelia Farm Research Campus, Ashburn, VA, USA
Learning from flies: Memory functions improve oriented walking and climbing in Drosophila

Flavio Roces
Thu 22/3/2012
University of Würzburg, Würzburg, Germany
Plant selection by leaf-cutting ants: decision-making by foragers and quality control through the symbiotic fungus

Francesco Battaglia
Thu 29/3/2012
Centre for Neuroscience-Swammerdam Institute for Life Sciences Universiteit van Amsterdam, Amsterdam, The Netherlands
Neural oscillations and communication between the hippocampus and the neocortex

| April 2012 |

David Schoppik
Wed 18/4/2012
Harvard University, Boston, MA, USA
Neuropeptide Hypocretin Modulates Neurons Responsible for Gaze Stabilization in Larval Zebrafish

Randolph Menzel
Thu 26/4/2012
Freie Universität Berlin, Institut für Biologie - Neurobiologie, Berlin, Germany
The Honeybee as a Model System in Neuroscience

| May 2012 |

Loren Looger
Thu 10/5/2012
Howard Hughes Medical Institute, Janelia Farm Research Campus, Ashburn, VA, USA
New tools for imaging and manipulating the brain

Christian Keysers
Thu 17/5/2012
Netherlands Institute for Neuroscience (KNAW, Amsterdam) and UMCG (RUG, Groningen), The Netherlands
The Vicarious Brain

Miguel Nicolelis
Thu 24/5/2012
Duke University Medical Centre, Durham, NC, USA
Freeing the Brain from the Body

Gerry Rubin
Tue 29/5/2012
Howard Hughes Medical Institute, Janelia Farm Research Campus, Ashburn, VA, USA
A Molecular Geneticist's Strategy for Understanding the Fly Brain

Andreas Luthi
Thu 31/5/2012
Friedrich Miescher Institute for Biomedical Research, Basel, Switzerland
Defining the neuronal circuitry of fear

| June 2012 |

Stephen Simpson
Thu 21/6/2012
The University of Sydney, Sydney, Australia
The Nature of Nutrition: A Unifying Framework from Animal Adaptation to Human Obesity

Bruce Cumming
Thu 28/6/2012
NIH - National Eye Institute, Bethesda, MD, USA
The nature of decision-related activity in the sensory cortex

| July 2012 |

Anatol Kreitzer
Thu 5/7/2012
Gladstone Institute of Neurological Disease, University of California, San Francisco, CA, USA
Mechanisms of Motor Control and Reinforcement Learning in the Basal Ganglia

Daniel A. Peterson
Thu 19/7/2012
Department of Neuroscience, Chicago Medical School at Rosalind Franklin University of Medicine and Science, Chicago, IL, USA
Recruiting endogenous tissue stem cell for repair

| August 2012 |

Tony Bell
Thu 23/8/2012
Redwood Centre for Theoretical Neuroscience, University of California at Berkeley, Berkeley, CA, USA
Levels, learning, and the new non-equilibrium statistical mechanics

|September 2012 |

Mark Churchland
Thu 6/9/2012
Colombia Neuroscience Department, Colombia University, New York, NY, USA
The neural dynamics of movement generation

Carlos Brody
Thu 20/9/2012
Howard Hughes Medical Institute, Ashburn, VA, USA, Princeton Neuroscience Institute and Department of Molecular Biology, Princeton University, Princeton, NJ, USA
Optimal accumulation of evidence for decision-making in the rat

| October 2012 |

Patricia Churchland
Mon 8/10/2012
Philosophy Department , University of San Diego, San Diego, CA, USA
Decisions, Responsibility and the Brain

Gadi Katzir
Thu 11/10/2012
Department of Evolutionary and Environmental Biology & Department of Marine Biology, University of Haifa, Haifa, Israel
Cormorants to chameleons: A sensory-ecological view of two unique visual systems

Daphne Bavelier
Thu 25/10/2012
University of Geneva, Geneva, Switzerland and University of Rochester, Rochester, NY, USA
Action video games as exemplary learning tools

| November 2012 |

Okihide Hikosaka
Thu 8/11/2012
Laboratory of Sensorimotor Research, NEI, NIH, Bethesda, MD, USA
Basal ganglia mechanisms for choosing valuable objects automatically

Herc Neves
Mon 26/11/2012
Biomedical Microsystems, Interuniversity Microelectronics Centre, Heverlee, Belgium
Challenges of in vivo neural probing

Alla Karpova
Tue 27/11/2012
Howard Hughes Medical Institute, Ashburn, VA, USA
Neural mechanisms underlying behavioural adaptation in variable and competitive environments

Lisa Boulanger
Thu 29/11/2012
Princeton Neuroscience Institute / Department of Molecular Biology, Princeton University, Princeton, NJ
What's histocompatibility got to do with it? Non-immune functions of MHCI in brain development, plasticity, and disease

| December 2012 |

Azad Bonni
Thu 6/12/2012
Harvard Medical School, Boston, MA, USA
Transcriptional Regulation of Neuronal Connectivity in Brain Development and Disease

Iain D. Couzin
Fri 14/12/2012
Ecology and Evolutionary Biology, Princeton University, NJ, USA
Distributed sensing and decision-making in animal and human collectives

Aljoscha Nern
Mon 17/12/2012
Howard Hughes Medical Institute, Ashburn, VA, USA
Genetic dissection of the early visual system of Drosophila

PRESENTATIONS AND MEETINGS ORGANISED AT INTERNATIONAL INSTITUTIONS

- PRESENTATIONS -

Megan Carey
25 Oct 2012
The cerebellar circuit: from synapse to behaviour
Centre for Neuroscience and Cell Biology, University of Coimbra, Portugal

13 Dec 2012
The cerebellar circuit: from synapse to behaviour
Neuroscience Seminar Series at the Friedrich Miescher Institute, Basel, Switzerland

Rui M. Costa

Jan 2012
Generating and shaping novel action repertoires
Ar|Respire Connosco event on Creativity, Lisbon, Portugal

Feb 2012
Generating and shaping novel action repertoires
Winter Meeting on Neural Plasticity, Symposium, St. Kitts

May 2012
Generating and shaping novel action repertoires
"The Striatum" Symposium, Sainsbury Welcome Centre, London, UK

May 2012
Generating and shaping novel action repertoires
Oxford University, Oxford, UK

Oct 2012
Generating and shaping novel action repertoires
Keynote lecture, 9th SiCA conference, University of Muenster, Germany

Oct 2012
Generating and shaping novel action repertoires
Brain.org conference, Gulbenkian Foundation, Lisbon, Portugal

Inbal Israely

16 Feb 2012
Dendritic domains defined by protein synthesis dependent cooperation and competition between spines
Winter Conference on Neural Plasticity, 24th Annual Meeting, St. Kitts & Nevis, Caribbean

15 Jul 2012
Interaction of different inputs within a dendritic domain during protein synthesis dependent spine plasticity
The Federation of European Neuroscience Societies (FENS), 8th Bi-annual Forum on Neuroscience, Barcelona, Spain.

6 Nov 2012
Protein synthesis dependent synaptic depression in competition for spine plasticity
Neural Circuit Basis of Behaviour and its Disorders, Cold Spring Harbor Asia, Suzhou, China

Adam Kampff

4 Oct 2012
Cephalopod Neuroscience: The comparative study of intelligent systems
CIIMAR, Porto, Portugal

5 Nov 2012
Moving with motor cortex: Control of behaviour in unpredictable environments
NERF Seminar Series, Leuven, Belgium

7 Nov 2012
Moving with motor cortex: Control of behaviour in unpredictable environments
Cortex Club, Oxford University, England

16 Nov 2012
How does the brain build an intelligent system from dumb algorithms: A neuroscience perspective
SAPO CODEBITS, Lisbon, Portugal

Susana Lima

Apr 2012
Female Reproductive Behaviour
University of Valencia, Spain

Set 2012
Female Reproductive Behaviour
Cold Spring Harbour Laboratory, USA

Christian Machens

Jan 2012
Revealing the dynamics of an oculomotor integrator through optogenetic perturbations
University of Munich, Munich, Germany

Feb 2012
Demixed Principal Component Analysis
Cosyne Workshop, Snow Bird, Utah, USA

Mar 2012
Demixed Principal Component Analysis
Northwestern University, Chicago, USA

May 2012
Revealing the dynamics of an oculomotor integrator through optogenetic perturbations
Max-Planck Institute, Goettingen

Jul 2012
Demixed Principal Component Analysis
Janelia Farms, USA

Jul 2012
The population level: A review
Janelia Farms, Dimensionality Reduction Workshop, USA

Sep 2012
Demixed Principal Component Analysis
PFC-Hippocampus Workshop, Heidelberg, Germany

Sep 2012
Demixed Principal Component Analysis
SISSA Trieste, Italy

Nov 2012
Demixed Principal Component Analysis
Frankfurt Institute for Advanced Studies, Frankfurt, Germany

Zachary Mainen

16 Jan 2012
Neural circuits and decision-making in the rat
Instituto de Medicina Molecular, Lisbon, Portugal

23 Feb 2012
Neural mechanisms for decision making in the rat: Uncertainty in brain and behaviour
CoSyNe, Salt Lake City, UT, USA

29 Feb 2012
Origins of uncertainty in olfactory decision-making
CoSyNe workshops, Snowbird, UT, USA

1 Mar 2012
Origins and use of uncertainty in olfactory decision-making
Stanford University, USA

23 Apr 2012
Odour-guided decisions in the rat: The origins and uses of uncertainty
NERF Neurotechnology Symposium, Leuven, Belgium

29 May 2012
The neural dynamics of waiting and giving up in the rat premotor cortex
Brain dynamics and decision making, Ascona, Switzerland

3-5 May 2012
Origins of uncertainty in neural circuits and behaviour
Canonical Neural Computation 2012, Villa La Pietra, Florence, Italy

17 Jul 2012
Neuronal basis of decision-making
"Some of the Science We Do", IGC 50 years conference, Calouste Gulbenkian Foundation, Lisbon, Portugal

19 Jul 2012
Olfactory perception
3rd International Summery School on Computational and Cognitive Neuroscience, Tsinghua University, Beijing, China

24 Jul 2012
The origins of decision uncertainty
Public Lecture, Tsinghua University, Beijing, China

25 Jul 2012
The origins of decision uncertainty
3rd International Summery School on Computational and Cognitive Neuroscience, Tsinghua University, Beijing, China

14 Sep 2012
The origins and use of decision uncertainty
Bernstein Conference, Munich, Germany

26 Sep 2012
Systems neuroscience: On how we choose to wait or to give up
FMUL, Masters/PhD Neurosciences, Lisbon, Portugal

2 Oct 2012
The neural dynamics of waiting and giving up in the rat premotor cortex
Champalimaud Neuroscience Symposium, Lisbon, Porugal

11 Oct 2012
The neural dynamics of waiting and giving up in the rat premotor cortex
McGovern Centre, MIT, Cambridge, MA, USA

12 Oct 2012
On the origins and use of uncertainty: Waiting and giving up
EMBO Members Meeting 2012, EMBL, Heidelberg, Germany
IKEN Brain Science Institute, Tokyo, Japan

Cristina Marquez

Jul 2012
Rats cooperate in the absence of direct benefit: Development of a new behavioural task
EBBS Satellite: Stress,the story of our social lives. FENS Forum 2012, Barcelona, Spain

Nov 2012
Neural mechanisms of abnormal aggression after peripuberty stress
Stress along the lifespan. Neurochemical and behavioural consequences (IBRO-Alumin Symposium), I Congreso FALAN (Federación de Asociaciones Latinoamericanas y del Caribe de Neurociencias)

Marta Moita

3 Sep 2012
Symposium: what is going on in the hippocampus? Experimental results and computational approaches to memory formation and spatial information processing
International Graduate School for Neuroscience at the Ruhr University of Bochum, Germany

Masayoshi Murakami

28 Feb 2012
Representation of waiting time in the rat premotor cortex
CoSyNe workshops, Snowbird, UT, USA

Michael Orger

26 Jul 2012
Neural circuits underlying visuomotor behaviours in the zebrafish
Centre for Neural Circuits and Behaviour, University of Oxford, England

1 Nov 2012
Whole brain imaging of neural circuit activity in behaving zebrafish
Workshop on Zebrafish Genetics, Transgenesis, and Systems Biology, Janelia Farm Reseach Campus, Ashburn, Virginia, USA

8 Dec 2012
Whole brain imaging of neural circuit activity in behaving zebrafish
European Symposium on Imaging Structure and Function in the Zebrafish Brain

Joe Paton
4 May 2012
Time for learning in the rodent striatum
Seminar series, Institut de Neurosciences de la Timone (INT), Marseille, France

Leopoldo Petreanu
3 Sep 2012
Optogenetics technology and application for circuit mapping
FENS-IBRO Imaging Training Centre, Lausanne, Switzerland

9 Oct 2012
The structure and function of long-range cortical connections
Cellular Mechanisms of Sensory Processing, Goettingen, Germany

23 Nov 2012
The structure and function of cortico-cortical connections
Instituto de Medicina Molecular, Lisbon, Portugal

Alfonso Renart
27 Apr 2012
The temporal structure of population activity in cortical circuits
Mathematical Neuroscience Workshop, University of Porto, Porto, Lisbon

11 Sep 2012
Neuronal variability and the accuracy of perception
Group for Neural Theory, Ecole Normale Superieure, Paris, France

14 Sep 2012
Variability of sensory neurons and the accuracy of perceptual choices
Instituto Gulbenkian de Ciência, Oeiras, Portugal

21 Nov 2012
Does the variability of sensory neurons constrain the accuracy of perception?
Neuroscience Centre, Universite de Geneve, Geneve, Switzerland

22 Nov 2012
Does the variability of sensory neurons constrain the accuracy of perception?
EPFL, Lausanne, Switzerland

Carlos Ribeiro
15 May 2012
Making essential and non-essential decisions
Instituto Gulbenkian de Ciência, Oeiras, Portugal

5 Oct 2012
Essential and non-essential decisions in Drosophila
Plenary lecture, FP7 MBG-BRIDGE - Development and Function of the Nervous System Workshop, Boğaziçi University, Istanbul, Turkey

22 Oct 2012
The gourmet fly - the molecular and neuronal basis of nutrient decisions in Drosophila
Instituto Superior de Psicologia Aplicada, Lisbon, Portugal

Maria Luísa Vasconcelos
18 Oct 2012
Circuits of the innate responses to the external world
Junior European *Drosophila* Investigators meeting, Foz do Arelho, Portugal

30 Jun 2012
Tracing olfactory circuits of innate responses
Society of Experimental Biology, Salzburg, Austria

MEETINGS ORGANISED BY CNP INVESTIGATORS

- MEETINGS AT THE CCU -

Advanced topics in reinforcement learning
26-30 Nov 2012

Organisers: Joe Paton, Eric Dewitt, Thomas Akam (all from CNP) and Jose Fernandes, Carlos Duik, Elliot Ludvig (all from Department of Neuroscience, Princeton University, USA).

This course assumed a basic knowledge of formal models for Reinforcement Learning. It was designed to give students and post-docs the opportunity to engage in more advanced topics in formal RL theory, as well as the connection of RL to Neuroscience. It involved didactic lectures, as well as active project-based learning opportunities.

- MEETINGS OUTSIDE OF THE CCU -

Towards a Common Framework to Study the Function of the Insect Central Complex
15-18 Apr 2012
Howard Hughes Medical Institute, Janelia Farm, Virginia, USA

Organisers: Eugenia Chiappe, Stanley Heinze & Vivek Jayaraman

The meeting gathered researchers studying the insect central complex and invited speakers studying higher sensory and sensorimotor processing in vertebrates. Its format (short talks and chaired panels at the end of a session) enabled focused discussions about the issues of each session. We asked that participants presented their data and ideas in the context of specific, testable hypotheses about the brain region's function and attempted to relate their findings to those of others in the field.

Dynamics of memory: what's the evidence?
12-13 Jul 2012
Satellite meeting at FENS 2012, Barcelona, Spain

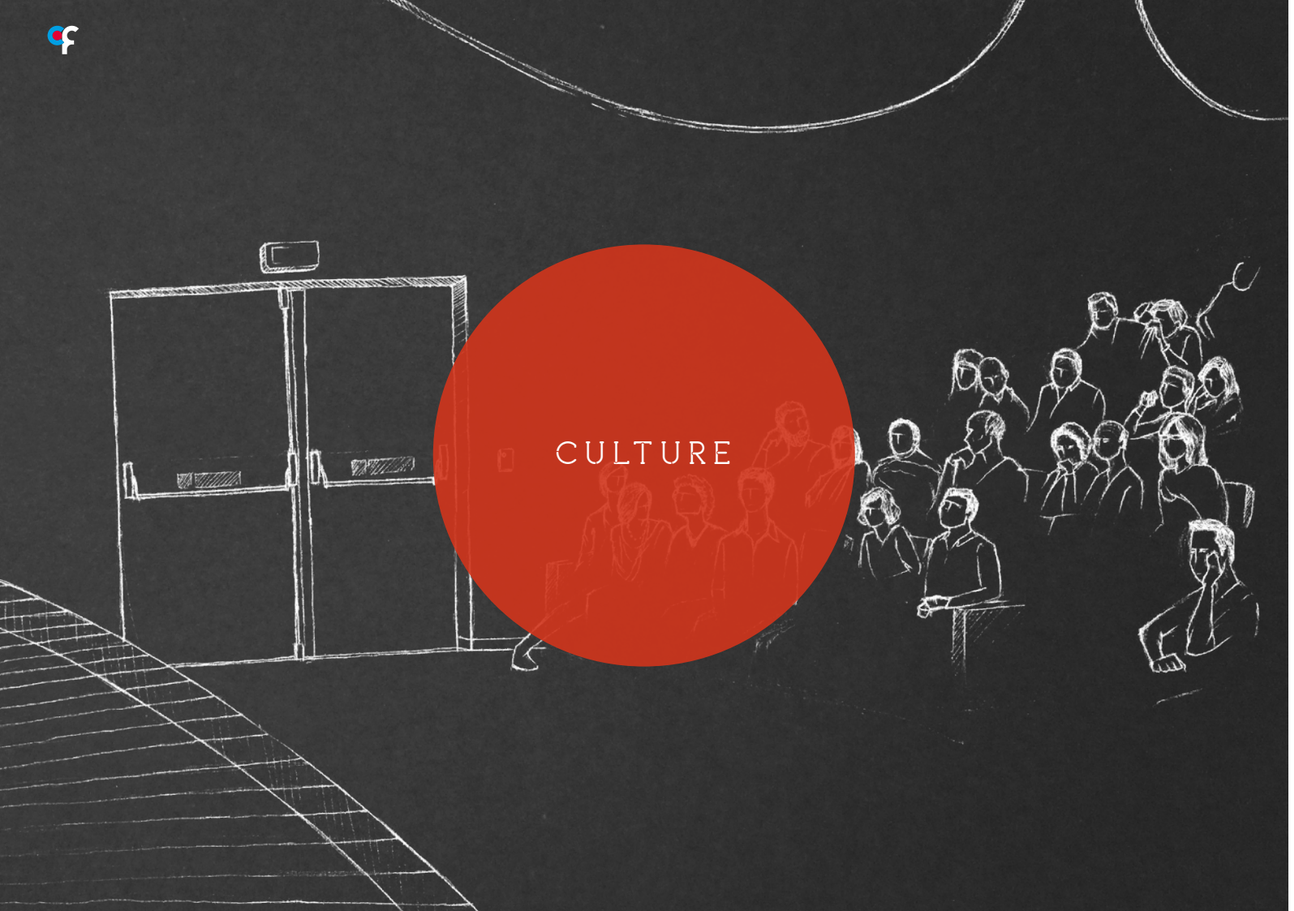
Organisers: Alfonso Renart and Albert Compte

The overall scientific goal of the conference is to discuss experimental approaches that would help to evaluate and assess different proposed theoretical frameworks comprising mechanistic explanations for how memories are stored, retrieved and maintained in the brain.

The return of the jedi: the second annual meeting of the junior european *drosophila* investigators
18-20 Oct 2012
Foz do Arelho, Portugal

Organisers: Carlos Ribeiro (CNP), Christen Mirth (IGC)

The meeting brought together independent *Drosophila* investigators in Europe at an early career stage and aimed at fostering scientific, professional and personal exchanges in an informal setting. Main topics were: how to strengthen the position of young team leaders within the established scientific community, how to create new, innovative and collaborative research structures, and how to strengthen the awareness and support for *Drosophila* research within Europe.



TO PROMOTE COLLECTIVE ACHIEVEMENTS

BEYOND THOSE REACHABLE BY INDIVIDUAL SCIENTISTS OR LABORATORY GROUPS

2012 CNP ANNUAL RETREAT

Each spring, the busy corridors of the CNP empty, as all CNP members travel together to a unique location. There, 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 2012, the retreat was held at the Vila Galé Clube de Campo in Alentejo. This remote and beautiful location offered an ideal setting for introspection and reflection on the on-goings of the CNP.

The symbol of this year's Champalimaud Neuroscience Programme (CNP) retreat, our fifth, is a seagull. The seagull was chosen because it is one of our new neighbours. The gull alighting on a Roman column represents our arrival at the Champalimaud Centre for the Unknown. After 5 years of incubating and over one year of being split in two, we are united at this fabulous facility on the banks of the Tejo. The seagull has landed.

CHAMPALIMAUD INTERNAL SEMINAR SERIES

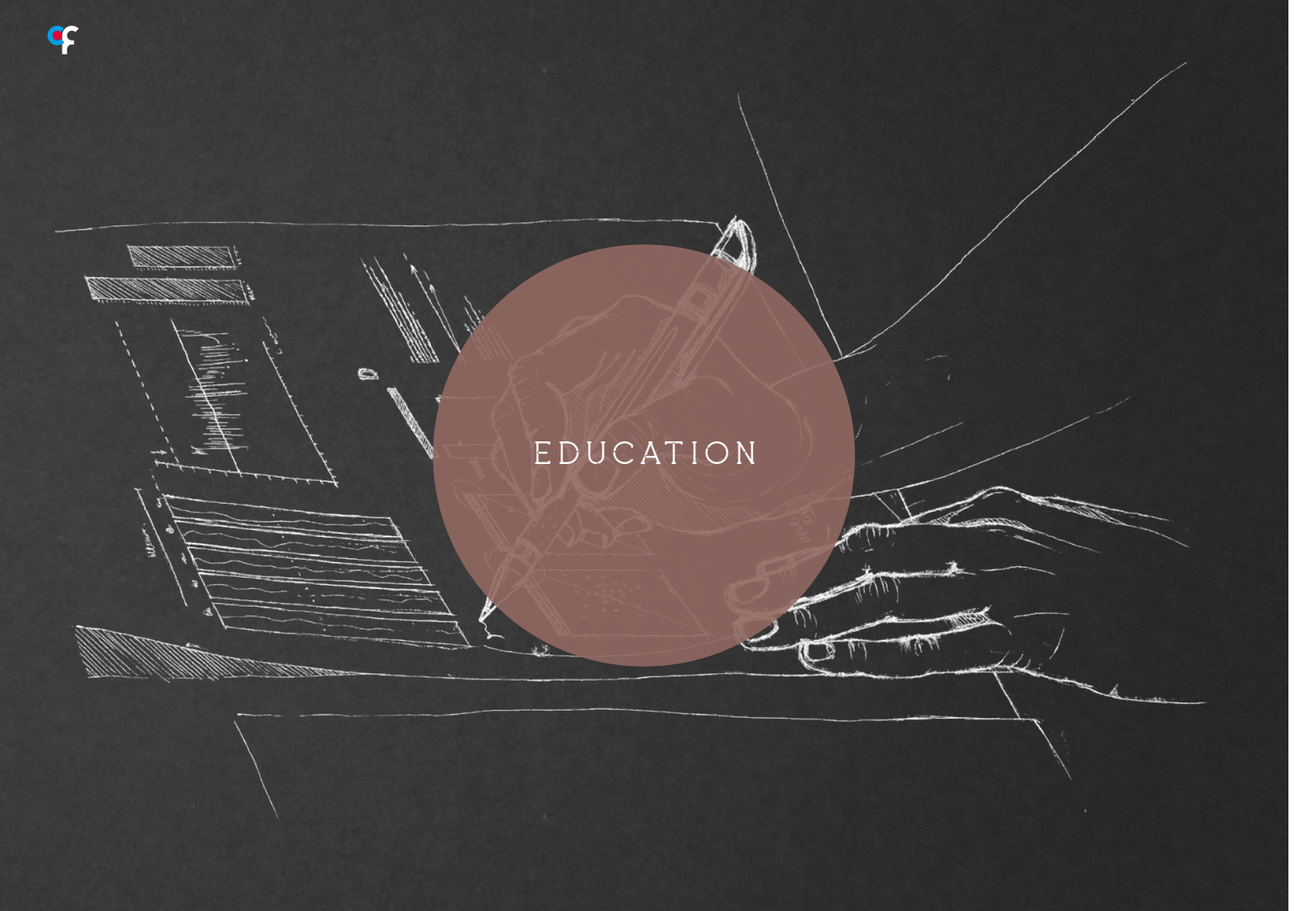
As one of the means to creating an environment where individual researchers, in all career stages, are familiar with the work of each other, an event series called Champalimaud Internal Seminars Series (CISS) was created. Each week, two CNP researchers deliver a 30 minutes presentation of their work, after which they receive feedback and questions from the CNP community. These events, in addition to creating an atmosphere that facilitates collaboration, also provide a platform for junior researchers to advance their skills at preparing and delivering oral presentations to large audiences.

LIFE@CCU

Life @ CCU is a series of meetings designed to address new initiatives, concerns and needs of the CNP community. Meetings are conducted in an open discussion format and are concluded with the formation of specific task teams.

FRIDAY HAPPY HOUR

These weekly events provide an informal setting where CNP members socialise over food and drink. Each week the Social is hosted by two different labs that create fun thematic events. Family members and children are also frequent visitors of the Friday Happy Hour, which is always a great way to start the weekend.



TO ENCOURAGE ACTIVE PARTICIPATION

CRITICAL THINKING AND INDEPENDENCE OF THOUGHT

INTERNATIONAL NEUROSCIENCE DOCTORATE PROGRAMME (INDP)

Programme Director: Alfonso Renart
Administrative Assistant: Alexandra Piedade

The INDP aims at providing students with a broad and integrative education in neuroscience with a focus on the neuronal and circuit basis of behaviour. A main goal of the programme is to foster and encourage active participation, independence and critical thinking on the part of the students. The first year of the programme, students attend courses structured as modules lasting one or a few weeks which cover basic topics in contemporary neuroscience such as basic cellular and synaptic physiology, sensation and action and cognitive neuroscience. Quantitative approaches are emphasised and students also receive background courses on basic biology, mathematics and programming. The following three years are dedicated to research on a specific topic leading to a PhD thesis. No previous background in neuroscience is required, but candidates with a background in biology or quantitative disciplines are encouraged to apply.

INDP STUDENTS

| 2012 Students |

Asma Motiwala
Masters Cognitive and Computational Neuroscience
University of Sheffield, Sheffield, UK

Danbee Kim
Bachelor's Brain and Cognitive Science
Massachusetts Institute of Technology, Cambridge, USA

Hedi Young
MSc in Cognitive Neuroscience
UCL & Birkbeck College, London, UK

Marina Fridman
Masters Neuro and behavioural Sciences
Universität Tübingen, Tübingen, Germany

Mert Erginkaya
BAchelor's Molecular Biology and Genetics
Bogazici Universitesi, Istanbul, Turkey

Michael Pereira
Master's Molecular Systems Biology
VU University Amsterdam, Amsterdam, The Netherlands

Nuno Calaim
MSc. Mathematics and Applications
Instituto Superior Técnico, Lisboa, Portugal

Nuno Loureiro
MSc. Degree in Physics Engineering
Instituto Superior Técnico, Lisboa, Portugal

Raphael Steinfeld
MSc. Molecular Biosciences
Ruprecht-Karls University of Heidelberg, Heidelberg, Germany

Rita Félix
MSc. Degree in Evolutionary and Developmental Biology
Faculdade de Ciências da Universidade de Lisboa, Portugal

| 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

2012 INDIVIDUAL COURSES

Techniques of experimental neuroscience I

16-20 Jan
Organisers: Adam Kampff (CNP), Michael Orger (CNP), Leopoldo Petreanu (CNP)
Teachers: Adam Kampff (CNP), Michael Orger (CNP), Leopoldo Petreanu (CNP)

Techniques of experimental neuroscience II

23-27 Jan
Organisers: Adam Kampff (CNP), Michael Orger (CNP)
Teachers: Adam Kampff (CNP), Michael Orger (CNP)

Anatomy, cellular physiology

30 Jan - 3 Feb
Organisers: Chris Braun (Hunter College, NYC), Josh Dudman (Howard Hughes Medical Institute, USA)
Teachers: Chris Braun (Hunter College, NYC), Beverley Clark (University College London, UK), Tiago Branco (University College London, UK), Jeffrey Diamond (National Institute of Health, USA)

Synaptic physiology

6-10 Feb
Organisers: Josh Dudman (Howard Hughes Medical Institute, USA)
Teachers: Beverley Clark (University College London, UCL), Tiago Branco (University College London, UK), Alasdair Gibb (University College London, UK), Nelson Spruston (Howard Hughes Medical Institute, USA) and Thomas Nevian (University of Berne-Switzerland)

PROJECTS 1

13-17 Feb
Organisers: Adam Kampff (CNP)

Synaptic plasticity

20-24 Feb
Organisers: Inbal Israely (CNP)
Teachers: Steven Kushner (Erasmus University Rotterdam, the Netherlands), Bartlett Mel (University of Southern California, USA)

Learning

27 Feb - 2 Mar
Organisers: Megan Carey (CNP)
Teachers: Diasynou Fioravante (Harvard Medical School - USA)

Sensory systems I - generic concepts in sensory systems

5-9 Mar
Organisers: Joe Paton (CNP), Luísa Vasconcelos (CNP), Alfonso Renart (CNP), Leopoldo Petreanu (CNP)
Teachers: Gabe Murphy (Howard Hughes Medical Institute, USA), Iris Salecker (NIMR, UK) and Alexander Fleischmann (CIRB, France)

Sensory systems II - applications to vision, taste, olfaction, audition, somatosensation

12-17 Mar
Organisers: Joe Paton (CNP), Luísa Vasconcelos (CNP), Alfonso Renart (CNP), Leopoldo Petreanu (CNP)
Teachers: Virginia Flanagin (BCCN Munich, Germany)

Neuroscience of eating

26-31 Mar
Organisers: Carlos Ribeiro (CNP)
Teachers: Matthew Piper (University College London - UCL)

Sensory-motor I

9-13 Apr
Organisers: Michael Orger (CNP), Eugenia Chiappe (CNP)
Teachers: Andrew Straw (California Institute of Technology Bioengineering, USA), Sam Sober (Emory University, USA), Kathrin Steck (Max Planck Institute for Chemical Ecology, Germany) and Matthias Wittlinger (University of Ulm, Germany)

Sensory-motor II

16-20 Apr
Organisers: Michael Orger (CNP), Eugenia Chiappe (CNP)
Teachers: David Schoppik (University of California, USA)

Reinforcement & bayes

23-27 Apr
Organisers: Christian Machens (CNP)
Teachers: Sophie Deneve (Ecole Normale Supérieure- Paris, France), Christian Machens (CNP)

Moving into action

30 Apr - 4 May
Organisers: Rui Costa (CNP)
Teachers: Jose Carmena ((UC Berkeley, USA), Joe McIntyre (CNRS and Collège de France, France) , Rich Ivry (UC Berkeley, USA) and Niels Birmbauer (Institute of Medical Psychology and Behavioural Neurobiology, Eberhard-Karls-University, Germany)

PROJECTS 2

7-12 May
Organisers: Adam Kampff (CNP)

Complex brain functions I - emotion, sex, and neuroscience of social behaviour

14-18 May
Organisers: Marta Moita (CNP), Zachary Mainen (CNP)
Teachers: Regina Christian Keysers (University Medical Centre Groningen, Netherlands), Jorge Pacheco (University of Minho, Portugal)

Complex brain functions II – emotion sex and neuroscience of social behaviour

21-25 May
Organisers: Marta Moita (CNP), Zachary Mainen (CNP)
Teachers: Ray Chung (Kinetic Designs, San Francisco) and Katarina Erikson (Kinetic Designs, San Francisco)

Project presentations

28 May - 1 June
Organisers: Adam Kampff (CNP)

THESES

Susana Lima

Msc Thesis awarded to Vanessa Urbano in October, 2012

Estrogénios e comportamento social: implementação de um método de quantificação de estrogénios e sua monitorização em murganhos selvagens

Instituto Superior de Ciências da Saúde Egas Moniz, Portugal

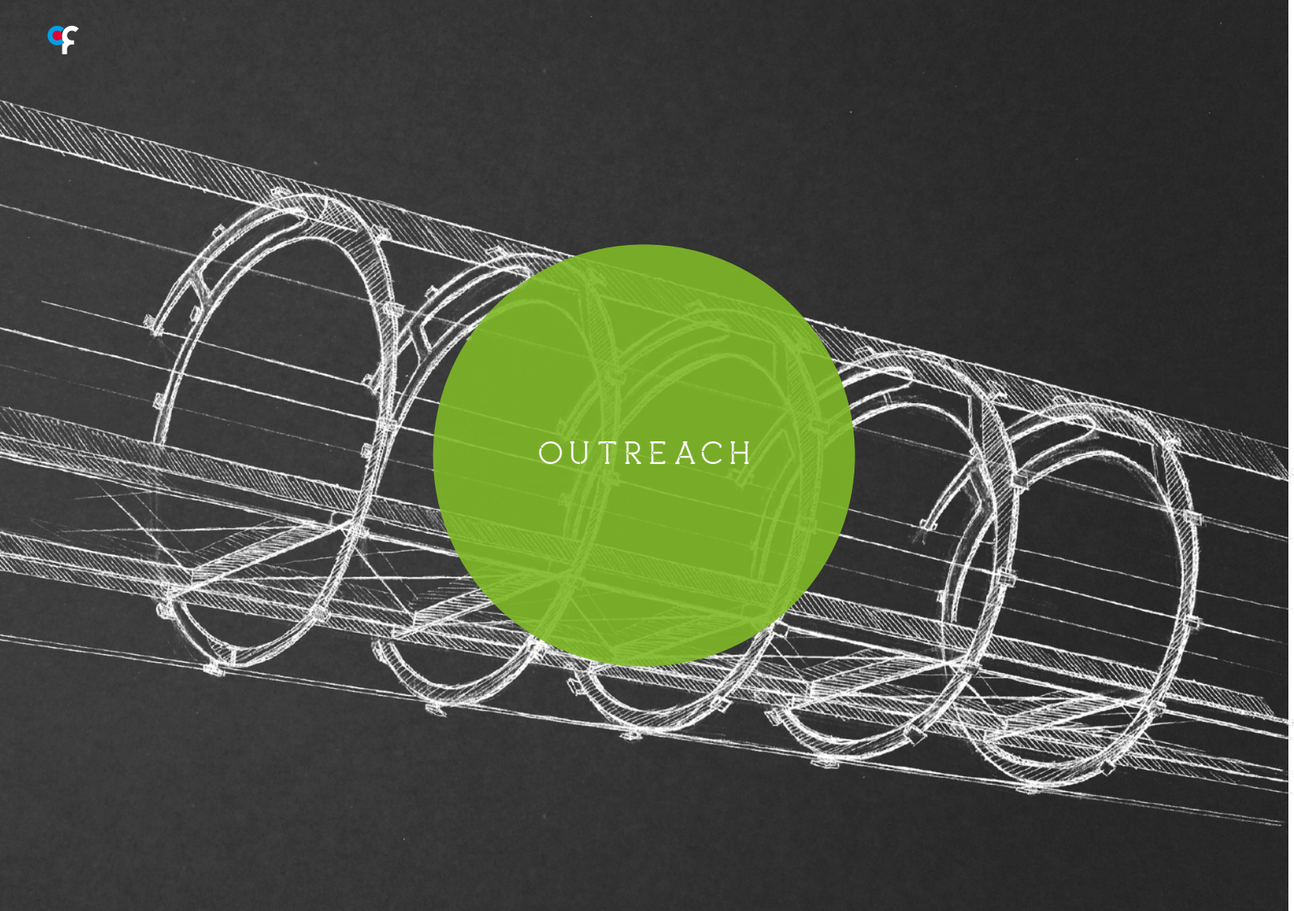
Christian Machens

PhD Thesis awarded to Pedro Gonçalves in September, 2012

A neural circuit model of the oculomotor integrator: theory for optogenetic dissection

UPMC Sorbonne Universites, Paris, France


PRINCIPLES OF
NEURAL SCIENCE



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.

In 2012, seven Ar events took place at the Champalimaud Auditorium. The first event of this vibrant series was dedicated to Creativity, with the participation of the artist Vik Moniz and the neuroscientist Rui Costa. This event was also a turning point for Ar, as it attracted the attention of individuals from Centro Cultural de Belém in Lisbon who invited members of Ar to participate in an event held there.

This was also the first time that Ar left Portugal to take part in two important initiatives: the Society for Neuroscience (SfN) Meeting in New Orleans - USA, and the Semana de la Sciencia in Madrid, the largest science communication event in Spain.

Supporting the events, the same group of students has im¬plemented 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.

Organisers:

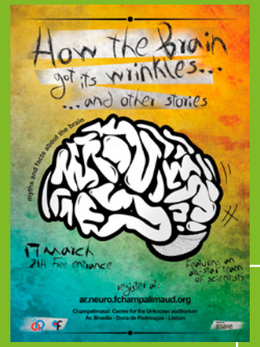
BAC Afonso, N Bonacchi, W Brendel, V. M. Corrales, PA Correia, GMP Costa, FA Dehmelt , EEJ Dewitt, AR Fonseca, AF Hobbiss, S Lackner, GC Lopes, TG Marques, SPS Matias, AG Mendonça, SV Meyler, C Monroy, CEL Ramos, SM Rennie, AM Vicente, E Vinnik, TS Gouvea, G Mello

AR EVENTS 2012

CREATIVITY

Jan 24th

Speakers: Vik Muniz (Artist, Brazil), Rui Costa (CNP)
MCs: Patrícia Correia, Rita Fonseca, Samuel Meyler (all CNP)



HOW THE BRAIN GOT ITS WRINKLES AND OTHER STORIES

Mar 17th

Discussion penal participants: Megan Carey, Adam Kampff, Susana Lima, Marta Moita (all CNP) and Rui Oliveira (ISPA/CNP)
MCs: Claire Monroy, Sofia Soares (all CNP)

HUMAN 2.0

May 24th

Speakers: Domingos Henrique (IMM/CNP), Neil Harbisson (Cyborg Artist, Catalonia/UK), Miguel Nicolelis (Duke University Medical Centre, USA)
MCs: Ekaterina Vinnik, Bruno Afonso, Thiago Gouvêa (all CNP)

FOOD FOR THOUGHT

Jun 21st

Speakers: Carlos Ribeiro (CNP), Stephen Simpson (Charles Perkins Centre at the University of Sydney, Australia), Paulo Morais (Chef, Umai restaurant, Lisbon, Portugal)
MCs: Veronica Corrales, Florian Dehmelt (all CNP)

THINK OF A NUMB3R

Jul 5th

Speakers: Christian Machens (CNP), João Blümel (Mentalist), Vince Lynch (Hypnotist)
MCs: Cristina Afonso (CNP), Elsa Abranches (IMM), Catarina Ramos (IMM), André Mendonça (CNP), Niccolò Bonacchi (CNP)

MIND INVADERS

Oct 25th

Speakers: Luís Vicente (University of Lisbon, Portugal), Daphne Bavelier (University of Rochester, USA), António Câmara (YDreams and Universidade Nova de Lisboa, Portugal)
MCs: Ricardo Zacarias, Maria Vicente, Gil Costa (all CNP)

SOCIETY

Dec 14th

Speakers: Iain Couzin (Princeton, USA), Simo Routarinne (Proimpro, Finland), Tamera (Tamera, Portugal)
Discussion Moderator: Zach Mainen (CNP)
MCs: Scott Rennie, Danbee "TaunTaun" Kin, Rita Venturini (all CNP)

Taken from the Ar Event Human 2.0:
"The drive to enhance human potential is as ancient as History itself. Some see this quest to surpass our limitations as fundamental, others regard it as dangerous arrogance. Are we up to the changes that technology and knowledge bring us today? Will the future change the very essence of who we are? "


LeaRNing
&
EduCAtioN
APRIL 4th // 21h00
GUEST SPEAKERS
PAUL HOWARD-JONES / NEUROSCIENCE AND EDUCATION
DOMINGOS FERNANDES / EDUCATIONAL ASSESSMENT
ESCOLA DA PONTE / NONTRADITIONAL EDUCATION

BRAIN AWARNESS WEEK

On March 17th the closing session of the Brain Awareness Week (BAW) 2012 took place at the CCU. This event brought together individuals from Champalimaud Foundation (President Dra. Leonor Beleza), Sociedade Portuguesa de Neurociências (President Dr. Nuno Sousa), CNP researchers, students and members of the general public of all ages.

For this event, CNP students organised a set of engaging activities – an interactive and informal presentation about the brain, which was prepared by the students in Portuguese and was designed to reach the general public of all ages (including the youngest). After the events, the audience was invited to visit stands that were placed outside the auditorium. These exhibit stands, which were also prepared by the students, had information and presentation about the experimental models and areas of research studied at the CNP.

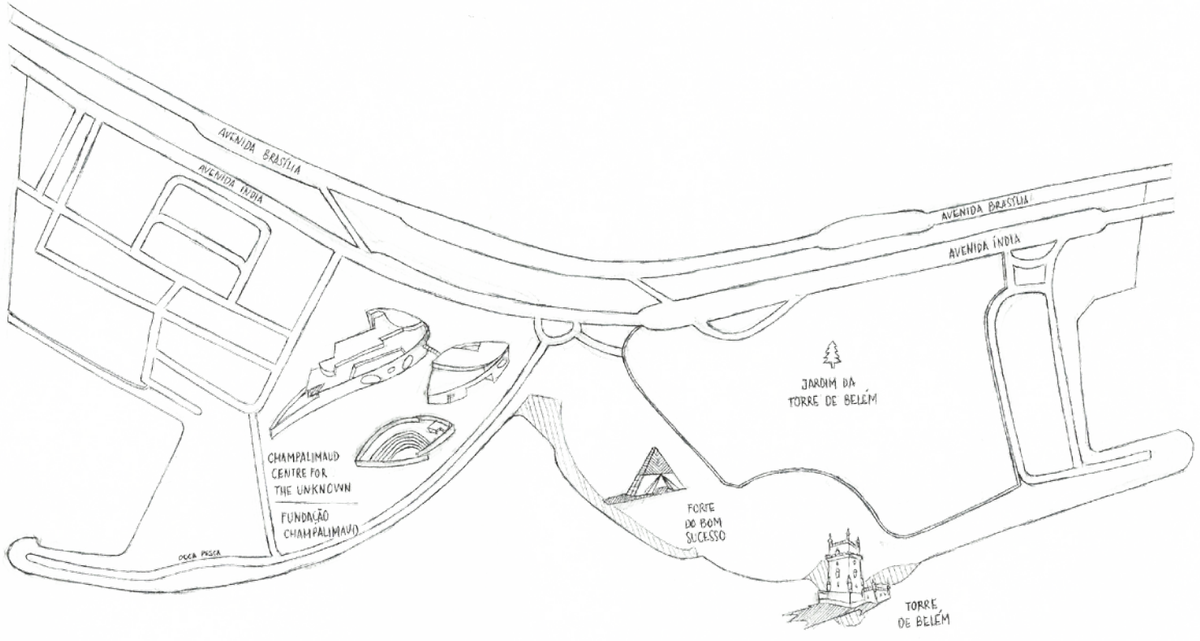
INVEST IN OUR FUTURE - INVEST IN SCIENCE VIDEO CAMPAIGN

In order to support the growing movement against cuts in the European science budget – Horizon 2020, a group of CNP Investigators launched a pro-science video campaign. The goal of this campaign was to engage society at large in the effort to secure the future of public funding of science in the European Union (EU). Each video featured in the campaign is a personal message from individuals who support this cause.

Invest in Our Future – Invest in Science has also become a partner of a movement named 'no-cuts-on-research' , organised by the Initiative for Science in Europe (ISE) that has been receiving strong public support, as over 150,000 individuals worldwide have already signed the 'no-cuts-on-research' petition.

The fun short-videos of Invest in Science have already reached thousands of people worldwide. In the short time the campaign has been running, the website was visited over 5000 times and the videos were viewed over 3000 times. In addition, the videos and website links have been widely shared in social networks, such as Facebook, where the number of visitors and fans keeps growing. In 2013, the Invest in Science team is transforming this campaign into a contest, drawing larger crowds and participation by more video creators.

Coordinators: Catarina Ramos, Liad Hollender, Rita Venturini, Zachary Mainen
Design: Gil Costa
Collaborators: Wolfgang Eppenschwandtner, Initiative for Science in Europe



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Printing

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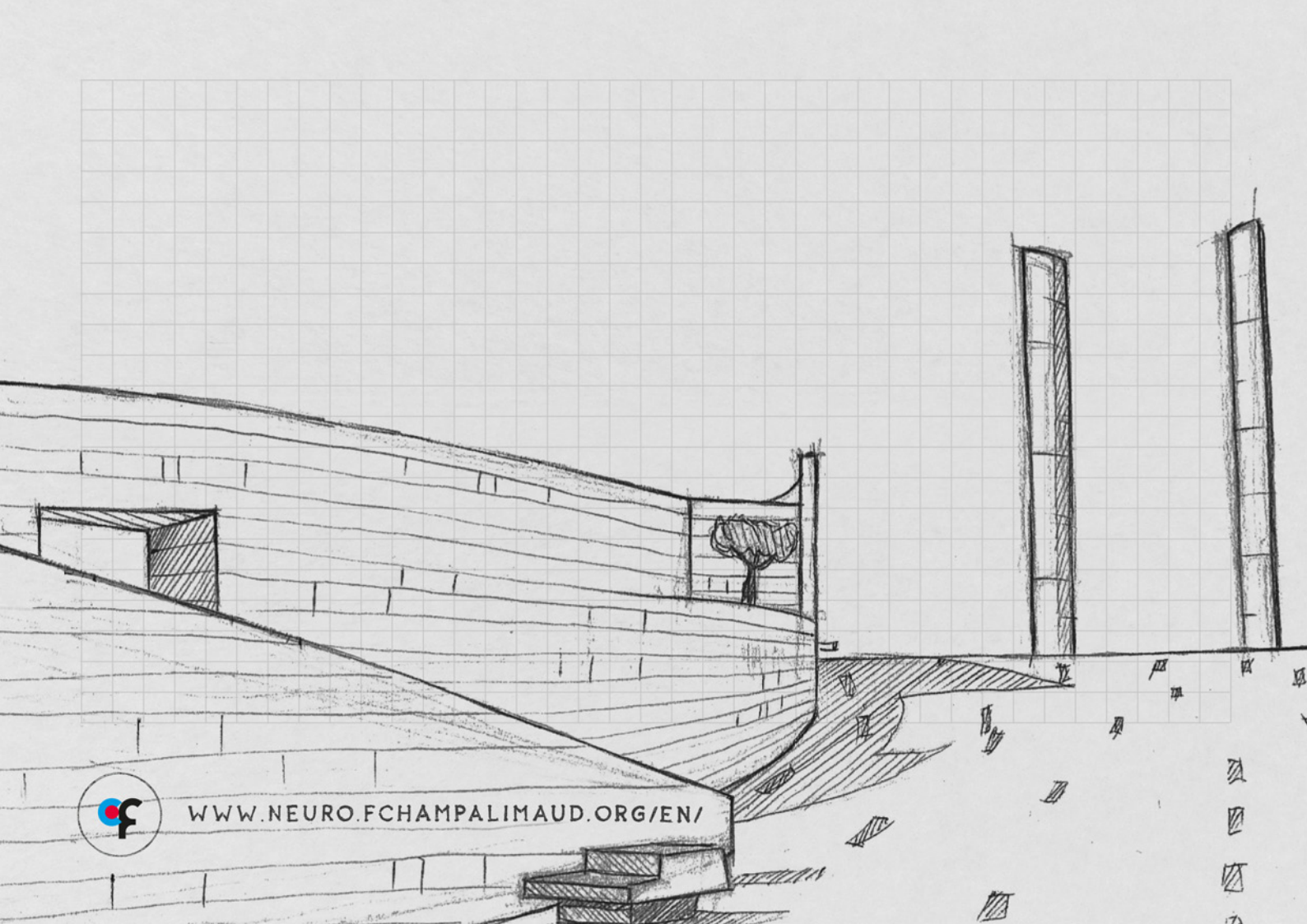
GABRIELA MARTINS
Photography

EVERYONE IN CNP
Thank you.
For your help and support
in the realisation of this publication.
Including the contribution of pictures,
materials and information.

With a special thanks to CNP
Administrative Support.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