

PEOPLE BEHIND THIS EDITION

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Stepping further into the unknown

"CHAMPALIMAUD ENCOMPASSING RESEARCH PROGRAMME SET OUT TO UNDERTAKE TWO GREAT CHALLENGES IN **BIOLOGY - THE NEURAL** BASIS OF BEHAVIOUR AND THE PHYSIOLOGICAL MECHANISMS OF CANCER."

t is perhaps surprising upon looking back, to be filled not with a sense of nostalgia, but with that of excitement and anticipation. As all years, 2015 began with its normal rhythms. Welcoming back a routine of research life with a steady flow of experiments and data, discussions and travel. And while it is true that all years bring with them new beginnings, 2015 gave rise to a set of pivotal ones.

One of the great leaps of 2015 was the official launching of Champalimaud Research (CR). In 2015, the envisioned goal of Each course is three-weeks long and accepts international the Champalimaud Foundation to form a sister programme applications from doctoral students. to the Champalimaud Neuroscience Programme (CNP), on We invite you to review this report to learn more about these the Biology of Systems and Metastasis (BSM), has come into and other exciting events of the past year. We feel fortunate fruition. The new programme focuses on a systems organismic to have spent a year full of fascinating debates, meetings approach to investigating the biology of cancer. Its ultimate goal and discoveries within a community of dedicated researchers is to understand and prevent cancer - especially metastasis. here at CR. We further invite you to follow our institute as the The two programmes come together under Champalimaud promise of the new beginnings of 2015 come into realisation Research - an encompassing research programme set out to across the next few years.

undertake two great challenges in biology – the neural basis of behaviour and the physiological mechanisms of cancer. In RESEARCH – AN June 2015, a symposium was held to select suitable group leaders for the BSM programme. This process culminated in the launching of three groups that will start in 2016.

> CR's research scope was broadened yet further with the implementation of cutting edge imaging technology in March of 2015. This technology has established the Champalimaud Centre for the Unknown (CCU) as one of the most advanced preclinical imaging institutions worldwide. Specifically, the newly installed two state of the art scanners of 9.4 and 16.4 Tesla, will provide novel insight onto brain's function, microstructure, and metabolism in health and disease.

> The expansion of research activities at CR coincided with the beginning of substantial financial support by the Fundação para a Ciênicia e a Tecnologia, as the CNP was evaluated as an Exceptional Research Unit in the previous year. This additional funding, amounting to a total of 1.3 M euros over three years will be directed to supporting the Unit in all its expenses, from personnel to equipment to programme-wide services.

> Finally, in the field of education, CR hosted the first edition of the CAJAL Advanced Neuroscience Training Programme in July. The Programme is a FENS and IBRO initiative in partnership with Bordeaux Neurocampus and the Champalimaud Foundation. This programme is the first of its kind in Europe, hosting recurring neuroscience training courses. CR hosts two advanced courses on a yearly basis; one on Behaviour and Neural Systems and the other on Computational Neuroscience.

THROUGH SCIENTIFIC BREAKTHROUGHS AND CLINICAL DEVELOPMENTS, THE FOUNDATION IS THERE TO HELP THOSE WHO NEED IT MOST.

he Champalimaud Foundation exists as the legacy of Portuguese entrepreneur and industrialist, the late António de Sommer Champalimaud. In accordance with the will of António Champalimaud, Leonor Beleza, former Portuguese Minister of Health, is the President of the Foundation, which was formally created in 2005 under its full title of the Anna de Sommer Champalimaud and Dr. Carlos Montez Champalimaud Foundation, in honour of the benefactor's parents.

The Foundation gives full backing to its researchers who work on the frontline of science and biomedicine. The Foundation's research scientists and doctors use their creativity, experience and talents to find new and innovative ways to approach the many questions of modern neuroscience and oncology.

hampalimaud Centre for the Unknown consists of two main branches. Champalimaud Research is made up of 20 groups working on unravelling the neural basis of behaviour and on the Biology of Systems and Metastasis, whereas in the Champalimaud Clinical Centre, healthcare professionals focus on managing and treating diseases. Both branches of the institute work harmoniously and



thus illustrate the Foundation's commitment to translational research: to bring the benefits of scientific developments out of the lab and to the patient as soon as possible by developing proximity between Fundamental Science and the Clinic.

Through the António Champalimaud Vision Award, celebrating its tenth edition this year, and the C-TRACER programme, the Champalimaud Foundation is reaching out in the global battle against blindness and vision disorders.

As an institute working at the forefront of both scientific innovation and disease management, The Foundation holds the fundamental belief that the work done at the Champalimaud Centre for the Unknown can benefit humanity. Through scientific breakthroughs and clinical developments, the Foundation is there to help those who need it most.



Leonor Beleza, President João Silveira Botelho, Vice President António Horta-Osório, Member of the Board









SCIENTIFIC ADVISORY BOARD

The Scientific Advisory Board (SAB) of CR is composed of internationally recognised scientists who meet annually to review the progress of CR researchers and programmes. It consists of regular members and additional external members who join on a yearly basis. In 2015, in addition to the annual review of CR, the SAB also discussed the launching of the Biology of Systems and Metastasis (BSM) Programme. Over multiple sessions held throughout 2 days in May, the SAB members, together with the CF Board, CR and Champalimaud Clinical Centre Directors, reviewed topics including the goals of the new programme, how the neuroscience and BSM programme will be integrated under CR and analysis of possible candidates. The conclusions of these discussions resulted in the recruitment of new group leaders for the BSM programme that will establish their labs at the Champalimaud Centre for the Unknown in 2016.

REGULAR SAB MEMBERS:

- J. Anthony Movshon. NY University, USA.
- Martin Raff. University College London, UK.
- Thomas Jessell. Columbia University, USA.

2015 SAB MEMBERS:

- Cornelia Bargmann. Rockefeller University, USA.
- Nicholas Hastie. University of Edinburgh, UK.
- Klaus Pantel. University Medical Center, Hamburg Eppendorf, Germany.
- Tyler Jacks. Massachusetts Institute of Technology, USA.

RENART ADMINISTRATIVE COORDINATOR PHILIPP TSOLAKIS

DIRECTOR

ALFONSO

INDP

ID

AC

CC

PD

COMMUNICATION COORDINATOR CATARINA RAMOS

PLATFORMS COORDINATOR TÂNIA VINAGRE











POSTCARDS FROM THE UNKNOWN



Principal Investigator MEGAN CAREY Joined CF in 2010

NEURAL CIRCUITS AND BEHAVIOR LAB

TAKING IT ONE STEP AT A TIME - INVESTIGATING HOW THE BRAIN CONTROLS COORDINATED MOVEMENT

It's obvious when we think about lead athletes, like gymnasts, that people are capable of remarkable feats of coordination. But in fact, keeping our bodies balanced and moving different parts of the body relative to each other in a coordinated manner while remaining stable are complex problems that the brain solves all the time. How does the brain control our movements and what happens when the underlying neural circuits malfunction?

Scientific Approach

The Neural Circuits and Behavior lab studies the cerebellum, a brain area that is critical for coordinated motor control and motor learning. The well-described cerebellar circuit is conserved across species, which enables the researchers to study it in mice, a powerful animal model that offers an array of genetic tools. Using these tools, the researchers are able to measure and manipulate activity in specific populations of neurons in the cerebellum. In some cases, these

manipulations mirror neural conditions that exist in humans who suffer damage to the cerebellum through illness or injury. Among the recent advances in the lab was the development of LocoMouse, an open-source tool that allows researchers to observe the fine details of movement with near-millisecond and millimeter resolution. The team developed this tool as the first step in their largescale project to reveal the neural circuits that generate coordinated walking, for which the lab has recently received significant support from the European Research Council.

NEURAL CIRCUITS AND BEHAVIOR LAB







MAIN INTERESTS:

How the brain generates and controls coordinated movement

METHODS:

Quantitative behavioural analysis, Electrophysiology, Optogenetics

ANIMAL MODEL /BRAIN REGION: Rodents / Cerebellum









LAB MEMBERS

POSTDOCTORAL RESEARCHERS

- 1. Dominique Pritchett
- 2. Hugo Margues
- 3. João Fayad
- 4. Dennis Eckmeier

PHD STUDENTS

- 5. Ana Machado
- 6. Catarina Albergaria
- 7. Dana Darmohray 8. Jovin Jacobs
- 9. Tatiana Silva

MASTER'S STUDENTS

10. Gonçalo Figueira

RESEARCH TECHNICIANS

11. Tracy Pritchett





Principal Investigator **EUGENIA CHIAPPE** Joined CF in 2012

SENSORIMOTOR INTEGRATION LAB

MOTION SELFIES HOW THE BRAIN CAPTURES THE BODY IN ACTION

Think about how difficult brushing your teeth might be if you didn't have a sense of where your arm is relative to your mouth. You might find the toothbrush in your eye, or up inside your nose... To ensure the success of the most trivial, or the most elaborate action, the brain has to simultaneously monitor the position of all body parts, their speed of movement and the posture of the individual. To accomplish this, it combines information about its internal movement plan with information from sensory feedback caused by the ongoing movement. Both vision and proprioception, the sense that informs the brain about the tension and position of each joint of the body, monitor how well the planned movement is being executed. Together, all these inputs are used to inform the brain about the movements of the individual and fine-tune them on a rapid, "onthe-fly" timescale. How is this internal representation of self-movement generated across neural networks in the brain?

Scientific Approach

To address this fundamental question, the Sensorimotor Integration lab focuses on transformations of visual information into

motor action in the fruit fly Drosophila melanogaster. Experiments in the lab combine quantitative analysis of behaviour with simultaneous monitoring and manipulation of neural activity in genetically identified populations of neurons. In this manner, the team can artificially silence or activate neurons of interest and observe what happens to the patterns of activity of other neurons within the network, as well as to the behaviour of the fly. In addition, to directly probe what features of the visual world the brain uses to control the behaviour of the fly, the lab also uses carefully constructed virtual reality environments. Ongoing work in the lab has revealed that a group of visual interneurons, previously thought to be purely sensory, receives quantitative information about the fly's speed and direction of walking. These results show that when the animal is engaged in locomotion, motor-related signals are forecasted with exquisite detail and specificity to sensory regions. This information may be used to distinguish self-generated from non self-generated sensory information, or in producing an accurate internal representation of selfmovement

SENSORIMOTOR INTEGRATION LAB





Whole-cell patch recordings from optic-flow processing neurons (HS cells) are performed in fruit flies walking on a air suspended ball while stimulated with wide-field visual stimuli (gratings). The activity of these non-spiking neurons is analysed with respect to both the visual stimuli and the head-fixed, walking behaviour.







The computational principles that govern integration of motor actions with sensory information.

METHODS Electrophysiology, Behaviour, Optogenetic, Virtual reality

ANIMAL MODEL /BRAIN REGION: Fruit fly / Sensory, Motor and Premotor brain areas

LAB MEMBERS

POSTDOCTORAL RESEARCHERS 1. Terufumi Fujiwara

PHD STUDENTS

2. Mert Erginkaya 3. Tomás Cruz

MASTER'S STUDENTS 4. Nuno Rito

RESEARCH ASSISTANT

- 5. James Bohnslav
- 6. Anabel Rodriguez







Principal Investigator **RUI COSTA** Joined CF in 2008

NEUROBIOLOGY OF ACTION LAB READY, SET, ACTION! *Our daily lives can be viewed as a series* | Compulsive Disorder. Work from the lab of actions. Some of them, like driving home, are well-rehearsed and habitual, while others, such as learning how to play a new sport, require goal-directed attention. This fact may seem trivial, but it raises many different questions. For example, are habitual and goal-directed actions controlled by the same, or different, neural processes? How does the brain learn how to perform new actions? What happens if the neural circuits that underlie action initiation or termination malfunction?

Scientific Approach

To find the answers to these questions, the Neurobiology of Action lab uses a cross-level approach, from molecules to neural circuits. Specifically, the lab focuses on the interaction of the Basal Ganglia, a brain region known to be involved in motor learning and in the control of movement, with areas in the cortex that are important in motor planning and decision-making. These brain areas are also affected in neural disorders such as Parkinson's Disease, Huntington's Disease and Obsessive

has generated various findings in the field, including the description of a process called "Chunking" in the basal ganglia in which single motor elements are joined, or "chunked" together to create a single entity. Through this process, for example, the neural representations of single syllables may become representations of entire words. In addition, the team has identified that mastering challenging motor tasks depends on the brain's ability to select the most important movement elements. Finally, most recently, the lab has produced groundbreaking observations challenging some of the previously held perceptions regarding the role of subcircuits in the basal ganglia.

NEUROBIOLOGY OF ACTION LAB



Neurons expressing GFP under the Arc promoter in premotor cortex; in the homecage (H) and after 1, 2 or 3 days of rotarod training (R)



MAIN INTERESTS: How the brain generates and selects actions

METHODS: Optogenetics, Electrophysiology, Behaviour

ANIMAL MODEL /BRAIN REGION: Rodents; Humans / Basal Ganglia; Orbitofrontal Cortex

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LAB MEMBERS

POSTDOCTORAL RESEARCHERS

- 1. Aaron Koralek
- 2. Alejandro Gomez-Marin
- 3. Ana Cruz
- 4. Andreas Klaus
- 5. Catherine French
- 6 Cátia Feliciano
- 7. Cristina Afonso
- 8. Gabriela Martins
- 9. Lauren McElvain
- 10. Paolo Botta
- 11. Rodrigo Oliveira
- 12. Thomas Akam
- 13. Vitor Paixão

PHD STUDENTS

- 14. Bruno Afonso
- 15. Inês Vaz
- 16. Ivo Marcelo
- 17. Joaquim Alves da Silva
- 18. Mafalda Vicente
- 19. Marcelo Mendonça
- 20. Nuno Loureiro
- 21. Patrícia Rachinas-Lopes
- 22. Pedro Ferreira
- 23. Sevinc Mutlu
- 24. Vivek Athalye

RESEARCH TECHNICIANS

25. Ana Vaz 26. Mariana Correia

CLINICAL RESEARCH FELLOWS

- 27. Albino Oliveira-Maia
- 28. Ana Fernandes
- 29. Ana Catarina Castro
- 30. Bernardo Barahona-Correa









Principal Investigator GONZALO DE POLAVIEJA Joined CF in 2014

COLLECTIVE BEHAVIOR LAB

SOCIETY: A WHOLE GREATER THAN THE SUM OF ITS PARTS?

How you understand the world is strongly | approaches to studying these questions. influenced by what people around you think. Our interactions with the others influence what we learn, how we act and the choices we make. This is true not only of humans, but also for other social species, such as ants and fish. The relation between the group and the individual has been studied for centuries. Yet, the rules by which the group influences the behaviour of the individual and vice versa are still largely unknown. For instance, which variables lead these influences to be more or less beneficial to the group? How can these rules explain the emergence of group patterns ranging from the captivating swirling of shoals of fish, or flocks of birds, to politics, or economics?

Scientific Approach

At the Collective Behavior lab, a multidisciplinary team that includes mathematicians, physicists and biologists applies computational, behavioural, molecular, imaging and virtual reality

The team implements this diverse set of tools in zebrafish and humans. In this way, insights gained by genetic and molecular probing in zebrafish enable the researchers to design models which they test and extend to human experiments. The lab's recent advances include the development of a mathematical model of decision-making in groups that works well across species, from ants to humans. With this model, the researchers were able to demonstrate how individuals faced with ambiguous sensory information, such as a disguised predator, can use social cues to improve the accuracy of their decisions. The team has also been able to use these models to propose new ways to tap into collective intelligence.

COLLECTIVE BEHAVIOR LAB





Distribution of answers given by humans to simple estimation problems before (blue) and after (red) social influence. Our model (blue and red lines), that we first derived for zebrafish behavior, gives a good description for human data.

MAIN INTERESTS:

Formulate the rules that explain the interaction between the group and the individual

METHODS: Behaviour, Neurobiology, Molecular Biology and Mathematical modelling

ANIMAL MODEL /BRAIN REGION:

Zebrafish; Humans / Whole brain











LAB MEMBERS

POSTDOCTORAL RESEARCHERS

1. Angel Roman

2. Maria Cano-Colino

PHD STUDENTS

- 3. Antonia Groneberg
- 4. Gabriel Madirolas
- 5. Júlian Vicente
- 6. Raúl Gil de Sagredo 7. Robert Hinz
- 8. Victoria Brugada

RESEARCH TECHNICIANS

- 9. Andres Laan
- 10. Marta Iglesias
- 11. Ivar Clemens



Zebrafish behaviour Theoretical models Human behaviour





Principal Investigator INBAL ISRAELY Joined CF in 2009

NEURONAL STRUCTURE AND FUNCTION LAB

THE SHAPE OF MEMORIES

From the moment we are born, our experiences continuously change our knowledge and abilities. These changes include both acquiring new memories and skills and forgetting others. It is widely believed that these changes are reflected in the potency of the connections between neurons. What physical processes underlie these changes in connectivity and can they be visualised as physical, structural modifications in the neurons themselves? We know that when information is transmitted between neurons, some of this activity leads to changes in the small protrusions at which they contact one another, called spines, but we do not understand how their physical organisation and reorganisation supports learning and memory.

Scientific Approach

In the Neuronal Structure and Function lab the investigators use optical, genetic, electrophysiological and computational techniques to study experience-induced structural changes in neuronal spines. Spines are the connection sites between excitatory neurons, and so it is there where information is stored, or lost. The group focuses on the neuronal spines of the hippocampus, a brain region that is known to be involved in memory formation. Using highly focused laser light, they are able to precisely stimulate individual contacts of a mouse neuron and follow how different patterns of activity can result in either the growth or shrinkage of spines. In addition, since abnormal spine shape is observed in several neurodevelopmental disorders in humans, including Autism, the lab also studies neurons from animal models of these disorders in order to better understand the connection between structure and cognitive function.

NEURONAL STRUCTURE AND FUNCTION LAB



A) A mouse hippocampal pyramidal neuron imaged with 2-photon microscopy showing the vast number of spines that are distributed throughout the branch like dendritic tree.

B) A closer look at spines on a dendritic branch and how the SpineS software that we developed allows us to automatically quantify the diverse volumes of these structures.



MAIN INTERESTS:

How does activity between neurons lead to changes both in the function and structure of synapses? METHODS: Imaging, Optogenetics, Glutamate uncaging, Synaptic plasticity, Computation ANIMAL MODEL /BRAIN REGION:

Rodents / Hippocampus



LAB MEMBERS

POSTDOCTORAL RESEARCHERS

1. María Royo

PHD STUDENTS 2. Ali Özgür Argunsah 3. Anna Hobbiss

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Principal Investigator ADAM KAMPFF Joined CF in 2011

INTELLIGENT SYSTEMS LAB

TECHNOLOGY IN MOTION

When we look at objects like a cup or a ball, we find it natural that we know what to do with them. We can imagine what the object would feel like if we picked it up, or sound like if we threw it around, and we use this information to guide our decisions and overcome obstacles. How do brains learn about the structure of their environment? How do they encode this information in networks, and how is it used to control adaptive behaviour? Answering these fundamental questions may be greatly facilitated by the realisation of two major technical advances: the development of virtual worlds in which the statistics and physics of the environment can be manipulated; and the design and construction of novel devices for simultaneously recording from large populations of neurons throughout the brain of a behaving animal.

Scientific Approach

To promote these technical advances, the Intelligent Systems lab has been focusing its efforts on several projects using rodents as a model animal. In one, the team constructed a "modular" environment where the properties of

| many variables can be changed easily, giving the researchers flexibility in their experimental design while creating an ever changing environment reminiscent of natural conditions for the animal. As part of this project, another independent endeavour emerged, which unexpectedly developed into a powerful open-source tool called Bonsai.

Bonsai is a programming language that enables the user to efficiently measure and control multiple variables within an experimental setup. Despite the fact that Bonsai was designed to help with the particular needs of the lab, it was quickly adopted by many labs both within and outside of the Champalimaud Centre for the Unknown and is currently used by at least 30 labs world-wide.

Finally, the lab also works on advancing current tools used to record the activity of neurons. Specifically, the team investigates novel electrode materials and structures, aiming to improve the electrode-tissue interface, optimise the signal to noise ratio and increase selectivity for specific types of neurons.

INTELLIGENT SYSTEMS LAB



A) Paired recordings with one cell labeled by a parallel juxtacellular recording (colour indicates size of juxtacellularly recorded spikes). B) Hybrid data with 7 units labelled (colour indicates the units, black is unlabeled spikes).

MAIN INTERESTS:

Designing advanced technological tools for Neuroscience Research

METHODS: Engineering, Software programming, Behaviour, Electrophysiology

ANIMAL MODEL / BRAIN REGION: Rodents /

Motor cortex



LAB MEMBERS

POSTDOCTORAL RESEARCHERS

1. João Frazão

PHD STUDENTS

- 2. Danbee Kim
- 3. Goncalo Lopes
- 4. Joana Neto
- 5. Lorenza Calcaterra
- 6. Atabak Dehban

MASTER'S STUDENTS

7. Pedro Lacerda

RESEARCH TECHNICIAN

8. Joana Nogueira









Principal Investigator SUSANA LIMA Joined CF in 2008

NEUROETHOLOGY LAB

THE NEUROBIOLOGY OF SEX

Life without sex and reproduction would not only be less interesting, it would be impossible. Yet, despite its importance for the existence of the species, unlike feeding, it is not actually necessary for the survival of the individual. Still, nature developed "ways" to ensure animals do engage in sex, such as making it highly rewarding. But on the other hand, sexual behaviour must also be tightly controlled, as sex can put animals at risk by placing them in a defenseless position. Given this complicated balance of benefits and risks, how does the brain ensure that animals engage in safe and productive sexual processes?

Scientific Approach

To tackle this multifaceted problem, the Neuroethology lab focuses on several variables that influence sexual behaviour in mice. For one, as the willingness of females to engage in sex is limited to periods of fertility, the team investigates how sex hormones modulate neural activity and behaviour throughout the

female reproductive cycle. Second, the team also studies the mechanisms that ensure termination of sexual interaction in males. Finally, as reward is a central component in sexual behaviour, the team also studies reward processing in the brain. To gain insight into how the brain controls these fundamental processes, the team uses a variety of techniques, including electrophysiology, geneticallybased imaging methods, anatomy and many different behavioural paradigms designed to address these various aspects of sexual behaviour. The team works on several brain regions, but most of their efforts are centred on the ventral tegmental area, which is fundamental for reward processing and learning and on the medial hypothalamus, an area that is particularly important for female sexual behavior. In fact, recent advances in the lab include the establishment of the medial hypothalamus as a brain region where hormonal state and social information are integrated.

NEUROETHOLOGY LAB



In rodents, female receptivity is characterised by the execution of lordosis, a posture that aids penetration by the male. Lordosis is a reflex controlled by the spinal cord, but is highly modulated by several different brain regions, including the brainstem and the hypothalamus and depends on the concentration of sex hormones which vary across the reproductive cycle.



MAIN INTERESTS:

How the brain controls key processes in sexual behaviour

METHODS: Electrophysiology, Optogenetics, Anatomy and Behaviour

ANIMAL MODEL /BRAIN REGION: Rodents / Medial Hypothalamus; Ventral Tegmental Area









LAB MEMBERS

POSTDOCTORAL RESEARCHERS

- 1. Francisco Esteves
- 2. Kensaku Nomoto

PHD STUDENTS

- 3. António Dias
- 4. Luís Moreira
- 5. Silvana Araújo
- 6. Susana Valente

MASTER'S STUDENTS

- 7. Alessandro Braga
- 8. Diogo Matias
- 9. Nadja Oellrich

RESEARCH TECHNICIAN 10. Margarida Duarte





Principal Investigator **CHRISTIAN MACHENS** Joined CF in 2011

THEORETICAL NEUROSCIENCE LAB THE MATHEMATICS OF

THE BRAIN

Major breakthroughs in science are often | formulate their ideas and intuitions in a accompanied by the identification of a mathematical way to describe complex phenomena, such as Newton's laws of motion, or the three dimensional structure of DNA. Though neuroscience has already produced several important models, it still lacks a mathematical description of how neurons in the brain coordinate their activity in order to process incoming sensory information and how they use it to act. It's one of the biggest and most complicated mysteries in the field of neuroscience. Big because little is understood at this point and complicated because it involves information. This theory resulted in the many interconnected autonomic units (neurons), which are intrinsically complex.

Scientific Approach

To develop models of information processing in the brain, the Theoretical Neuroscience lab uses mathematical analysis and numerical simulations. These tools allow the researchers to

precise manner and thereby put them to a test using real data. Specifically, the team focuses on several 'higher-order' regions such as the frontal cortices that are involved in turning sensory information into decisions. As part of the recent advances in the lab, the team has developed a new method that visualises how populations of neurons represent sensory information and decisions simultaneously. In addition, other advances in the lab include the development of a theory that describes how neurons communicate shared successful explanation of a large set of experimental observations.

THEORETICAL NEUROSCIENCE LAB



A) Schematic of a neural population (middle) providing a representation (right) of a natural image (left). This image representation is formed when neurons respond to an image patch x with a so-called sparse representation.

B) Following the death of neurons that represent vertical orientations, the image representation degrades substantially for image segments that contain vertical lines (blue circle), and less so for image segments that contain horizontal lines (green circle).

C) Following optimal compensation, the image representation is recovered.

MAIN INTERESTS: Formulating computational theories of brain function and animal behaviour

METHODS: Mathematical analysis and Numerical simulations

ANIMAL MODEL /BRAIN REGION: Rodents, Monkeys/ Frontal lobes



LAB MEMBERS

POSTDOCTORAL RESEARCHERS

1. Dmitry Kobak

PHD STUDENTS

- 2. Asma Motiwala
- 3. João Semedo 4. Michael Pereira
- 5. Nuno Calaim

image of tree branches

image decoded from neural activities



Orientation column death





Optimal compensation





ZACHARY MAINEN Joined CF in 2007

Principal Investigator

SYSTEMS NEUROSCIENCE LAB

CREATING AND EVALUATING SUBJECTIVE REALITY We do not perceive the world directly. Rather, our brains must decipher what is out there using the window of information we receive from our senses. The result of this process is referred to as a 'model' of the world. Understanding how brains construct and use internal models is a central problem in neuroscience. This problem can be approached by thinking of the brain as a kind of an intuitive scientist. collecting and analysing data, constructing and testing hypotheses based on those data, and revising them in light of new data. Each brain gets different data and produces a different model, making the beliefs that guide our actions subjective and sometimes wrong. Fortunately, like a good scientist, our brains can and do evaluate the quality of the data. This gives us a sense of confidence in our beliefs and decisions, helping us to know when our our subjective reality is worth acting on and when to question it. Understanding how all this works in terms of neural circuits is the long-term goal of research in the Systems Neuroscience lab.

Scientific Approach

Until recently, most research on cognitive phenomena, such as perception and decision-making was done mainly in human and non-human primates. Together with

| a handful of colleagues, Mainen, head of the System Neuroscience lab, has helped to show that rodents, in fact, share many of primates' cognitive abilities. Indeed, in 2008, his lab was the first to discover neural activity that reflected decision confidence in any species, a feat that was done in rats. Though research projects with human subjects have more recently started in the lab, this approach still dominates the Systems Neuroscience lab today, where rodents are the stars, allowing the use of advanced genetic and molecular tools not available in humans and non-human primates. Using these tools, the team is able to combine multiple techniques, which allow them to record and manipulate the neural circuits that control confidence and decision-making in relevant brain regions, such as the cortex and the midbrain. The team places a major focus on the midbrain serotonin system, which they believe to play a key role, along with other neuromodulators, in regulating beliefs. Theory and modeling are also a vital component of the work done in the lab because of the inherent complexity involved. The members of the Systems Neuroscience lab are a diverse group, with backgrounds ranging from biology to mathematics, engineering and even philosophy. Lab members also counts on collaborations with many groups at the CR.

MAIN INTERESTS:

How brains use perceptual information to create and act on models of the world, the role of confidence, uncertainty and neuromodulators in these processes METHODS: Optogenetics, theory, Behaviour, Electrophysiology ANIMAL MODEL /BRAIN REGION: Rats, Mice, Humans/ Cortex and Raphe Nuclei

SYSTEMS NEUROSCIENCE LAB















LAB MEMBERS

POSTDOCTORAL RESEARCHERS

- 1. Bassam Atallah
- 2. Cindy Poo
- 3. Eran Lottem
- 4. Eric DeWitt
- 5. Eva Kobak
- 6. Masayoshi Murakami
- 7. Paul Bush 8. Rita Venturini

PHD STUDENTS

- 9. Ana Rita Fonseca
- 10. André Mendonça 11. Madalena Fonseca
- 12. Niccolò Bonacchi
- 13. Patrícia Correia
- 14 Samuel Viana
- 15. Sara Matias

RESEARCH TECHNICIANS

16. Ana Sofia Cruz

LAB MANAGER

17. Ana Nunes

A) A schematic drawing of the optogenetic approach to photostimulate DRN and promote waiting behaviour. DRN neurons are infected with AAV2/1-Dio-ChR2-EYFP. In SERT-Cre mice, 5-HT neurons will express ChR2-YFP (green cells) and can be photoactivated with blue light delivered through an optical fiber implant.

B) Dose-dependent increase in the fraction of patient trials for the population of SERT-Cre mice (n = 7). Percent changes in the fraction of patient trials with respect to nonstimulated trials, averaged across mice, are shown. Error bars indicate SEM.



Principal Investigator MARTA MOITA Joined CF in 2008

BEHAVIORAL NEUROSCIENCE LAB

THE NEUROSCIENCE OF SURVIVAL - FROM DEFENCE TO COOPERATION

Behaviours that are crucial for survival are likely to have shaped the brain throughout evolution. For instance, animals face a multitude of dangers, many of which can be life threatening, such as the encounter with a predator. Therefore, they have evolved several mechanisms of defensive behaviours, of which many are similar across the animal kingdom. Another type of behaviour crucial to the survival of many species is social behaviour. Living in groups provides a number of advantages, including protection against predators, a great example of this is the use of alarm signals from other animals, and division of labour, such as when groups of females take care of their young together. These two different types of behaviour raise many questions such as how animals detect threats in the environment, how they choose which defensive strategy to adopt and what drives animals to cooperate with each other.

Scientific Approach

To study how animals detect potential threats the Behavioural Neuroscience lab uses rats, since a great deal is known about the mechanisms in the brain that drive defensive behaviours in rodents. Most studies in rodents have focused primarily on the mechanisms that allow animals to learn about cues that predict impending danger. Still, how social information is used to detect threats remains largely unanswered. Therefore, a major effort in the lab is to unravel how animals use cues from conspecifics for threat detection.

To address this question the lab started by developing new behavioural tasks that allow the dissection of the social cues that rats use when exposed to threats. The team has been focusing on the amygdala, a brain structure that regulates defensive responses, and the areas that send information to it. To do so, experiments in the lab combine genetically based techniques and pharmacology to manipulate the activity of neurons in the brain regions of interest.

Once a threat is detected animals need to choose the appropriate action. While the action an animal displays depends on a number of factors, there is little understanding of how the choice between different defence modules is made. Again the social environment plays a crucial role in regulating defensive responses. Many times defensive behaviours are carried out at the level of the population, such as shoaling in fish. To address the question of the neural mechanisms of social defense responses, the Behavioral Neuroscience group uses a model system that is both amenable to the search for the neural mechanism of behaviour, while at the same time allowing the study of the behaviour of large groups of individuals, the fruit fly. This is the ideal model system, for its large collection of powerful genetic tools, a rapidly increasing number of approaches to study neural circuits and expanding set of behavioural paradigms. Therefore, the team is developing an assay to dissect social

Silence

Movement induced sound

Medial geniculate

Lateral amygdala

MAIN INTERESTS:

Defensive and social behaviour

METHODS: Development of behavioural tasks, Optogenetics, Pharmacology and Physiology

ANIMAL MODEL /BRAIN REGION: Rat and Fruit flies / Amygdala, Auditory thamalus and Cortex

BEHAVIORAL NEUROSCIENCE LAB









LAB MEMBERS

POSTDOCTORAL RESEARCHERS

- 1. Cristina Márquez
- 2. Clara Ferreira

PHD STUDENTS

- 3. Andreia Cruz
- 4. Ricardo Zacarias
- 5. Scott Rennie
- 6. Elisabeth Rickenbacher
- 7 Ana Pereira

MASTER'S STUDENTS

8. Matheus Farias

RESEARCH TECHNICIANS

9. Alexandra Medeiros 10. Diana Costa

Rats use freezing displayed by others, a defensive behaviour displayed in the absence of escape, as an alarm cue. Freezing is sensed by the sudden cessation of movement evoked sound. The dorsal portion of the medial geniculate, the auditory thalamus and the lateral amygdala play a crucial role in silence triggered freezing.



Defensive response



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Principal Investigator MICHAEL ORGER Joined CF in 2010

VISION TO ACTION LAB

WATCHING HOW THE BRAIN NAVIGATES THE WORLD Standing on the beach on a clear, sunny day you are watching the waves when you suddenly notice an airborne object speeding towards you. Do you jump out of its path, or do you try to catch it? Your reaction depends on your brain's ability to extract relevant features of sensory visual input and guide appropriate motor actions. Similar reflexive behaviours can also be seen in zebrafish larvae that, at just a week old, are naturally able to escape predators, or catch a prey. Though seemingly relatively simple, reflexive behaviours such as these actually depend on activity generated in complex networks of neurons that are distributed across the entire brain. Discovering how these dynamics unfold throughout brain on the level of single neurons during behaviour is crucial in order to formulate the principles on which these sensorimotor circuits are organised.

Scientific Approach

To tackle these challenges, the Vision to Action lab uses a combination of advanced optical, genetic and behavioural methods in zebrafish. In recent years, zebrafish have emerged as an attractive model system, as they exhibit a robust set of instinctive visually guided behaviours, while their brain, which follows a typical vertebrate pattern, is sufficiently small and transparent so that researchers can non-invasively image the activity of each of its neurons. Specifically, the team follows the activity of neurons by imaging changes in calcium levels inside neurons, a marker of neural activity, while performing high-speed behaviour tracking to make a detailed, quantitative analysis of visually evoked swimming and eye movements. In addition, the team develops genetic tools in order to probe and manipulate defined circuit elements with high specificity.

Recent work from the lab described, at single neuron resolution, the neural activity dynamics throughout the brain of behaving zebrafish. While even very simple behaviours involve activity in hundreds of neurons distributed across many brain regions, the team found that these elaborate patterns are consistent across individuals down to a very fine anatomical spatial scale. In addition, the team has also developed a high-speed, real-time tracking system that has allowed them to systematically characterise the swimming behaviour of zebrafish larvae in response to a variety of different stimuli. Using a computational approach to behaviour classification, called unsupervised machine learning, they have identified a core set of swimming movements, and demonstrated how they are used flexibly across different behaviours.

VISION TO ACTION LAB





A) Optomotor response Zebrafish swim to follow translational whole-field motion, which serves to stabilize their position in moving water.



MAIN INTEREST

Determine the principles on which sensorimotor circuits are organised and reveal how activity dynamics unfold throughout the whole brain during behaviour

METHODS

High-speed behaviour tracking, Optogenetics, Whole-brain calcium imaging, Computation ANIMAL MODEL /BRAIN REGION: Zebrafish / Whole brain









LAB MEMBERS

POSTDOCTORAL RESEARCHERS

- 1. Ana Raquel Tomás
- 2. Claudia Feierstein
- 3. Sabine Renninger

PHD STUDENTS

- 4. Jens Bierfeld
- 5. João Marques
- 6. Rita Félix
- 7. Simone Lackner

MASTER'S STUDENTS

8. Rita Esteves

RESEARCH ASSISTANT

9. José Lima 10. Marta Oliveira 11. Alexandre Laborde

 B) Optokinetic response.
Rotational motion induces conjugate horizontal eye movements.





Principal Investigator JOE PATON Joined CF in 2008

> LEARNING LAB

PINNING DOWN THE NEURAL CLOCK

For our ancient ancestors learning was necessary for survival. Will these berries make me ill? Which birdcalls announce the approach of a tiger? Millennia have passed, but to be a successful, or at least an adequate human, we still need to learn about the world. Even trivial tasks such as calling the elevator require learning making a mental connection between two events separate in time. How is the brain able to create these connections, which can happen either seconds, minutes, or even hours apart? Are there neural clocks known to be important for timing, the ticking away somewhere inside our brains \mid team also studies the thalamus and *drawing invisible lines between cause and* | frontal areas of the cortex. These frontal effect?

Scientific Approach

One of the major challenges in studying timing is that time is inevitably associated with changes in other variables, such as movement, or sensation. Therefore, the behaviours tested in the Learning lab are carefully chosen to help separate neural activity which is related to time from other ongoing variables. The team studies these behaviours in rats and mice while simultaneously recording

the activity of multiple neurons and manipulating their activity. This way, the team can observe how information about time can be encoded across networks of neurons. Indeed, one of the lab's largest contributions thus far has been to discover that information about elapsed time can be encoded in a kind of wave of activity that travels slowly across populations of neurons in the Basal Ganglia.

In addition to the Basal Ganglia, an area areas specifically are optimal sites for studying timing behaviour as they are thought to be involved in the association of experienced positive outcomes with the choices and actions that have led to them, or in other words, creating a mental connection between causes and positive effects. A deeper understanding of these areas could have far reaching implications for grasping how people function in both healthy and pathological conditions such as addiction or Parkinson's disease.

LEARNING LAB





A) As rats categorised intervals as longer or shorter than 1.5 seconds.

B) Neurons in the striatum fire maximally at different times, tiling the time intervals rats had learned to judge. This pattern of activity proceeded more quickly or more slowly when rats categorised a given interval as "long" or "short" respectively.

Δ

Short

0.6s



Duration judgments

MAIN INTERESTS:

How the brain learns what to do and when to do it

METHODS:

Behaviour, Neurobiology, Molecular biology and Mathematical modelling ANIMAL MODEL /BRAIN REGION:

Rodents / Basal Ganglia, Thalamus and frontal areas of the Cerebral Cortex

LAB MEMBERS

POSTDOCTORAL RESEARCHERS

1. Tiago Monteiro

PHD STUDENTS

- 2. Bruno Cruz
- 3. Gustavo Mello
- 4. Sofia Soares
- 5. Thiago Gouvêa

RESEARCH TECHNICIAN

6. Alessandro Braga











Principal Investigator LEOPOLDO PETREANU Joined CF in 2012

CORTICAL CIRCUITS LAB

EAVESDROPPING ON THE BRAIN: WHAT DO DIFFERENT AREAS TALK ABOUT?

outermost part of the brain. But appearances can be deceiving. In fact, the neocortex is the part of the brain that endows us with the advanced cognitive abilities that we are capable of. Despite its uniform appearance, the neocortex is composed of a set of specialised areas that interact with each other, thereby forming a complex network. Each action we take depends on the network's ability to communicate information across different regions and combine functions. For example, we wouldn't be able to catch a ball if different parts of our visual system were not engaged in continuous and rapid interaction. Communication among brain areas is done through a part of the neuron called an axon, which functions as a long "wire" that connects neurons both locally and across different brain areas. However, it still remains to be known what is the exact nature of the information that is sent out across areas and how it is "heard" by the target

areas and incorporated into their own

functioning.

The neocortex is a seemingly simple

sheet of neurons located at the

Scientific Approach

The members of the Cortical Circuits lab study the cortical areas that are required for visual processing in rodents. Using advanced microscopy methods, they study the axons that link distant visual areas of the neocortex. Specifically, team members use optical methods to map the connectivity of these axons with unprecedented detail. They also record and manipulate these axons while the animals perform visual tasks in order to understand the logic of these inter-areal interactions. It is important to note that recording the activity of single axons is no small feat, as axons are extremely thin wires, whose diameter measures a mere micrometer (a millionth of a meter) or less. Recent advances in the lab include the development of a novel technique to study how information received from distant brain areas is integrated by groups of neighbouring neurons in the target area.

> A) Connectivity maps of long-range axons in visual cortex and circuit wiring diagram.

B) Optical recordings of neural signals in axons linking visual areas.

MAIN INTERESTS: How different brain areas interact

with each other

METHODS: Imaging, Electrophysiology and Behaviour

ANIMAL MODEL /BRAIN REGION: Rodents / Visual Cortex

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LAB MEMBERS

POSTDOCTORAL RESEARCHERS

- 1. Nicolas Morgenstern
- 2. Nicolas Gutierrez-Castellanos

PHD STUDENTS

- 3. Gabriela Fioreze
- 4. Hedi Young
- 5. Marina Fridman
- 6. Tiago Marques

MASTER'S STUDENTS

7. Rodrigo Dias

RESEARCH TECHNICIANS 8. Julia Nguyen







Principal Investigator ALFONSO RENART Joined CF in 2011

CIRCUIT DYNAMICS AND COMPUTATION LAB

UNDERSTANDING COMPUTATIONS PERFORMED BY NETWORKS OF NEURONS Processes such as sensing, remembering, they believe that, at the moment, the or deciding are computations most effective approach to achieve the

accomplished through the exchange of nerve impulses by networks of neurons in the brain. Although the way in which single neurons use electrical activity to emit pulses is relatively well understood, neurons in the brain do not operate in isolation, and the trains of pulses from one neuron affect and are affected by the nerve impulses of the neurons with which it is connected. Since it is now possible to monitor the activity of hundreds of neurons simultaneously, it is becoming feasible to describe how neurons coordinate their activity in the living brain. Formulating general principles describing how neurons in key brain areas work together while animals solve specific tasks is an important step for understanding how the brain computes.

Scientific Approach

The goal of the Circuit Dynamics and Computation lab is to understand how the dynamics of networks of neurons allows them to solve particular problems. Although the team's ultimate objective is to understand neural computation at the circuit level in mathematical terms,

most effective approach to achieve this goal is to use a combined experimentaltheoretical approach. This is because the available experimental evidence describing the activity of neuronal circuits during specific computations is too scarce to formulate accurate theories. The lab's approach is therefore to first design behavioural tasks for rats and mice that isolate a specific computation, second, to record the simultaneous activity of many neurons during performance of these tasks, and finally to use mathematical methods to analyse this data and to generate models of how these computations are implemented. Specifically, the team is studying a variety of problems, among which two central ones are the way in which sensory areas in the cerebral cortex represent auditory information and use it to make simple decisions, and the way in which associative areas in the prefrontal cortex mediate short-term memory, by guiding actions using sensory information no longer present in the environment. Some of this work is done in collaboration with the Theoretical Neuroscience Lab and with the Systems Neuroscience Lab.

CIRCUIT DYNAMICS AND COMPUTATION LAB



Representation of the activity of 100 simultaneously recorded neurons from the rat auditory cortex in response to sounds of different intensity in the two ears (color) at different overall loudness (size of the dots) in the plane of the first two principal components.

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MAIN INTERESTS:

Identifying generic principles governing the dynamics of cortical circuits and the way in which they produce function METHODS: Behaviour, Electrophysiology, Analysis, Theory ANIMAL MODEL /BRAIN REGION:

Rodents, Human / Auditory Cortex and Prefrontal Cortex









LAB MEMBERS

POSTDOCTORAL RESEARCHERS

- 1. José Pardo-Vazquez
- 2. Nivaldo Vasconcelos
- 3. Tor Stensola

PHD STUDENTS

- 4. Jacques Bourg
- 5. João Afonso
- 6. Raphael Steinfeld
- 7. Roberto Medina

MASTER'S STUDENTS

8. Julien Fiorilli 9. Ana Mafalda Valente

RESEARCH ASSISTANT 10. Juan Castiñeiras





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Principal Investigator **CARLOS RIBEIRO** Joined CF in 2009

BEHAVIOR AND METABOLISM LAB

THE HUNGRY BRAIN PURSUING THE NEURAL CIRCUITS THAT DETERMINE FOOD CHOICE

The food we eat affects all aspects of our | implement an integrative neuroscience lives, including aging, ability to reproduce, lifespan, mental state and mood. For better or worse, we are what we eat. Yet, how the brain controls food choice is still a mystery. What are the neural processes that drive us to choose a pretzel over an apple, or a steak over ice cream? To tap into this problem researchers have to tackle difficult questions such as how does the brain know which nutrients the body needs to stay healthy and how is this information translated into action?

Scientific Approach

The Behavior and Metabolism lab addresses these questions by using the fruit fly Drosophila melanogaster, one of the most powerful genetic animal models currently available. The fruit fly offers an impressive set of tools and techniques, which include, among many others, genetic circuit manipulations, activity imaging, automated, quantitative methods for studying behaviour, and neuroanatomy. Team members use the full set since it enables them to

approach, necessary in solving this whole-organism problem. Since nutrient decisions have implications that pertain to the entire organism, the lab's work leads it to probe neural circuits ranging from those that mediate taste and smell perception to those involved in the mating response. One of the lab's recent advances, for instance, was the discovery of a female neuronal pathway that begins with mating, continues with changes in sensory salt perception in female flies and culminates with alterations in their preference for salty food. Bringing to mind the well-known phenomenon of food cravings during pregnancy.

BEHAVIOR AND METABOLISM LAB





In fruit flies, mating induces a salt appetite, resembling that seen during reproduction in many species. This appetite is induced by a change in taste processing, driven by a malederived signal acting on specific neurons in the female



Yeast

MAIN INTERESTS:

The neural mechanisms of nutrition

METHODS: Optogenetics, Nutritional manipulations,

Molecular and Biochemical methods, Neuroanatomy, Microbial manipulations of the host and Behaviour

ANIMAL MODEL /BRAIN REGION: Fruit fly / Whole brain









LAB MEMBERS

LAB MANAGER

1. Ana Paula Elias

POSTDOCTORAL RESEARCHERS

- 2. Kathrin Steck
- 3. Pavel Itskov
- 4. Ricardo Gonçalves
- 5. Zita Santos

PHD STUDENTS

- 6. Samantha Herbert
- 7. Samuel Walker
- 8. Verónica Corrales

MASTER'S STUDENTS

9. José Maria Moreira

RESEARCH TECHNICIANS

- 10. Patrícia Francisco
- 11. Celia Baltazar







Principal Investigator NOAM SHEMESH Joined CF in 2014

NEUROPLASTICITY AND NEURAL ACTIVITY LAB

NO ONE EVER RECORDS FROM THE SAME BRAIN TWICE

When the Greek Philosopher Heraclitus spoke about how change is central to the universe, coining the phrase "no one ever steps into the same river twice", one wonders if he could have foreseen the implications his words would have on the human brain. Throughout normal development, experience and learning, or injury and disease, our brain's activity and structure are always in motion. So much so that one can almost even say that no one ever records from the same brain twice. How do these different processes influence the brain's functionality and structure over time?

Scientific Approach

To find the "missing link" between behaviour and changes on the molecular, or cellular level, the Neuroplasticity and Neural Activity lab develops pioneering functional magnetic resonance imaging (fMRI) techniques. fMRI is a non-invasive, powerful tool for studying various neuroscience and biomedical questions. Current fMRI methods work by performing

indirect measures of neural activity by following accompanying changes in blood volume and oxygenation level. However, changes in blood flow, in addition to being an indirect measure, occur over a timescale of seconds, while neural activity occurs within a fraction of a single second. This difference in timescale points out an obvious limitation of current fMRI techniques – they are too slow to resolve many important processes in the brain. To address these issues, the team's first steps, for which they have recently received support for from the European Research Council, have been focused on developing novel techniques that harness the power of MRI to perform direct measurements of neural activity on a much faster timescale. For instance, the team will use ultrahigh magnetic fields to image the dynamics of neurotransmitters in the brain. These various measurements will be performed *in-vivo* using state of the art 9.4T and 16.4T scanners, in both anesthetised and behaving rodents.

NEUROPLASTICITY AND NEURAL ACTIVITY LAB



Different tracts in the rodent spinal cord were mapped using a robust newly developed method for quantifying the axon density, by using ultrahigh field MRI, making possible the contrasting of different tracts.

MAIN INTERESTS: Direct functional MRI based on cell

METHODS: Functional Magnetic Resonance Imaging

(fMRI), Optogenetics, Behaviour

ANIMAL MODEL /BRAIN REGION: Rodents / Whole brain

swellings and neurotransmitter release





LAB MEMBERS

POSTDOCTORAL RESEARCHERS

- 1. Daniel Nunes
- 2. Ekaterina Vinnik
- 3. Tal Shemesh

PHD STUDENTS

- 4. Annelene Dahl
- 5. Madalena Fonseca

RESEARCH ASSISTANTS

- 6. Frederico Severo
- 7. Rita Gil





Principal Investigator LUÍSA VASCONCELOS Joined CF in 2011

INNATE BEHAVIOR LAB

WHEN INSTINCTS TAKE OVER

your stomach rumbling when you suddenly catch a whiff of a delicious smell. Without giving it a second thought you decide to follow it, making a few wrong turns until you find yourself in a nice bakery. This behaviour, common to humans and other animals, is called foraging, the active seeking of food. It is actually only one example of a group of behaviours defined as instinctive, or innate behaviours. These behaviours do not require learning, nor experience, they are often involuntary and can occur in individuals even without their awareness. Other well-known examples of innate behaviours include nest-building and courtship. Fortunately, unlike other behaviours such as decision-making, the neural circuits that underlie innate behaviours are hardwired, which means that they are invariant from animal to animal. This fact makes these behaviours an excellent case study in neuroscience, where the neural processes involved can be mapped out from sensory input to motor output

You are walking down the street with

Scientific Approach

To dig down into the neural circuitry of innate behaviour, the Innate Behavior lab focuses on two main behaviours - the

| relatively simple avoidance of a repulsive odour and the more intricate courtship behaviour. Both are studied in the fruit fly Drosophila melanogaster, a powerful model system that offers a wide range of advanced techniques. These include genetic tools and manipulations to help to identify which neurons are involved in specific behaviours and optogenetic tools to monitor the activity of neurons by using changes in calcium level for instance, a proxy for neural activity. Together, these tools enable the researchers to pin down the anatomical and functional components of neural circuits. The team uses these tools together with highly detailed video monitoring to establish the most precise relationship between behaviour and neural activity. The team studies different brain areas to understand each of these behaviours. Specifically, to study odour avoidance, the team investigates how two higherorder olfactory centres of the fly's brain interact to generate escape behaviour. Studying the more complex courtship behaviour, however, may lead to any part of the brain, turning it into a very exciting journey, which began with the lab's recent discovery of a set of neurons that is required for the female to respond adequately to male courtship.

INNATE BEHAVIOR LAB



As a normal part of courtship, female flies walk away from males but at a lower speed than when walking alone. When the activity of neurons that express the gene apterous is silenced during courtship (by placing them in a 30°C environment) females walk away from the male faster than normal female flies.

MAIN INTERESTS.

Identification of the neural circuits and mechanisms that control innate. or instinctive. behaviours

METHODS:

Optogenetics, Imaging, Behaviour and Genetics

ANIMAL MODEL /BRAIN REGION: Fruit fly /

Whole brain







POSTDOCTORAL RESEARCHERS

- 1. Cecilia Mezzera
- 2. Márcia Aranha
- 3. Nélia Varela

PHD STUDENTS

- 4. Cristina Ferreira
- 5. Dennis Herrmann
- 6. Eliane Ochôa Arez
- 7. Miguel Gaspar

RESEARCH TECHNICIANS

- 8. Hugo Cachitas
- 9. Sophie Dias



BSM

The Biology of Systems and Metastasis Programme

IN 2015, THE CHAMPALIMAUD FOUNDATION LAUNCHED A NEW PROGRAMME FOCUSED ON A "WHOLE BODY" INTEGRATIVE APPROACH TO INVESTIGATING THE BIOLOGY OF CANCER. ITS ULTIMATE GOAL IS TO UNDERSTAND AND PREVENT CANCER.

Understanding how cancer emerges, how cancer cells escape the organism's defence mechanisms, how they multiply and metastasise, will depend on more than understanding the biology of the cancer cells; it will also depend on understanding how cancer cells interact with the various systems of the organism, including the vascular, immune, lymphatic, and endocrine systems, and how these interactions change over time.

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The first three groups of the programme were recruited in 2015. They will research how non-tumour cells contribute to tumour initiation, growth and metastasis; how tumour and regular cells compete in organisms, and how stem cells are reactivated.

A - Systems Oncology Lab

Tumor-associated cells (green) adjacent to tumor cells (red) at a metastatic site.

B - Cell Fitness Lab

Winner epithelial cells in magenta growing at the expense of neighboring normal tissue, shown in black. All cell membranes are marked in green, due to the expression of epithelial marker E-cadherin GFP.

C - Stem Cells and Regeneration Lab

6 days after brain injury, new neurons (marked in red and green) have integrated into the damaged brain area marked by the dashed line. Cell nuclei are stained in blue. Inset: quiescent neural stem cell in the adult fly brain.





Systems Oncology Bruno Costa da Silva





Cell Fitness Eduardo Moreno Humans are able to detect fitness decay in colleagues by looking at the greying of their hair or the wrinkles in their faces. Work from the lab in the last few years has shown that cells can also detect the fitness level of neighbouring cells by using a molecular code. These "fitness fingerprints" can be used to mediate cell selection by recognising and eliminating cells which are less fit during ageing, regeneration and cancer. The lab has recently shown that these mechanisms are at play during cell





Stem Cells and Regeneration Christa Rhiner Unraveling how stem cell populations are activated physiologically and upon damage is important for understanding and preventing conditions such as cancer and brain injury. For instance, recent results from the lab include the discovery of damage-responsive neural stem cells in the fruit fly *Drosophila melanogaster*. These cells proliferate after traumatic brain injury and efficiently produce new neurons in the injured brain region. By taking advantage of the fly's genetic accessibility, the team aims to uncover

The general interest of the Systems Oncology group is to understand how non-tumour cells contribute to tumour initiation, growth and metastasis. More than focusing on specific tumour types, the group investigates the biological systems that support oncologic disease. For instance, tumour cells can produce and release proteins and extracellular vesicles that affect and modify healthy tissue. These modifications then facilitate tumour growth and metastasis. By using animal models of tumour initiation, progression and metastasis, in combination with thorough analysis of extracellular vesicle composition isolated from patients with diverse clinical profiles, the team intends to characterise novel cellular and molecular determinants of cancers.

competition in cancer, and can be used as potential therapeutic targets.

the molecular mechanisms that activate stem cells and contribute to regenerative neurogenesis in the brain and to cancer. In addition, the team is also focused on understanding how altered neural stem cell plasticity (hyper-activation or adult loss of neural stem cells) impacts tissue regeneration, aging and cancer.

Publications Highlights

THE DISCOVERIES RESULTING FROM THE WORK OF CR RESEARCHERS ARE REGULARLY PUBLISHED IN HIGH IMPACT JOURNALS, MIRRORING THE SIGNIFICANT POTENTIAL REACH OF THE RESEARCH DONE BY CR INVESTIGATORS



Behavior And Metabolism Lab

Pass the salt - Using the flv to understand how pregnancy drives food cravings

By piecing together a complicated puzzle, researchers were able to demonstrate that salt-craving exists in flies much as it does in mammals and that this craving plays an important role in their reproductive abilities. They were also able to identify the trigger for saltcraving and map several steps in the neural circuitry that brings about this behavioural change.

Walker SJ, Corrales-Carvajal VM, Ribeiro C. (2015). Postmating circuitrv modulates salt taste processing to increase reproductive output in Drosophila. Current Biology. 25(20):2621-30.



Behavioral Neuroscience Lab

Lending a hand, or a paw - what drives us to help others?

Is our tendency to act to benefit others without benefit to ourselves unique to humans, or is this apparent virtue common to other species such as rats? In this study, researchers find that similarly to humans, rats offer help without added self-benefit. This behaviour, however, is found to depend on certain behavioural variables, which are outlined in this study.

Márquez C, Rennie SM, Costa DF, Moita MA (2015). Prosocial choice in rats depends on food-seeking behaviour displayed by recipients. Current Biology. 25(13):1736-1745.25(20):2621-30.



Intelligent Systems Lab

Bonsai - the art of creating new worlds

This study represents a special example of a research side project that became a powerful open-source tool. Bonsai is a programming language that enables the user to efficiently measure and control multiple variables within an experimental setup.

Lopes G, Bonacchi N, Frazão J, Neto JP Atallah BV Soares S Moreira L, Matias S, Itskov PM, Correia PA, Medina RE, Calcaterra L, Dreosti E, Paton JJ, Kampff AR (2015). Bonsai: An event-based framework for processing and controlling data streams. Frontiers in Neuroinformatics. 9:7.

Publications



How does the brain keep track of time?

According to this study, time is represented by a slow wave of sequential activity across neurons in the striatum. This wave shrinks or expands to encode different durations, implying that time in the brain is relative, not absolute, as it is measured as a position within an interval and not as a unit, such as a second or an hour.

Mello GB*, Soares S*, Paton JJ. (2015). A Scalable Population Code for Time in the Striatum Curr. Biol. S0960-9822 (15): 00205-5 (doi:10.1016/j. cub.2015.02.036)

A state-of-the-art open-source tool that captures fine details of locomotion in mice and offers new insights onto the neural basis of balance and coordination.

deficits

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Machado AS, Darmohray DM, Fayad J, Marques HG, Carey MR. (2015). A quantitative

framework for whole-body coordination reveals specific deficits in freely walking ataxic mice. eLife. doi: 10.7554/eLife.07892.

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McElvain LE, Faulstich M, Jeanne JM, Moore JD, du Lac S (2015). Implementation of Linear Sensory Signaling via Multiple Coordinated Mechanisms at Central Vestibular Nerve Synapses. Neuron 15 (00043-4), [Epub ahead of print]

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Akam T, Costa R, Dayan P (2015). Simple Plans or Sophisticated Habits? State, Transition and Learning Interactions in the Two-Step Task. PLoS Comput. Biol. 11 (12):e1004648 .

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Banerjee A, Marbach F, Anselmi F, Koh MS, Davis MB Garcia da Silva P Delevich K Oyibo HK, Gupta P, Li B, Albeanu DF (2015). An Interglomerular Circuit Gates Glomerular Output and Implements Gain Control in the Mouse Olfactory Bulb. Neuron. 87(1):193-207.

Barahona-Corrêa JB. Camacho M. Castro-Rodrigues P, Costa R, Oliveira-Maia AJ. (2015). From Thought to Action: How the Interplay Between Neuroscience and Phenomenology Changed Our Understanding of Obsessive-Compulsive Disorder Front. Psychol. 6:1798. doi: 10.3389/fpsyq.2015.01798.

Bush PC, Mainen ZF (2015) Columnar architecture improves noise robustness in a model cortical network. PLoS ONE. 10(3):e0119072.

Cao VY, Ye Y, Mastwal S, Ren M, Coon M, Liu Q, Costa RM, Wang KH (2015). Motor Learning Consolidates Arc-Expressina Neuronal Ensembles in Secondary Motor Cortex. Neuron. 86 (6):1385-1392.

Fonseca MS, Murakami M, Mainen ZF (2015). Activation of Dorsal Raphe Serotonergic Neurons Promotes Waiting but Is Not Reinforcing. Curr. Biol. 25(3):306-15.

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Neural Circuits and Behavior Lab

LocoMouse - Innovative tool sheds light on motor



Neuroethology Lab

The neural basis of 'being in the mood'

What determines receptivity or rejection towards potential sexual partners? In this study researchers discover neurons in the hypothalamus of female mice that respond differently to interactions with males depending on the hormonal state of the female, thereby corroborating the existence of a brain region that combines social information with hormonal state

Nomoto K, Lima SQ (2015). Enhanced Male-Evoked Responses in the Ventromedial Hypothalamus of Sexually Receptive Female Mice. Current Biology 25(5): 589-594.



Systems Neuroscience Lab

Good things come to those who wait? Study finds that more serotonin, more patience

In this study, researchers from the find a causal link between the activation of serotonin neurons and the amount of time mice are willing to wait, and reject a possible link between increased serotonin and reward.

onseca MS, Murakami M, Mainen ZF (2015), Activation of Dorsal Raphe Serotonergic Neurons Promotes Waiting but Is Not Reinforcing. Current Biology. 25(3): 306-315.

Publications

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Funding **Highlights**

CR IS SUPPORTED BY FUNDS PROVIDED BY THE CHAMPALIMAUD FOUNDATION AND BY EXTERNAL FUNDS FROM A DIVERSE GROUP OF NATIONAL AND INTERNATIONAL ORGANISATIONS.

FCT Fundação para a Ciência e a Tecnologia

Funding 1.3 M € Awarded to the Champalimaud Neuroscience Programme (CNP)

Following both phases of the recent review of Research and Development units in 2014, the CNP was classified as Exceptional, the highest grade possible in this evaluation. This classification places the CNP among the best research institutes in Portugal, awarding it with support in the form of a budget of approximately 450,000€ per year for the duration of 3 years, beginning June, 2015.



ERC **European Research Council**

Funding 2.5 M € Awarded to Zachary Mainen

This research grant is the second consecutive ERC advanced grant awarded to Dr. Mainen, representing the first time a researcher working in Portugal has received this award two successive times. The grant will be dedicated to studying how serotonin influences the way we perceive the world and consequently our behaviour.

Funding 1.8 M € Awarded to Megan Carey

This ERC Starting Grant was awarded to Dr. Carey to study the neural circuits that coordinate locomotion in mice. In this project, Dr. Carey's team will work to elucidate the mechanisms through which the cerebellum contributes to locomotion.

Funding 1.5 M € Awarded to Noam Shemesh.

Dr. Shemesh was awarded this ERC Starting Grant to establish cutting edge Magnetic Resonance Imaging methodologies that will provide novel insights onto neural function during health and disease.

European Research Council

Carey, Megan. Cerebellar circuit mechanisms of coordinated locomotion in mice. ERC Starting Grant. (Started 2015).

Mainen, Zachary. Modulation of cortical circuits Fundação Para a Ciência e a Tecnologia and predictive neural coding by serotonin. ERC Advanced Grant. (Announced 2015).

Shemesh, Noam. Sensing activity-induced cell swellings and ensuing neurotransmitter releases for in-vivo functional imaging sans hemodynamics. ERC Starting Grant. (Announced 2015).

Fundação Bial

Carey, Megan & Prichett, Dominique. Optogenetic circuit dissection of neural instructive signals for cerebellum-dependent learning. Bial Science Research Grant. (Started 2015).

Costa, Rui & Koralek, Aaron. The role of dopamine in behavioral exploration and action selection. Bial Science Research Grant. (Started 2015).

Machens, Christian & Kobak, Dmitry. Demixing and visualizing neural population activity in higher cortical areas. Bial Science Research Grant. (Started 2015).



Horizon 2020, Marie Skłodowska-Curie

Shemesh, Noam (with Mainen, Zachary). From surrogate hemodynamics-based fMRI towards direct functional imaging of neural activity via sensing activity-induced cell swellings and neurotransmitter releases in vivo. Marie Sklodowska Curie Individual Fellowship. (Started 2015).

Koralek, Aaron (with Rui Costa). The role of dopamine in behavioral exploration and action selection. Marie Sklodowska Curie Individual Fellowship. (Declined by fellow)

2015).

(FCT)

A - FCT grant 1.3 M € awarded to the CNP

B - ERC Awarded to Megan Carey Continuous 3D trajectories



Ribeiro, Carlos. Identifying and characterizing the neuronal circuits required for nutrient choice and their effects on aging. Bial Science Research Grant. (Started 2015).

Champalimaud Neuroscience Programme. Evaluation level: Exceptional. R&D Units Evaluation. (Started 2015)

Costa, Rui. Determining the basal ganglia circuits involved in repetitive behaviors in Autism Spectrum Disorders. Scientific research and technological development Project. (Announced 2015).

Lima, Susana. Female socio-sexual behavior: role of hypothalamic neuronal activity across the reproductive cycle. Scientific research and technological development Project. (Announced 2015).

Oiveira, Rui, de Polavieja, Gonzalo. Behavioural and evolutionary ecology of social cognition: experimental approaches in zebrafish. Scientific research and technological development Project. (Announced 2015).

Orger, Michael. The neural circuit basis of oculomotor behavior in zebrafish. Scientific research and technological development Project. (Announced 2015).

Polavieja, Gonzalo. Decision-making in animal groups: a multidisciplinary approach to understand how social information is processed. Scientific research and technological development Project. (Announced 2015).

Shemesh, Noam. Mapping specific neural activity by coupling ultrahigh field functional-MRI, optogenetics, and calcium recordings. Scientific research and technological development Project. (Announced 2015).

Portugal 2020

Costa, Rui (partner). Sondas neuronais dotadas com interação elétrica, ótica e comunicação sem fios para controlo de neurónios-alvo. Projecto de I&DT em Copromoção. (Announced 2015).

External Funding 2007-2015

Fundação Para a Ciência e a Tecnologia

INDP Class of 2014: Cruz, Bruno; Romero, Vertechi, Pietro; Silva, Tatiana; Khoboko, Thabelo; Cruz, Tomás. Doctoral Fellowship. (Started 2015).

Pritchett, Dominique (with Carey, Megan). Optogenetic circuit dissection of neural instructive signals for cerebellum-dependent learning. Postdoctoral Fellowship. (Announced

Simons Foundation

Koralek, Aaron (with Costa, Rui). The role of dopaminergic network dynamics in behavioral Francisco; Vaz da Cunha, Inês; Gaspar, Miguel; exploration. Simons Collaboration on the Global Brain Postdoctoral Fellowship (Started 2015)

Swiss National Science Foundation

Botta, Paolo (with Costa, Rui). Dissecting specific amygdala-striatal circuitries on exploration. Early Post-doc Mobility Fellowship. (Started 2015).

Education Highlights

NCE THE BEGINNING.

THE CR HAS REGARDED DUCATING FUTURE UROSCIENTISTS AS ONE 1AIN OBJECTIVES TO THIS END. THE CR 5 BEEN DEDICATINO)FVFI OPMFN' ND IMPLEMENTATION OF SES AND WORKSHOP

INDP

International Neuroscience **Doctoral Programme** INDP Director: Alfonso Renart

Administrative Assistants: Alexandra Piedade and Teresa Carona, Tânia Li Chen

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.

During the first year of the programme, students attend courses that cover basic topics in contemporary neuroscience. The courses have a strong practical component, which includes a variety of experimental preparations. During this year, students also perform lab rotations, which allow them to familiarise themselves with the research done in the different labs and help them with selecting the lab where they will conduct their doctoral research.



INDP Class of 2015

Rodriao Dias MSc in Physics Engineering Universidade de Lisboa

Severin Berger MSc in Bioinformatics University of Basel

Theses

December 3, 2015 PhD awarded to: André Mendonça Title: The role of reinforcement learning in perceptual decision-making. Thesis Advisor: Zachary Mainen, CR

Thesis Advisor: Zachary Mainen, CR

December 15, 2015 PhD awarded to: Rodrigo Abril Abreu Thesis Advisor: Rui Oliveira, CR and ISPA

December 10, 2015 PhD awarded to: Sara Matias Title: Dynamics of serotonergic neurons revealed by fiber photometry.

Title: Social Eavesdroppping in Zebrafish

In 2015, the new CAJAL Advanced Neuroscience Training Programme was launched. The programme consists of four yearly courses, two held at the Champalimaud Centre for the Unknown in Lisbon and two in the Bordeaux Neurocampus. These two institutes were chosen to be the first centres in Europe that will host recurring neuroscience training courses, following a model that has been successfully running in the US for decades.

Advanced Course in Behaviour and Neural Systems

Course Directors: Adam Kampff (CR), Zachary Mainen, (CR) and Florian Engert (Harvard University, USA)

This three-week course is a practical "hands-on" introduction to advanced methods in behavioural neuroscience and provides sufficient background such that all participants will be able to establish these techniques in their home laboratories. Popular model organisms (rodents, fly fruits, and zebrafish) are used to demonstrate how modern technology (e.g. video tracking, virtual reality, automation, etc.) can be combined with traditional behavioural approaches to perform truly innovative neuroscience investigations.

The course is composed of two phases. The first consists of a series of day long "mini-projects". These hand on exercises introduce new model organisms and the relevant core techniques. The second phase involves deploying these new skills to design and implement them in a week-long research project that consolidates this new knowledge. This extended project offers an opportunity for the participants to undertake novel state-of-the-art research supervised by experts in the field.

Advanced Course in Computational Neuroscience

Course Directors: Christian Machens (CR), Gilles Laurent (Max Planck Institute for Brain Research, Frankfurt, Germany), Máté Lengyel (Cambridge University, UK)

Computational Neuroscience is a rapidly evolving field whose methods and techniques are critical for understanding and modelling the brain, and also for designing and interpreting experiments. Mathematical modelling is one of the few tools available to cut through the vast complexity of neurobiological systems and their many interacting elements.

This three-week school teaches the central ideas, methods, and practice of modern computational neuroscience through a combination of lectures and hands-on project work. Each morning is devoted to lectures given by distinguished international faculty on topics across the breadth of experimental and computational neuroscience. During the rest of the day, students work on research projects in teams of two-three people under the close supervision of expert tutors and faculty. Research projects are proposed by faculty before the course, and included, in 2015, the modelling of neurons, neural systems, and behaviour, the analysis of state-of-theart neural data (behavioural data, multi-electrode recordings, calcium imaging data, connectomics data, etc.), and the development of theories to explain experimental observations.

February 09, 2015

April 13 2015

tinnitus patients

June 01, 2015

melanogaster.

UK

Tata Institute of Fundamental Research **Baylor Brangers**

BS in Physics, BS in Astronomy&Astrophysics Indiana University Dennis Goldschmidt MSc in Neural Systems and Computation

University of Zurich/ETH Zurich".

PhD awarded to: Fernando Santos

dynamics during novel skill learning.

Thesis Advisor: Rui Costa, CR

Title: Learning new tricks: Corticostriatal

PhD awarded to: Ana Isabel Aires Amaral

Title: Functional MRI of stimulus interference

on auditory processing in normal listeners and

Thesis Advisor: Dave Langers, NIHR Notting-

ham Hearing BRU, University of Nottingham,

Title: Investigation of Novel Circuits Involved in

Thesis Advisor: Maria Luisa Vasconcelos. CR

PhD awarded to: Dennis Herrmann

Virgin Female Receptivity of Drosophila

Marta Iglesias BS in Biology Universidad Autonoma de Madrid

July 08, 2015

Mauricio Toro MSc in Biological Sciences Universidad de Chile Patrícia Francisco

MSc in Human Biology & Environment Universidade de Lisboa

PhD awarded to: Gil Costa Title: The title is neural and behavioral correlates of decision confidence. Thesis Advisor: Zachary Mainen, CR

July 27, 2015 PhD awarded to: Maria Inês Vicente Title: Uncertainty in olfactory decision-making. Thesis Advisor: Zachary Mainen, CR

September 21, 2015 PhD awarded to: Ana Pereira Title: Auditory cues in Social Transmission of Fear. Thesis Advisor: Marta Moita, CR

November 27 2015 PhD awarded to: Patrícia Correia Title: The role of serotonin in behavior: Shining light on the maestro of the brain. Thesis Advisor: Zachary Mainen, CR



Courses. **Workshops** & Events Highlights

TO COMPLEMENT RESEARCH RELATED ACTIVITIES, THE CR ALSO ORGANISES SCIENTIFIC EVENTS ON A REGULAR BASIS. THESE EVENTS, WHICH INCLUDE A COLLOQUIA SERIES AND CONFERENCES, BRING TO THE CCU DISTINGUISHED INTERNATIONAL NEUROSCIENTISTS. THE EVENTS ARE OPEN TO THE PUBLIC, THOUGH PRE-REGISTRATION AND SELECTION PROCESSES ARE OFTEN APPLIED.

Round Table Discussion

Science Funding as an Engine For **Develoment**

May 20, 2015

Organisers: Rui Costa and Megan Carey What are the challenges facing private foundations to promote research? How does the interaction between private foundations and public bodies work to advance science? High-level representatives from both private and public sectors came together to discuss these and other topics.

The discussion titled "Science Funding as an Engine For Development" was held as part of

the visit of Robert Tjian, President of Howard Hughes Medical Institute, to Champalimaud Centre for the Unknown. The panelists, in addition to Tjian, were Leonor Parreira, Portuguese Secretary of State for Science; Leonor Beleza, President of the Champalimaud Foundation and Marcal Grilo. Board member at the Calouste Gulbenkian Foundation. The discussion was moderated by Rui Costa, codirector of Champalimaud Research.

Following the discussion, the panelists replied to questions and engaged in conversations with members of the audience.



Courtesy of Christa Rhiner

Symposium Biology of Systems and Metastasis Programme June 16-18, 2015

Organisers: Zachary Mainen and Rui Costa

In 2015, the Champalimaud Foundation launched a new programme on the Biology of Systems and Metastasis (BSM) focused on a systems organismic approach to investigating the biology of cancer. Its ultimate goal is to understand and prevent cancer especially metastasis. To select the most suitable group leaders for the programme, the call was aimed at candidates with ambitious research

programmes using advanced techniques to elucidate metastasis and cancer biology with an organismic perspective. Researchers using both experimental and theoretical approaches were encouraged to apply. More than 40 researchers applied from top institutions around the globe and ten were selected for a symposium that took on June 2015.

This process culminated in the recruitment of four new group leaders for the BSM programme: Bruno Costa-Silva, Eduardo Moreno, Christa Rhiner and Henrique Veiga-**Fernandes**

4th Champalimaud Neuroscience Symposium Perspectives on Social Behavior

September 16 - 19, 2015 Organisers: Gonzalo de Polavieja, Susana Lima and Christian Machens Administrative coordination: CR Administrative Units At the 4th Champalimaud Neuroscience

Symposium, researchers working on a broad

Dirk Helhina

Eric Fortune

ogy, US

lain Couzin

ogy, Germany

Jav Van Bavel

New Jersey Institute of Technol-

Gonzalo G. de Polavieia

Programme, Portugal

New York University, US

Champalimaud Neuroscience

Max Planck Institute for Ornithol-

List of speakers

Aanes-Melinda Kovacs Central European University Buda- ETH ZURICH, Switzerland pest, Hungary Alex Mesoudi

Durham University, UK Andreas Olsson

Karolinska Institutet Solna, Sweden

Audrey Dussutour Universite Paul Sabatier, France Christian Keysers University Medical Center Groningen, The Netherlands

Christopher F. Chabris Union College NY, USA range of areas in social behaviour, including social neuroscience, psychology, sociology, behavioural ecology and anthropology came together at the Champalimaud Centre for the Unknown

This year's programme included talks by distinguished invited speakers, talks selected from abstracts and three poster sessions demonstrating the most recent results of ongoing research from around the world.

Jens Krause

Germany

Keith Jenser

gie und Binnenfischerei (IGB),

Maria Luisa Vasconcelos

Programme, Portugal

P. Read Montague

leae London, UK

Champalimaud Neuroscience



Rui Oliveira

Leibniz-Institut für Gewässerökolo-Instituto Superior de Psicologia Aplicada, Instituto Gulbenkian de Ciência, Champalimaud Neuroscience Programme, Portugal

The University of Manchester, UK Ruth Mace University College London, UK

> Steven Kushner University Medical Center Rotterdam , The Netherlands

Tali Kimchi Weizmann Institute Israel

Ralph Adolphs California Institute of Technology, US

Virginia Tech, US, University Col-

Jan 08

Colloquium Mo-

lecular and cellular mechanisms of synaptic plasticity

Ana Luisa Carvalho (CNC-Center for 05 Neuroscience and Cell Biology & Depart-

ment of Life Sciences University of Coimbra. Portuaal).

22 Colloquim Rethinking Depression and

its Treatment: Insights from Studies of Deep Brain Stimulation.

26-29

Oraanisers: Caro-

Polavieja, Simone

Lackner (All CR)

Colloquium The

Stressed Brain.

(School of Health

Minho, Portugal)

Colloquium Roles

of cytoskeleton in

Yasunori Hayashi

Institute, Japan)

hippocampal synaptic

(RIKEN Brain Science

Nuno Sousa

Feb

plasticity.

05

12

29

Helen Mayberg (Emory University School of elegans. Medicine, USA)

> tute of Neuroscience University of Oregon, USA)

19

26 Social insect behaviour.

lina Doran, Eugenia Chiappe, Gonzalo de

pean Molecular Biology Laboratory, Monterotondo, Italvtondo, Italv)

Apr Science,University of 16

Colloquium Circuit principles of behavioral choice in Drosophila. Marta Zlatic (Janelia

Group Leader, Howard Huahes Medical Institute, USA) 23

Colloquium The Dynamics of the Unconscious Brain Under General Anesthesia.

Emery Brown (Depart-

ment of Brain and

Cognitive Sciences,

Technology, USA)

MIT-Harvard Division

Colloquium Volitional Control of neuronal spatiotemporal patterns via Brain-Machine Interface.

Filon Vaadia (Edmond and Lily Safra Center for Brain Sciences, He brew University, Israel)

19 Colloquium On the

single-trial variability of motor cortical populations.

Maneesh Sahani (Gatsby Computational Neuroscience Unit, University College London, UK)

26

cerebellum in forebrain motor circuits.

Clément Léna (Depart ment of Bioloay. École normale supérieu, France)

May

14

learn

Cornelius Gross (Euro-

Engine For Development. Organiser: Rui Costa

21

Zebrafish. of Health Sciences and

Exploring the role of first person experience in neuroscience

Organisers: Rita Venturini. Thabelo Khoboko and Alex Gomez-Marin

(All CR)



Colloquium To model the Connectome, or not: a case study in C.

Shawn Lockery (Insti

Colloquium Primal threats - the neural circuitry of predator and social fear.

USA) 20



(All CR)

28

27-29

Advanced Course

Colloquium Fitting the

COURSES, WORKSHOPS, EVENTS

Mar 2015

Colloquium Olfactory Signaling in Mushroom Body Output Neurons - Neural coding as a Circuit Converges.

Glenn Turner (Cold Sprina Harbor Laboratory, USA)

Colloquium How populations of neurons

Aaron Batista (Center for Neuroscience. University of Pittsburgh,

Round Table Discussion Science Funding as an

Colloquium Specificity and modules in circuits for motor control.

Silvia Arber (Friedrich Miescher Institute for **Biomedical Research** Basel, Switzerland)

Colloquium The Cellular Basis of Directional Mechanosensation in

Hernán López-Schier (Helmholtz Zentrum , München, Germany)

Jun

12

Colloquium Cortical circuits underlying auditory decision making.

Anthony Zador (Cold Spring Harbor Laboratory, USA)

16-18

Biology of Systems and Metastasis Programme Organisers: Zacharv

Mainen and Rui Costa (All CR)

Jul-Aug 12/7-05/8

Advanced Course Behaviour and Neural Systems

Oraanisers: Adam Kampff (CR), Zachary Mainen, (CR) and Florian Engert (Harvard University, USA).

Aug 09-29

Advanced Course Computational Neuroscience

Organisers: Christian Machens (CR), Gilles Laurent (Max Planck Institute for Brain Research, Frankfurt, Germany), Mate Lengyel (Cambridge University, UK)

Sep

Colloquium The first steps in vision: computation and repair. Botond Roska (Friedrich Miescher Institute for Biomedical Research, Basel, Switzerland)

10-14

Summer School Learning from the Lord of the Genes

Oraanisers: Carlos Ribeiro, Samuel J Walker (All CR) *Organized as part of the European doctoral training network, FLi-ACT- Systems neuroscience of Drosophila. from aenes to circuits to behaviours

16-19

4th Champalimaud Neuroscience Perspectives on Social Behaviour

Gonzalo de Polavieja, Susana Lima & Christian Machens (All CR)

21

Colloquium Primitive hypothalamic circuits controlling behaviors.

Marcelo Dietrich (Yale School of Medicine, USA)

Oct 08

Colloquium

Adriano Aguzzi (Institute of Neuropathology, University Hospital of Zurich, Switzerland)

09

Colloquium From star to neuron: wavefront shaping for clearer, deeper, and faster brain imaging.

Na Ji (Janelia Reseach Campus, USA)

27

Colloquium The emergence of a circuit model for addiction: from synaptic mechanisms to therapeutic implications.

Christian Lüscher (University of Geneva, Switzerland)

Nov

Colloquium Neural mechanisms for the genesis, expression and control of emotional behaviour.

Daniel Salzman (Columbia University, USA)

12

Colloquium Neural Mechanisms for Predicting the Sensory Consequences of Behavior

Nathaniel Sawtell (Columbia University. USA)

27

Colloquium Benefits limitations, and algorithms of social and cultural learning.

Richard Hahnloser (Institute of Neuroinformatics. University of Zurich / ETH Zurich Switzerland)

Dec 03

Colloquium The representational structure of complex movements in the human neocortex.

Joern Diedrichsen (Institute of Cognitive Neuroscience, Univer sity College London. LIK)

10

Colloquium Arithmetic and neural circuits underlying dopamine reward prediction errors.

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

11

CONGENTO on Applications of CRISPR to Genetically Tractable Organisms

Organisers: Ana Catarina Certal (Fish Platform, CF), Isabel Campos (Fly Platform (CE) and Ana Casaca (CR Administrative (Jnit)

17

Colloquium Dendritic Channelopathies and Fragile X Syndrome.

Dan Johnston (UT-Austin, USA)

Culture

Highlights

AS ONE OF THE MEANS TO REATE AN ENVIRONMENT ESEARCHERS, IN ALL CAREER ARE FAMILIAR WITH rk of each othef REGULARLY AT THE CCU

CISS

Champalimaud Internal Seminar Series

Each week, two CR researchers deliver a 25 minute presentation of their work, after which they receive feedback and questions from the CR community. These events, in addition to creating an atmosphere that facilitates collaboration, also provide a platform for junior researchers to advance their skills in preparing and delivering oral presentations to large audiences.





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CR Annual Retreat @Alentejo

AN TO AN AND A AND A

A central event shared by all CR researchers is the CR annual retreat. Each June, all members travel together to a remote location where they dedicate five days to getting reacquainted with each other's research and to simply having a good time together.

In 2015, the retreat committee organised a different scientific activity each day. These activities stressed group interactions and discussion on topics in science and science policy.

Support Highlights

VO MAIN BODIES FACILITATE TH FI INCTION 'OR THE UNKNOWN

CRAU CR Administrative Unit

Coordinator: Philipp Tsolakis

The CR Administrative Unit is responsible for providing comprehensive administrative services, including budget and financial management, purchasing, procurement, human resources services and science communication.

The vision of the Administrative Unit is to be an exemplary resource in the field of research administration by providing management tools, educational opportunities and exceptional service. The members of the Unit strive to support the CR by addressing any question or concern and by maximising the time spent in research.

- CR Administrative Unit:
- Lab Administration
- Purchasing, Logistics and Controlling
- Human Resources & Fellow's Office
- INDP, Courses & Teaching Lab
- Guests, Meetings & Events
- CR Direction & Faculty Assistance
- Science Communication Office.

A - Scientific Hardware Platform Development (HWP) An electrode Interface Board with

62

32 or 64 channels, redesigned and produced by the HWP team

PLATFORMS

Scientific and Technological Platforms

Coordinator: Tânia Vinagre

The Champalimaud Centre for the Unknown operates nine scientific and technological platforms, which are the core technical support structure available to the research community. The Platforms offer cutting-edge shared resources and services from model organisms' facilities (rodent, fish and fly), imaging and microscopy, histopathology, molecular biology and viral production, media preparation, software and hardware development.

The Platforms are widely involved in all research activities of CCU, providing services, tools, technology development and training as well as international networking and collaborations.

The Champalimaud Platforms are widely used by laboratories at the CCU but are also available to external users in academia and industry. In 2015, a significant part of platforms activities was dedicated to providing services to external users.

Scientific & Technological Platforms:

- Optical imaging & Microscopy
- Molecular Biology
- Scientific Software (SWP)
- Scientific Hardware Development (HWP)
- Fly Platform
- Fish Platform
- Vivarium
- Histopathology
- Glasswash & Media Preparation
- Office of Sponsor Programmes (OSP)

B - Scientific Hardware Platform Development (HWP) Open Ephys IO board., produced by

the HWP team

C - Preclinical imaging

An ultra-high field 9.4T horizontal wide-bore scanner.

D - Scientific Software Platform Development (SWP) A screen shot of 3D tracking software,

developed by the SWP team.

E - Fish Platform

Aquariums which house, breed and maintain Zebrafish.

F - Brain Machine Patent Application

A scheme from the submitted patent application, supported by the platforms/OSP.

Large scale production and distribution of open-source tools

Through a partnership with Open Ephys, an MIT spinoff initiative to distribute open-source electrophysiology tools to the neuroscience community, in 2015 the scientific hardware development platform produced and distributed electrophysiology equipment to 23 countries and to more than 50 research institutions.

3D Tracking of marine animals

The development of this unique tool for tridimensional tracking of marine animals was done by the Scientific Software Platform for a collaborative project involving the Neurobiology of Action Laboratory, MARE-ISPA and Zoomarine.

This software tool received the second place in the Outernet Technologies International Award of the international marine animals trainers association.

Brain Machine Interface Technology Patent issued for the Neurobiology of Action Laboratory

The Neurobiology of Action laboratory led by Rui Costa featured an important technological development in 2015. The inventors, Rui Costa, Fernando Santos, Nuno Loureiro and Vitor Paixão, developed a new paradigm of a fixed decoder to Brain Machine Interface (BMI), which includes an algorithm leading to fewer noise and muscular artefacts. This decoder can be readily learned by individuals, easily consolidated and generalizable among applications.

This technology was secured through a patent application that was managed by the Office for Sponsored Programmes.

0



D

Installation and support of cuttingedge imaging technology at CCU

In 2015, the CF

made a significant investment to create a preclinical research imaging facility at the CCU. The Platforms supported the installation of two preclinical MRI scanners (a 9.4T horizontal-bore and a ultrahigh field 16.4T vertical-bore) that will establish the CCU as one of the most advanced preclinical imaging institutions worldwide.

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International Workshop 'Applications of CRISPR to genetically tractable organisms'

In December 2015, the Animal Platforms organised an international workshop 'Applications of CRISPR to genetically tractable organisms' in the context of CONGENTO, a Portuguese initiative to support and expand the use of genetic tools in research.

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Outreach & **Science** Communication Highlights

ONE OF CR'S STATED GOALS S TO SHARE ITS KNOWLEDGE NOT ONLY WITHIN THE CIENTIFIC COMMUNITY, BUT LSO WITH THE COMMUNITY AT LARGE, MANY CR ESEARCHERS, AT ALL CAREER ADOPT THIS VISION ND CHOOSE TO ORGANISE RTICIPATE IN VARIOU UTREACH ACTIVITIES. BOTH

AT AND OUTSIDE OF THE CCU.

Science Communication Office PRESS OFFICE

Coordinator: Catarina Ramos

The Science Communication Unit is responsible for disseminating information on the activities and ongoing or emerging objectives of the Champalimaud Research (CR) to all relevant parties. In particular, this unit is responsible for maintaining fluent internal and external communication channels, including CR's online presence, liaising with the media, the production of communication documents/materials, such as the annual report. In parallel, this Unit coordinates science communication initiatives that range from science education and outreach events to the organisation of scientific meetings. The team is also able to support the CR community in their scientific endeavours, with in-house scientific design and illustration.

To realise these aims, the on-going activities of the Science Communication Unit were expanded in 2015 with two new areas of activity: 1. Visualisation creating design solutions for accurate scientific content with a high visual impact, with the purpose of communicating research with both scientists and the general public; 2. Education – developing tools grounded on hypothesis-driven approaches via game-based learning and orchestrating citizen science projects relating to questions relevant to our community. The tools and services developed within these additional fields will enhance the efficacy of the Science Communication Office in both internal and externally-targeted projects.

CR presence in the media

The Science Communication Unit manages requests from the media and issues press releases regularly. In 2015, 19 press releases were produced, resulting in 159 references in national media and 106 references in international media. In addition, the team mediated 21 requests from national media, including requests for interviews of CR scientists to various Portuguese: i) journals such as Expresso, Público, Observador, i; ii) magazines such as Visão and Sábado; iii) TV channels like RTP, SIC, Euronews and i) radio channels like Antena 1 and Ant3na

A - Brain Awareness Week

Exploring emotions and the brain with elementary school students at Externato Santa Catarina, in Algés. Brain Awareness Week.

B - Roots of Curiosity

Round table with artists and scientists at the "Roots of Curiosity" conference.

C - AR Event

A full auditorium "meditating" during the Ar event "Mindfulness -Finding Peace in a Frantic World".

D - School visits

High school students during one of the monthly school visits to the Champalimaud Centre for the Unknown.

ROOTS OF CURIOSITY Art and Science Cycle

Roots of Curiosity, (Raízes da Curiosidade), was an art-science project designed by three students from CR and developed through a partnership between the Centro Cultural de Belém (CCB) and the Champalimaud Foundation. Roots of Curiosity evolved into an artscience cycle where different formats were produced for different audiences. In 2014, this cycle included three days of performance and one month of workshops for schools and families. In 2015, the cycle was concluded with a 2-day conference, a documentary film and the release of a book about the process.

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BRAIN AWARENESS WEEK

International Science Education Initiative

Each year, in March, CR coordinates outreach activities for the annual Brain Awareness Week. In 2015, among other activities, five CR members spent one day at Externato Santa Catarina in Lisbon, where they engaged students ages 6-10 in special activities. Among the activities were demonstrations of real brains, modeling of neurons and various neurogames that exposed the children to basic concepts in neuroscience.

AR | RESPIRE CONNOSCO CR Outreach Initiative

Drawing on the enthusiasm of the CR community and spearheaded by young researchers at CR, a series of science communication events called Ar was established by a group of volunteers. 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-scientists, such as chefs, dancers, group facilitators, economists and others, engage the public to think, interact and debate their ideas.

In 2015, three events were organised by Ar dedicated to Depression, Mindfulness and Pain.

