ANNUAL REPORT 2018

Champalimaud Research

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"We all have forests on our minds. Forests unexplored, unending."

Ursula K. Le Guin, The Wind's Twelve Quarters

Champalimaud Research



Foreword

In the last two years, the Champalimaud Research (CR) has become a fully operational, two-pronged programme. In its first years, it was chiefly dedicated to the study of the links between behaviour and underlying neural processes (also known as the Champalimaud Neuroscience Programme, or CNP). Now its also geared towards understanding the links between the maintenance of a healthy body and the spread of cancer (the Biology of Systems and Metastasis Programme, or BSM). During this short period, original findings have emerged from the gap between these non-related areas of research.

One example is the work on Alzheimer's disease (AD), stemming from a collaboration between the Cell Fitness and Stem Cells and Regeneration labs. Their results suggest, unprecedently, that neuronal death in AD may be a protective reaction against the disease—and that the early stages of its progression, are not to blame for the cognitive havoc wreaked in the brain of patients. These results resonate with a discovery made by the Theoretical Neuroscience lab a few years ago, where the team demonstrated that due to redundancy, the brain is extremely resilient against neuronal loss, and can maintain function despite a progressive decline in numbers.

Another "gap-bridging" finding, between neuroscience and physiology, was the work of the Immunophysiology lab. In 2017, the team showed that immune cells in the gut are not able to develop their protective actions against infections without establishing a "dialogue" with neurons residing at that site—neurons of the socalled "second brain". In addition to exciting new findings at the intersection between neuroscience and physiology, in 2018, CR teams have advanced knowledge in their respective fields: the role of the neurotransmitters serotonin and dopamine in behaviour, the untangling of the neural basis of decision-making, learning, motor behaviour or food craving and the study of long-range neural connectivity in the brain through computerbased modelling and imaging techniques. The approaches to tackling these questions have been varied and progress has been sustained.

Here too, a collaboration between teams has proven fruitful, such as the one between the Behavioural Neuroscience and Innate Behaviour labs. Together they have begun to unravel the mystery of how the brain chooses which defensive strategy to apply in the face of danger.

As proof of the quality of their ongoing research, in 2018. CR researchers were awarded a total of 19 million euros from various national and international funding entities. Some of the most relevant awards were the Allen Distinguished Investigator Award, given to Henrique Veiga-Fernandes (Immunophysiology lab) and the H2020 ERC Consolidator Grant from the European Commission given to Marta Moita (Behavioural Neuroscience lab) - who in 2018 was appointed deputy-director of CR. Carlos Ribeiro (Behaviour and Metabolism lab) and Leopoldo Petreanu (Cortical Circuits lab) received funding from the "la Caixa" Foundation, while Michael Orger (Vision to Action lab) received funding from the Volkswagen Foundation through a collaboration with a group at the Max Planck Institute of Neurobiology.

Eleven years into its history, CR is embracing its evolution into a multidisciplinary programme and is thriving with many new insights and discoveries.

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The Foundation



Champalimaud Foundation Board of Directors

President: Leonor Beleza Vice President: João Silveira Botelho → Member of the Board: António Horta-Osório ← Through scientific breakthroughs and clinical developments, the Champalimaud Foundation is there to help those who need it most.

The Champalimaud Foundation exists as the legacy of Portuguese entrepreneur and industrialist, the late António de Sommer Champalimaud. It was formally created in 2005 under the full title: Anna de Sommer Champalimaud and Dr Carlos Montez Champalimaud Foundation. Thus, honouring the benefactor's parents, with Leonor Beleza as President, as set out in the will of António Champalimaud. The Foundation gives full backing to its researchers who work on the frontline of science and biomedicine. Its scientists and doctors use their creativity, experience and talents to find new and innovative wavs to approach the many questions of modern neuroscience and oncology.

In September 2018, during the António Champalimaud Vision Award ceremony, the Champalimaud Foundation announced the creation of the first pancreas cancer research and treatment centre in the world, due to be inaugurated on October 5, 2020. Mauricio Botton Carasso and his wife, Charlotte Botton, decided to work with the Champalimaud Foundation, contributing 50 million euros to build an innovative facility where scientists, doctors and physician-scientists can work together to advance knowledge, take control and fight the hitherto irreducible character of a disease that has defied science for decades.

The Champalimaud Foundation was born of a visionary and patriotic gesture from a genius entrepreneur, who left it to Portugal and the world. Now comes a new gesture, this time from Spain, as an illustrious name joins that of António Champalimaud in the construction of projects and finding of solutions that will benefit humanity.



↑ The future Pancreatic Botton-Champalimaud Cancer Centre (in colour).

2018 Overview



5

Outreach & educational events at the CCU

Structure & Diversity





35 countries of origin

56% Female

Administrative Technical

66

support staff

206

37

support staff

Angola Germany Argentina Greece Austria India Belgium Iran Brazil Israel Canada Italy **Cape Verde** Jamaica Chile Japan Colombia Lesotho **Mauritius** Croatia Estonia Norway France **Philipines**

61% Portuguese

227

143

Poland

Portugal

Romania

Switzerland

The Netherlands

United Kingdom

United States of

39% Non-portuguese

Russia

Spain

Turkey

America

Venezuela

Research Groups

↓ The CR group photo is taken at the yearly retreat. Neither rain, nor sleet, nor gloom of night shall stand in the way of this tradition.



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 for measuring and manipulating activity in specific populations of neurons. In some cases, these manipulations mirror neural conditions that exist in humans who suffer damage to the cerebellum through illness or injury.

Recently, the lab has revealed a link between ongoing locomotor activity and the enhancement of learning within the cerebellum. These results, published in the journal Nature Neuroscience in 2018, indicate a novel role for behavioural states in the modulation of motor learning and suggest a potential mechanism through which engaging in motor activities may improve an individual's ability to learn.

Megan Carey talks about the lab highlights of 2018.

"One highlight is the publication of a new research article in the journal Nature Neuroscience, where we reported the existence of a direct relationship between how fast mice walked and how fast they learned.

Another highlight is that in the summer of 2018, a previous postdoctoral researcher in the lab, Dominique Pritchett, left to start his lab as an Assistant Professor in the Department of Biology at Howard University in the United States."

Neural Circuits & Behaviour

Megan Carey

Joined CF in 2010

Model Rodents

Cerebellum

Brain

region

Research Methods

Quantitative behavioural analysis Optogenetics Chemogenetics Electrophysiology





tarta Maciel — MSc Stud. Jana Darmohray — PhD Stud. Satarina Almeida — Rsch. Tech. Jiogo Duarte — Rsch. Asst. Satarina Albergaria — PhD Stud. éonard Dupont — MSc Stud. Jugo Marques — Postdoc. Rsch. Yirginia Casasnovas — Rsch. Tech.

not in photo co-supervised by Michael Orger, CR Ana Gonçalves – PhD Stud.
 Ana Machado – Postdoc. Rsch.
 Megan Carey – PI
 Jovin Jacobs – PhD Stud.
 Margarida Nunes – Lab Admin. *
 Rita Félix – PhD Stud. * I
 Jorge Ramírez – PhD Stud. *

* Cerebellum

In Latin Cerebellum means "little brain", possibly because of its appearance as a separate structure attached at the bottom of the cerebral hemispheres.

How the brain

generates and

coordinated

movement

controls

The research strategy of the Sensorimotor Integration* lab focuses on connecting neural activity dynamics to the locomotive behaviour of the fruit fly, Drosophila melanogaster. The researchers employ multiple methods to record and reversibly perturb neural activity in behaving flies, to analyse the structure of interconnected neurons, to quantify different aspects of the fly's locomotive behaviour, and to model functional networks. This multidisciplinary approach, together with the ever-expanding genetic toolkit of the fruit fly, allows the team to find mechanistic explanations for how multi-sensory and sensorimotor integration processes in the brain are used to guide adaptive behaviour.

Eugenia Chiappe explains the results of a series of new experiments.

"Using a combination of virtual reality technology, electrophysiology and modelling, in 2018 we finished up a series of exciting experiments. These experiments showed that the fly brain uses self-generated visual motion-signals to control walking performance during exploratory behaviour. In turn, non-visual, walking-related internal signals, such as those related to walking speed motor commands, coordinate which populations of visual motion-sensitive cells will contribute to walking performance."

Sensorimotor Integration

Eugenia Chiappe

Principal Investigator Joined CF in 2012

Model Fruit fly

Sensory Premotor Motor

Brain

Regions

Research **Methods**

Electrophysiology **Optical Tools** Behavior Virtual reality Whiteboard Literature

iva — Lah Ad





* Sensorimotor integration

The

computational

principles that

govern motor

and sensory

coordination

Sensation and movement may seem like distinct processes, but they are tightly linked through behavioural and neural connections. This connectivity, by which sensory and motor information are combined, is crucial for the successful execution of actions and for learning how to perform actions more efficiently in the future.

The Neurobiology of Action lab focuses on the interaction of the Basal ganglia*—a brain region known to be involved in motor learning and the control of movement—with areas in the cortex that are important in motor planning and decisionmaking. These brain areas are also affected in neural disorders such as Parkinson's disease, Huntington's disease and obsessive-compulsive disorder. Work from the lab has generated various findings in the field, including groundbreaking observations challenging some of the previously held perceptions regarding the role of subcircuits in the basal ganglia.

Rui Costa talks about a new study about how the brain initiates movement.

"In a new study in mice, we showed that the initiation of movements is accompanied by a brief increase in dopamine release in the brain, as opposed to a steady increase throughout the movement. Since dopamine substitutes are one of the main treatments for Parkinson's disease, this finding may have important implications for the development of future therapies, which could try to mimic this newly found biological mechanism."

Neurobiology of Action

Rui Costa

Principal Investigator Joined CF in 2008

Models Brain Rodents Regions

Humans

Basal ganglia Orbitofrontal cortex

Research Methods

Optogenetics Electrophysiology Behaviour



1 2 3 4 5 6 8 10 7 7 16 18 17 16 15

Daniela Pereira – Rsch. Scientist
 Sara Abalde – MSc Stud.
 Andreas Klaus – Postdoc. Flw.
 Joaquim Alves da Silva – PhD Stud.
 Jonathan Tang – Postdoc. Flw.
 Gatarina Carvalho – Postdoc. Flw.
 Marcelo Mendonça – PhD Stud.
 Nicolas Morgenstern – Postdoc. Flw.
 Vitor Paixão – Postdoc. Flw.
 Michael Pereira – PhD Stud. I
 Sofin Marques – Rsch. Tech.

Cristina Álcacer – Postdoc. Flw.
 Rodrigo Oliveira – Postdoc. Flw.
 Ana Cruz – Postdoc. Flw.
 Cristina Afonso – Postdoc. Rsch.
 Ana Fernandes – Postdoc. Rsch.
 Ana Isidro – MSc. Stud. *
 Catherine French – Postdoc. Flw. *
 Sara Oliveira – MSc. Stud. *
 Sevinç Mutlu – Postdoc. Flw. *
 Ana Rita Afonso – Rsch. Tech. *
 João de Araújo – Rsch. Tech. *

not in photo co-supervised by Christian Machens, CR

How the brain

generates

actions

and selects

* Basal ganglia

Located deep inside the brain, the basal ganglia is crucially important for movement. It is a structurally complex brain area that contains many types of neurons, including some that produce the neurotransmitter dopamine. The death of these dopamine-producing neurons in Parkinson's disease is the cause of the severe motor problems associated with this condition.

Systems Óncology

Bruno Costa-Silva

Model Region of Interest Mice

Whole organism

Research Methods

Principal Investigator Joined CF in 2016

Flow cytometry Cell culture Animal models of cancer



ian Bodo — Senior Rsch. Tech

not in phote

How the exchange of extracellular vesicles, a natural form of communication in the body, can be utilised by cancerous tumours for growth and metastasis

* Extracellular vesicles

bloodstream.

One of the means by which cells participate

in the smooth functioning of the body is by

exchanging long-distance messages with

each other. One of the ways they do this

is by producing nano-sized liquid-filled spheres (called extracellular vesicles),

which are released from the cells and

are carried to remote locations via the

Many natural, physiological processes

work through the exchange of these tiny

extracellular ("out of the cell") vesicles, but

recent findings show that they can also be

utilised by cancer to promote metastasis.

SCIENTIFIC APPROACH

The general interest of the Systems Oncology lab is to understand how the crosstalk between tumour cells and non-tumour cells supports or prevents oncologic disease. Specifically, the lab studies how the exchange of extracellular vesicles*, a natural form of communication in the body, can be utilised by cancerous tumours for growth and metastasis.

Recent results from the team have shown not only that these vesicles are different in cancer patients, but also that they can activate healthy cells at remote locations to support tumour metastasis. Following these results, the lab currently focuses on developing animal models of tumour initiation. progression and metastasis, in combination with the characterisation of extracellular vesicles isolated from tumour cell lineages and oncologic patients with diverse clinical profiles. By using this approach, the lab aims to gain a mechanistic understanding of this form of communication with the end goal of developing tools for early detection, follow-up and treatment of cancer.

In 2018, the group developed a new technology, based on High-Resolution Flow Cytometry, that enables a multi-parameter analysis of extracellular vesicles populations derived from both tumour and non-tumour cells in biofluids. It also dramatically reduces the processing time and volume requirements of biofluids for extracellular vesicles. By doing so, it has great potential to simplify and accelerate the analysis of these vesicles in patientderived biofluids for diagnostic applications.

Bruno Costa-Silva explains a new research method developed in the lab.

"By studying extracellular vesicles one-by-one, this method facilitates the study of differential packaging of biomolecules in extracellular vesicles and has the potential to identify novel cell-cell communication systemic networks involving extracellular vesicles in vivo. It may also help us understand how these vesicles are formed and how can we modify their content to block cancer progression. Our new method may also help us to study extracellular vesicles in biofluids with intrinsically small volumes, such as lacrimal, vitreous humour and synovial fluids. This has the potential of opening new avenues, both in the biology and diagnosis, of ophthalmologic, rheumatic and orthopaedic diseases."

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At the Collective Behaviour lab, a multidisciplinary team that includes mathematicians, physicists and biologists implements a diverse set of computational, behavioural and virtual reality tools in zebrafish and humans.

In this way, insights gained by genetic and molecular probing in zebrafish are used by the researchers to design models which they test and extend to human experiments. The lab also works on the development of tools and techniques aimed at obtaining richer datasets essential to the formulation of better models of collective behaviour.

Several recent publications by the lab have identified rules that capture how elements such as modulation of swimming speed and the choice of which conspecific to follow, help explain the emergence of schooling behaviour in fish.

Gonzalo de Polavieja shares some insights about a new system capable of learning.

"One of the fields we focus on is the development of computer algorithms that can learn. These types of algorithms could be used for various types of programmes that require learning, such as image recognition.

In a new preprint, published in 2018, we presented a system that can learn small algebraic models using Universal algebra* that function under a wide range of conditions. These algebraic models can learn not only from data, but also from other learning systems based on the same. or different information.

The learning of the system can also be shaped by a set of formal rules. This is important because not all learning needs to happen from seeing many examples but also from explicit knowledge about the task. We are currently using insights gained in this study to determine which elements facilitate learning in these systems, with the end goal of building improved learning systems that maximally use these properties."

F. Maroto and G.G. de Polavieja, 'Algebraic Machine Learning' https://arxiv.org/abs/1803.05252

Collective Behaviour

Gonzalo de Polavieja

Brain Models Zebrafish

Humans

Principal Investigator Joined CF in 2014

Region Whole brain

Behaviour Mathematical modelling Machine learning

Research

Methods



- ata Cruz MSc Stud.
- no Ferreira Software Eng es Wichert — MSc Stud
- nia Groneberg PhD Stud. ¹
- o Costa PhD Stud II ia Fortunato – MSc Stud
 - icisco Romero PhD Stud
 - nzalo de Polavieia PI

not in photo co-supervised by Michael Orger, CR pervised by Alfonso Renart, CR

9 Victòria Brugada - PhD Stud. 10 Fernando Martin-Maroto - Rsch. Sci Robert Hinz – Postdoc. Francisco J. Heras - Postdoc. Andres Laan - PhD Stud. Marta Iglesias — PhD Stud. •

* Universal algebra

Field of Mathematics that studies sets of objects with one or more operations defined on them.

Understanding emergent properties in collectives of interacting units

Neuroethology

Susana Lima

Principal Investigator Joined CF in 2008

Model Rodents

Hypothalamus Ventral tegmental area

Brain

Region

Research Methods

Electrophysiology Optogenetics Anatomy Behaviour



12

Francisco Esteves — Postdoc Luís Moreira — PhD Stud. nger – PhD Stud, I rgarida Duarte — Rsch. Tec na Husain — PhD Stud

and Lacoste — Postdoc, II iliana Ferreira — Rsch. Tech. III Inês Dias — MSc Stud.

usana Lima — PI

icolas Gutierrez — Postdoc

Silvana Araújo — PhD Stud

António Dias — PhD Stud. 📍

Susana Valente — PhD Stud.

stanze Lenschow — Postdoc

 not in photo I co-supervised by Zachary Mainen, CR II co-supervised by Christian Machens, CR

III co-supervised by Ana Catarina Certal, CR

controls key processes in sexual behaviour

* Reproductive cycle

The ability of females to become pregnant

varies along their reproductive cycle. The

cycle itself is determined by fluctuating

and estrogen. In addition to regulating

influence the behaviour of female animals

levels of the hormones progesterone

reproduction, these hormones also

towards males through a mechanism

that is not yet fully understood.

How the brain

The Neuroethology lab focuses on several

SCIENTIFIC APPROACH

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, genetically-based 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 learning, and on the medial hypothalamus, an area that is particularly important for female sexual behaviour. 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.

Susana Lima presents two new researchers that joined the lab.

"During 2018, we started implementing the European Commission (ERC) Consolidator Grant that we received in the previous year.

Of particular interest, two new postdoctoral researchers joined the lab to complement ongoing research: Bertrand Lacoste, in collaboration with the laboratory of Christian Machens, started using computational tools to build models that can explain specific features of sexual behaviour; Nicolas Gutierrez built the lab's first in-vitro setup to interrogate the dynamics of brain regions whose activity is modulated by the reproductive cycle, thereby bridging cellular properties and behavioural changes."

Formulating

theories of

and animal

behaviour

* Numerical simulation

One of the means by which cells participate

in the smooth functioning of the body is by exchanging long-distance messages with

each other. One of the ways they do this

is by producing nano-sized liquid-filled

spheres called extracellular ("out of the cell") vesicles. They are released from the cells and are carried to remote locations via the bloodstream. Many natural, physiological processes work through the exchange of these tiny extracellular vesicles, but recent findings show that they can also be utilised by cancer to promote metastasis.

computational

brain function

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 formulate their ideas and intuitions in a precise manner and thereby put them to 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.

The team is currently developing methods to summarise the activity of neural populations in useful ways and to compare population activity across areas. In turn, the researchers seek to relate the population activity to behavioural, computational, and mechanistic problems or constraints that organisms are facing. They work in close collaboration with several experimental labs, both within and outside of the Champalimaud Centre for the Unknown.

Christian Machens talks about two graduations that happened in 2018.

"Two PhD students from our lab successfully defended their theses in 2018: Asma Motiwala and João Semedo. Asma was the lab's first student that was trained at CR's doctoral programme (INDP). Her thesis was titled: 'Internal representations for time-based decisions'; João was a student of the Carnegie-Mellon-Portugal doctoral programme, his thesis was titled 'Inter-area communication in the brain: a population-level approach'."

Theoretical Neuroscience

Data

Rodents

Zebrafish

Christian Machens

Principal Investigator Joined CF in 2011

Sources Regions Monkeys

Frontal lobes Visual cortex Auditory cortex Striatum hindbrain

Brain

Mathematical analysis Numerical simulations

Research

Methods



- ncalo Guiomar PhD Stud. V

Podlaski — Postdoc. Flw Iotiwala — PhD Stud. • V nedo — PhD Stud. • VI

9 Sander Keemink – Postdoc. Flw.
 10 Nuno Calaim – PhD Stud.
 11 Christan Machens – PI

Systems Neuroscience



Principal Investigator Joined CF in 2007

Models Rodents Humans

Methods Regions

Brain

Cortex

Raphe nuclei

Optogenetics Theory

Research

Behaviour Electrophysiology



22

ago Quendera - PhD Stud. eni Smaragdi - Rsch. Tech sé Teixeira - MSc Stud nsola - Postdor Solène Sautory - PhD Stud Inês Laranieira - Rsch Asst Eric DeWitt - Rsch. Assoc Romain Ligneul - Postdoo 11 Lucas Soares - MSc Stud.

12 Mattia Bergomi – Postdoc 13 Susana Silva — MSc Stud. 14 Dario Sarra — PhD Stud. Margarida Duarte — Rsch. Tech Niccolò Bonacchi – Senior Tech 17 Zachary Mainen – PI 18 Catarina Pimentel — Lab Mng 19 Kcénia Bougrova – PhD Stud 20 João Morais - MSc Stud. Fanny Cazettes - Postdo

22 Beatriz Godinho – Rsch Asst

not in photo

I co-supervised by Noam Shemesh, CR co-supervised by Susana Lima, CR III co-supervised by José Pedro Serra, FLUL 23 Cindy Poo – Postdoc 24 Olivier Winter - Senior Tech Bassam Atallah — Postdoc. Flw. 🏾 Gautam Agarwal — Postdoc ena Fonseca — PhD Stud. • I Megha Patwa — Rsch. Asst. Pietro Vertechi — PhD Stud. Eran Lottem — Rsch. Assoc. Masayoshi Murakami — Post<u>doc</u>. Baylor Brangers — PhD Stud. • II Samuel Viana — PhD Stud. • III

How brains use perceptual information to create and act on models of the world, using role of confidence, uncertainty and neuromodulators in these processes

SCIENTIFIC APPROACH

Until recently, most research on cognitive phenomena, such as perception and decisionmaking 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 nonhuman 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 learning and decision-making. Theory and modelling 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 count on collaborations with many groups at the CR.

Zachary Mainen talks about the lab's involvement in the International Brain Laboratory.

"Our lab is part of an international consortium called the International Brain Laboratory (IBL), which is composed of 21 labs across the world. The lab / CCU is now the headquarters of a team counting six members involved in the optimisation of the behavioural setups that will be shared between the experimental labs of the consortium. Besides four of our team members working on IBL projects, the lab is also hosting the Data Coordinator and the Scientific Programmer for the whole consortium."

* Serotonin

Serotonin is a small molecule that functions in the brain as a neurotransmitter, meaning that it influences the activity of neurons. The serotonin produced in the midbrain, (a region at the base of the brain), projects widely across the cortex. It is thought that this system has an important role in various functions, including learning, decision-making and mood.

Behavioural Neuroscience

Marta Moita

Principal Investigator

Joined CF in 2008

Models Brain Regions

Fruit fly

Amygdala

Auditory thalamus

Development of behavioral tasks Pharmacology Physiology

Research

Methods





- na Mendes Tech. eus Farias PhD Stud

Mirjam Heinemans — MSc Stud. Ricardo Vieira — MSc Stud.

Defensive and social behaviour

SCIENTIFIC APPROACH

Once a threat is detected animals need to choose the appropriate action. While the action displayed by an animal depends on several factors, there is little understanding of how the choice between different defence strategies* is made. One of the factors that play a crucial role in regulating defensive responses is the social environment. For instance, 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 defence responses, the Behavioural Neuroscience group uses the fruit fly as a model system. It's amenable to the search for the neural mechanism of behaviour, and it allows the study of the behaviour of large groups of individuals. This is the ideal model system due to its large collection of powerful genetic tools, a rapidly increasing number of approaches to study neural circuits, and an expanding set of behavioural paradigms. Therefore the team is developing assays to dissect social defence mechanisms in Drosophila.

Marta Moita speaks about a new grant for studying defensive behaviour.

"In 2018, I was awarded a Consolidator Grant by the European Commission. This grant will allow me, together with my team, to advance our innovative work on the neural basis of defensive behaviours. Specifically, we will be focusing on understanding the contribution of the social and the spatial environment to the choice of defensive strategy and on identifying the brain circuits that process the relevant information and execute these decisions."

* Defence strategies

The three fundamental defence strategies are fight, flight, or freeze in place with the hope of remaining unnoticed. Though they are universal across the animal kingdom, the neural mechanisms that lead animals to choose a particular strategy at any given situation are largely unknown.

Cell Fitness

Eduardo Moreno

Principal Investigator Joined CF in 2016

Models Region of Interest

Epithelial & Neuronal tissue Methods Genetics

Research

Genetics Microscopy Live imaging





Iariana Reis — PhD Stud. ntónio Palm — MSc Stud. liguel Pinto — Tech. ndres Gutierrez — PhD Stu

ea Spinazzola — PhD Stud. a Bettencourt — PhD Stud. a Couceiro — Tech.

> ho — PhD Stud. 18 gues — PhD Stud. 19

17 Eduardo Moreno – P
18 Rajan Gogna – Visitin
19 Dina Coelho – Postdo

The mechanisms by which cells of multicellular animals perform fitness detection and selection of neighbouring cells

* Cell competition

Like humans, single cells grow old and

their performance decays through use or damage. Cells can recognise decay in their

neighbours, and once they do, they bring

about the death of less fit cells to protect

the crucial importance of this fundamental process and its implication into several

broader fields, such as development, ageing,

the overall health of the tissue. Despite

regeneration and cancer, the molecular mechanisms that underlie it are only now

starting to be uncovered.

SCIENTIFIC APPROACH

The group studies the mechanisms of cell competition* in processes such as ageing, development, tissue regeneration and cancer. Work from the team has provided significant insight into these mechanisms, including the identification of "fitness fingerprints", a molecular code used by cells to exhibit their fitness level. According to their findings, fitness fingerprints allow neighbouring cells to recognise and eliminate less-fit cells. The team showed that this process happens during ageing, regeneration and cancer. Specifically, they found that fitness-based cell selection could be manipulated to delay ageing and tissue fitness decay as well as to prevent the expansion of cancer (cancer cells often exhibit themselves as "superfit" cells, which leads to the elimination of healthy cells around them). A new type of competition was discovered and named "mechanical competition" in which a high density of cells leads to compression of tissue and thereby to cell elimination. They are currently in the process of testing whether mechanical competition is important for tumour expansion into healthy tissue.

Work in the lab is done in the fruit fly animal model, where they apply advanced genetic techniques to manipulate the functions of genes related to cell fitness, in combination with microscopy and live imaging. The team studies epithelial tissue, which is known to give rise to 95% of cancer types, including breast, lung and skin cancer. They also study the role of fitness-based cell selection among neurons during brain development, neurodegeneration and brain ageing. Also, they have recently started studying the conservation of the process in human cells and mouse models.

Eduardo Moreno explains how the findings of a collaborative study may change how we think about Alzheimer's disease.

"Current thinking about Alzheimer's disease is that neuronal cell death in the brain is to blame for the cognitive havoc caused by the disease, but a new study by our lab and the Stem Cells and Regeneration lab suggests that neuronal death in Alzheimer patients may actually be a protective reaction against the disease, this could lead to a complete rethinking of therapeutical approaches to Alzheimer's disease."

Vision to Action

Michael Orger

Animal Brain <u>Model Reg</u>ion

Zebrafish W

Research Methods

Principal Investigator Joined CF in 2010 h Whole brain

High-speed behaviour tracking 2-photon calcium imaging Light-sheet microscopy Optogenetics



- 1 Aaron Ostrovsky Senior Rsch. 2 Pedro Tomás – MSc Stud.
- Sabine Renninger Postdoc. R
- Jens Bierfeld PhD Stud. Alexandre Laborde – Rsch. Tech
- Adrien Jouary Postdoc. I
- 7 Rita Félix PhD Stud. II
- Sofia Freitas Rsch. Tech.
- 9 Claudia Feierstein Rsch. Asso
 10 Bernardo Esteves Rsch. Tech.
- 11 Edite Figueiras Senior Rsch. Tech
- 2 Joaquim Contradanças PhD Stud

not in photo
 co-supervised by Christian Machens. CF

- II co-supervised by Megan Carey, CR
- III co-supervised by Gonzalo de Polavieia. CF
- 13 Elena Hindinger PhD Stud.
 14 António Lucas Martins PhD Stud.
 15 Raquel Jacinto Postdoc.
 16 Antonia Groneberg PhD Stud. III
 17 Michael Orger PI
 18 Ruth Diez del Corral Rsch. Assoc. Simone Lackner – PhD Stud. • Adinda Wens – Rsch. Tech. • Rita Esteves – Rsch. Tech. •
 - Adinda Wens Rsch. Tech. Rita Esteves — Rsch. Tech. • Elisa Morbiato — Intern • João Martins — Intern •

Determine the principles on which sensorimotor circuits are organised and reveal how activity dynamics unfold throughout the whole brain during behaviour 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 images changes in levels of calcium ions, a marker of neural activity, while performing high-speed behavioural 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.

Recently, the team has developed a highspeed, 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.

Michael Orger talks about a new machinevision based method developed in the lab.

"In 2018, our team published a research article in the scientific journal Current Biology, where the movements of zebrafish larvae were analysed with the help of a novel machine vision computer programme developed in the lab. Using this method, we were able to demonstrate that the animals' motor behaviour is formed by sequences of distinct, discrete movement types."

* Unsupervised machine learning

Unsupervised machine learning programmes use mathematical tools in order to discover hidden structures within complex data sets. In particular, these programmes search for a way to divide data points into distinct categories. This is in contrast to supervised machine learning, where the categories are already defined and the programme has to match points within a data set to those pre-existing categories.

patonlab.org

Learning

Joe Paton

Principal Investigator Joined CF in 2008

Model Rodents

Regions Basal Ganglia Thalamus Frontal areas of the cerebral cortex

Brain

Research Methods

Behaviour Neurophysiology Calcium imaging Optogenetics Mathematical modelling





Ben Zarov — Rsch. Tech. Gonçalo Guiomar — PhD Stud. I Cristina Domnisoru — Postdoc. Filipe Rodrigues — PhD Stud. 9 Georg Raiser - Postdoc

11 Mauricio Toro – PhD Stud.

12 Joe Paton – PI

10 Daniela Domingues — Rsch. Tech

Asma Motiwala — PhD Stud. • I

Margarida Duarte — Rsch. Tech. *

ipe Rodrigues — PhD Stud. uno Cruz — PhD Stud.

argarida Pexirra — MSc Stud. ago Monteiro — Postdoc. _____

Margarida Sousa — PhD Stud

not in photo
 I co-supervised by Christian Machens, CR

Learning, decisionmaking and cognition

The Learning lab studies how information about

SCIENTIFIC APPROACH

dynamic, internal variables can be encoded across networks of neurons. One of the lab's contributions to the field was the discovery that information about elapsed time can be encoded in a wave-like activity pattern that travels across populations of neurons within a brain region called the striatum*. An additional discovery made by the lab showed that subjective time perception can be directly controlled by manipulating the activity of dopamine neurons within a brain structure called the substantia nigra* in mice. The loss of these neurons is the major contributing factor to symptoms of Parkinson's disease, a condition which is known to be associated with impaired timing capabilities in patients.

Other projects in the lab target genetically and anatomically targeted cell types across the basal ganglia, thalamus and frontal areas of the cortex. These frontal 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.

Joe Paton describes a recently published review article about time encoding in the brain.

"In a review published in the scientific journal Neuron, Joe Paton and his colleague Dean Buonomano from the University of California in Los Angeles, provide an encompassing view of how time is encoded in the brain. Particularly, we illustrate how a multitude of circuits and mechanisms in the brain generate temporal patterns that subserve the diverse functions performed by the brain areas they are embedded in. The upshot is that there is not just one clock in the brain, instead, there are many."

The Review: Paton JJ, Buonomano DV (2018). The Neural Basis of Timing: Distributed Mechanisms for Diverse Functions. Neuron. DOI:10.1016/j.neuron.2018.03.045.

* Striatum & substantia nigra

These are part of a collection of brain regions that together make up the basal ganglia. The basal ganglia play a key role in the selection and execution of voluntary movement. The striatum, specifically, receives inputs from all cortical areas and relays them to motor areas; whereas the substantia nigra contains dopamine-producing neurons that modulate the activity of the striatum.

The Cortical Circuits lab applies a structure-tofunction approach to understand the neural basis of visual perception. The researchers use optical and electrophysiological techniques to study the wiring logic of cortical circuits in areas that are required for visual perception in rodents. The team applies advanced optical methods to map the connectivity of axons that link distant areas of the neocortex* with unprecedented detail. They also measure the activity of the same circuits in mice performing perceptual tasks using twophoton imaging, high-density microelectrode arrays and whole-cell recordings.

This combined approach allows the researchers to understand both the computations implemented by cortical circuits as well as how they emerge from the underlying neuronal network. They are testing to what extent conserved circuits motifs perform similar computations across the neocortex and how sensory evidence and internal factors are combined to build a coherent model of the world.

Leopoldo Patreanu talks about a new research article and a graduation.

"In a paper published in the scientific journal Nature Neuroscience, we demonstrated that connections going from higher to lower visual areas in the cortex are exquisitely organised, suggesting how they might shape visual perception."

Tiago Marques, the first author of this paper and the lab's first PhD student, also graduated in 2018. His PhD Thesis was titled 'Mechanisms of Visual Perception in Mouse Visual Cortex'."

Marques T, Nguyen J, Fioreze G, Petreanu L (2018). The functional organization of cortical feedback inputs to primary visual cortex. Nat Neurosci. DOI:10.1038/s41593-018-0135-z.

Cortical Circuits

Leopoldo Petreanu

Principal Investigator

Joined CF in 2012

Model Rodents

l Brain Region

Visual Cortex

Methods Imaging

Research

Electrophysiolog Behaviour





na Fridman – PhD Stud. 7 Mar iela Fioreze – PhD Stud. 8 Rad § Fayolle – MSc Stud. 9 Rod Young – PhD Stud. 10 Leo ille Mazo – Postdoc. 11 Bea H Horno – PhD Stud. I Tiag

not in photo co-supervised by Christian Machens, CR

brain builds a representation of the environment from sensory stimuli

How the

* Neocortex

Neo is Latin for new, signifying that the Neocortex is relatively recent in the

evolutionary tree, existing in mammals,

though not in older species such as reptiles, or fish. The basic structure of the Neocortex is a 6-layer sheet that surrounds the cerebral hemispheres. It is divided into different areas dedicated to various functions including sensory processing, association and executive functions, such as attention and decision-making.

Circuit Dynamics & Computation

Alfonso Renart

Principal Investigator Joined CF in 2011

Models Humans Rodents

Auditory cortex Prefrontal cortex

Brain

Regions

cortex Behaviour al cortex Electrophysiology Analysis

9 André Monteiro – Rsrch Tech.

Margarida Duarte — Rsrch Tech.

10 Ildefonso Pica — MSc Stud

11 Íris Damião — MSc Stud

Research

Methods

Theory



1²³4₅6⁷8 119 10 1 Raphael Steinfeld — PhD Stud. 2 Tiago Costa — PhD Stud. 3 Juan Castiñeiras - PhD Stud. 4 Alfonso Renart — P1 5 Mafalda Valente — PhD Stud. 5 João Afonso — PhD Stud. 7 Davide Reato — Postdoc.

not in photo co-supervised by Gonzalo de Polavieja, CR co-supervised by Noam Shemesh, CR

Identifying the specific computations underlying flexible sensory and memory-guided decisions and describing their

implementation in terms of the dynamics of populations of neurons

* Psychophysics

A branch of psychology that aims to capture

the mathematical relation between sensory

experience and the physical properties of a stimulus (such as the loudness

of sound, or the intensity of light).

SCIENTIFIC APPROACH

The Circuit Dynamics and Computation lab is interested in identifying generic principles governing the dynamics of cortical circuits and the way in which they produce function. Their current work revolves around two lines of research: sensory perception in the auditory modality with an emphasis on the relationship between the response variability of sensory neurons and the accuracy of perceptual discriminations and working memory, with a focus on the mechanisms underlying the maintenance of information across time in the prefrontal cortex.

The lab's research strategy relies both on identifying characteristic signatures of population organisation—through recordings of the simultaneous activity of neuronal populations during controlled behavioural tasks—as well as on developing a mechanistic understanding of how these patterns of population activity emerge which they investigate by developing mathematical models of the underlying neuronal circuits.

Alfonso Renart talks about a new discovery in the field of psychophysics*.

"In a preprint published in 2018, we identified a mechanistic explanation to a well-known psychophysical phenomenon called Weber's law. According to Weber's law, the ability of an individual to discern the difference between two sensory stimuli (such as whether one sound is louder than another), depends on the ratio between their respective loudness levels, instead of the absolute difference between them.

Using a combination of innovative experimental and computational approaches, we were able to show that there is another important variable associated with Weber's Law—reaction time. Using this newly found observation, we constructed a mathematical model that provides novel insight into the biological basis of Weber's Law."

Jose Luis Pardo-Vazquez, Juan Castineiras, Mafalda Valente, Tiago Costa, Alfonso Renart. Weber's law is the result of exact temporal accumulation of evidence. bioRxiv 333559; doi: http://sci-hub.tw/10.1101/333559

renartlab.org

How adult stem

cells can switch

actively dividing

tumour formation

from being

dormant to

in situations

relevant for

regeneration

after injury

or tissue

* Stem cells

All body tissues are composed of cells. The majority of these cells (such as skin

cells, neurons, heart cells, etc.), have

strictly defined features and functions that

they maintain as long as they are viable.

In contrast, stem cells have the ability to

transform into different types of cells. This

flexibility is important for many processes

including ageing and tissue repair.

The Stem Cells and Regeneration lab is interested in isolating the factors that bring about the activation of adult stem cells* during tissue regeneration after injury or tumour formation. To that end, the team studies the molecular mechanisms through which neural stem cells are activated and produce new nerve cells in the adult brain.

The methods utilised in the lab include genetics, RNA-sequencing, high-end confocal microscopy and behavioural assays to test recovery of neural function. The team applies these methods in the adult fruit fly brain, within a region called the optic lobe.

Recent work from the lab has resulted in the discovery of damage-responsive stem cells in this area and the identification of several candidate genes that are thought to underlie this process. Currently, the team is characterising these genes while concurrently working on identifying other brain regions that are able to regenerate. Ultimately, the team's discoveries may lead to new therapies to facilitate tissue repair, such as brain regeneration after stroke, and preventing dysregulated stem cell proliferation that may lead to tumour formation.

Christa Rhiner talks about the lab highlights.

"In 2018, we published our first research paper, in collaboration with the Cell Fitness Lab. In this study, Silvia Schwartz demonstrated that efficient removal of impaired neurons in a fly model of Alzheimer's disease protects against loss of long-term memory and locomotion defects.

In addition, we were awarded a grant by the Portuguese Science and Technology Foundation (FCT), which will allow us to interrogate the molecular mechanisms of stem cell activation upon brain injury."

Coelho DS, Schwartz S, Merino MM, Hauert B. Topfel B. Tieche C. Rhiner C. Moreno E (2018). Culling Less Fit Neurons Protects against Amyloid-β-Induced Brain Damage and Cognitive and Motor Decline. Cell Reports. DOI:10.1016/j.celrep.2018.11.098.

Stem Cells & Regeneration

Christa Rhiner

Model

Fruit fly

Region

Brain

Principal Investigator Joined CF in 2016

Whole brain Genetics

RNA-sequencing Confocal microscopy Behavioural assays

Research

Methods



eia Augusto — MSc Stud os – PhD Stuc

Carmo Soares - Rsch. Tec Sara Uldry Júlio — MSc Stud

not in photo

Behaviour & Metabolism

Carlos **Ribeiro**

Mode **Brain**

Joined CF in 2009

region

Methods Whole brain

Research

Neurogenetics **Optogenetics** Molecular & Biochemical methods Neuroanatomy Behaviour Microbial manipulations of the host





vic – Lab Adr

The neural mechanisms of nutrition

SCIENTIFIC APPROACH

To study the neural mechanisms of nutrition, the lab uses the fruit fly, one of the most powerful and versatile genetic animal model currently available due to its long history of important contributions to medicine and our understanding of biology. The fruit fly allows researchers to combine a wide array of tools and approaches: genetic circuit manipulations, activity imaging, automated quantitative methods for studying behaviour, microbiome* manipulations and tissuespecific large scale RNAi screens. Team members use these tools to implement an integrative neuroscience approach, necessary to solve this whole-organism problem.

When animals lack dietary proteins they develop a craving for protein. The mechanisms in the brain driving animals to like protein-rich food are largely unknown. Recently, the team identified a set of taste neurons on the "tongue" that allow the fly to taste protein-rich food. They used a special microscope capable of observing the activity of these neurons in the brain of living flies while they were eating different foods. These neurons were more active in flies which lacked proteins than in fully fed flies, this shows that flies craving proteins "sense" protein-rich food more intensely, which biases their preference toward such foods.

Carlos Ribeiro talks about new collaborations and microbiome discoveries.

"Recently, our team showed, for the first time, that gut microbes direct the appetite of animals for specific nutrients. To investigate the biological basis of this discovery, with the support of funding agencies such as the Kavli Foundation and the "la Caixa Foundation", we put together an interdisciplinary group of researchers that study the mechanisms by which the microbiome directs feeding decisions.

New lab members are leveraging quantitative behavioural assays, neuronal circuit imaging, metabolomics, genomics and microbial genetics. These techniques are used to identify the metabolic, molecular and neuronal circuit mechanisms by which specific gut microbes interact with the brain to guide behaviour and nutrition. This work is done in collaboration with teams located in Switzerland, the UK, France and Germany."

* Microbiome

A population of many millions of microorganisms that live inside our digestive systems and on the surface of our bodies.

Neuroplasticity & Neural Activity

Noam Shemesh

Model Rodents

Principal Investigator Joined CF in 2014

Brain region Whole brain

Research Methods

Functional Magnetic Resonance Imaging (fMRI) Optogenetics Behaviour





- andes Rsch Tech

- niel Nunes Postdoc. drada Ianus Rsch. Associate. II s Santiago PhD Stud. •
- Madalena Fonseca PhD Stud. III •

- ervised by Daniel C Alexander, UCL rvised by Noam SHemesh, CR

Direct functional MRI based on cell swellings and neurotransmitter release

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 time scale 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 received support from the European Research Council, have been focused on developing novel techniques that harness the power and versatility of MRI to perform direct measurements of neural activity on a much faster timescale. For instance, the team harnesses ultrahigh magnetic fields and diffusion to image the dynamics of (hypothetical) cell swellings that are known to be coupled with neural activity, as well as neurotransmitter release in the brain. These various measurements are performed in-vivo using state of the art 9.4T and 16.4T scanners. in both anaesthetized and behaving rodents.

Noam Shemesh speaks about a new technology that was implemented in the lab.

"Since its establishment at the CCU, our lab has been using ultra-high-field MRI scanners for pre-clinical and basic research and to develop novel imaging techniques. In 2018, the imaging infrastructure was upgraded with the arrival of a new cryogenic microimaging probe, the first and only one of its kind in the world. This new probe, maintained at about -230 degrees Celsius, significantly increases the resolution of the images acquired with the scanners, thereby providing higher-quality data essential for tackling the hard problems our team is set out to solve."

* Magnetic Resonance Imaging

Our bodies are composed of ≈70% water. When the protons that make up the water molecules are exposed to the strong magnetic field generated by MRI scanners, they behave like bar magnets that naturally align with the magnetic field, similar to how a compass needle would align with the earth's magnetic field.

To gain insight into the structure of the tissue that is being imaged, the MRI scanner sends radiofrequency pulses that perturb the magnetic moment of the water protons and registers how they realign with the field. The dynamics of this realignment process encode the highly informative images that are commonly used in research and medicine.

To dig down into the neural circuitry of innate behaviour, the Innate Behaviour* lab focuses on two main behaviours – the relatively simple avoidance of a repulsive odour and the more intricate courtship behaviour. Both behaviours are studied in the fruit fly Drosophila melanogaster, a powerful model system that offers a wide range of advanced techniques. These include genetic manipulations to help identify which neurons are involved in specific behaviours, optogenetic tools to monitor the activity of neurons, and highly detailed video monitoring to establish the most precise relationship between behaviour and neural activity.

Using this combined approach, the team was able to establish a direct link between neural activity and behaviour, when they discovered a group of neurons (called apterous neurons) that have direct control over sexual receptivity in female flies. When the researchers silenced these particular neurons, females significantly reduced their receptivity towards males. Besides, they were able to pinpoint a specific behavioural hallmark that was affected - the walking pace of the female. Together, these results represent an important step towards gaining a better understanding of the neural mechanisms that control female receptivity. For the next step, the team is trying to pin down the neural circuitry these neurons tap into to find out how they exact this powerful effect on the behaviour of the female.

Luísa Vasconcelos talks about a new grant.

"In 2018, the lab was awarded a grant from the Portuguese National Ministry for Science and Technology (FCT) to support the research project: 'Communication during courtship: the role of ovipositor extrusion'.

During courtship, the female fly extrudes the ovipositor, the organ through which she deposits her eggs. This action is exclusive to courtship, but its function is unknown. Recently, the team found a way to manipulate ovipositor extrusion. Using this new finding, we plan to determine how this action impacts the course of male-female interactions during courtship."

Innate Behaviour

Maria Luísa Vasconcelos

Principal Investigator Joined CF in 2011 Model

Brain

Region Methods Whole brain Optogenetics Imaging Behaviour

Research

Genetics

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

* Innate behaviour

Innate, also called instinctive, behaviours

they are often involuntary and can occur in

individuals even without their awareness.

Well-known examples of innate behaviours include nest-building and courtship.

do not require learning, nor experience,

2 4 1 3 5 6

1 Sophie Dias – Rsch. Tech. 2 Miguel Gaspar – PhD Stud. 3 Maria Luisa Vasconcelos – PI 4 Cecilia Mezzera – Postdoc. 5 Cristina Ferreira – PhD Stud. 6 Eliane Ochôa Arez – PhD Stud. Margarida Brotas – MSc Stud.

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Immunophysiology

Henrique Veiga-**Fernandes**

Principal Investigator Joined CF in 2017

Model Rodents

Mucosal barriers such as the intestine and the lungs

Regions

Research of Interest Methods

Genetic, molecular and cellular approaches Flow cytometry Confocal microscopy In vivo models of disease





- Ana Rasteiro MSc Stud quel Silva — MSc Stud
- linho da Silva Postdoc, Elv
- Bruno Raposo Rsch. Tech. Sara Correia – Rsch Tech
- Roeland Klein Wolterink Postdoc
- Vânia Cardoso Postdoc, Flw Vasco Correia — Tech
- 10 David Brea Lopez Postdoc .Flw
- 11 Raquel Soares MSc Stud 12 Miguel Rendas — PhD Stud

- 13 Julie Chesné Postdoc, Flw
- 14 María Martínez-Lopez Postdoc. Flw 15 Marko Šestan – Postdoc. Flw.
- 16 Ana Filipa Cardoso PhD Stud
- Gonçalo Malpica MSc Stud.
 Kristin Fischer PhD Stud.
- 19 Hélder Ribeiro Lab Mngr
- 20 Henrique Veiga-Fernandes Pl
- 21 Roksana Pirzgalska Postdoc .Flw Manuela Ferreira — Postdoc. Flw. Telmo Catarino — PhD Stud. •

The role of crosstalk between neurons of the peripheral nervous system and the immune system in the prevention and resolution of disease

SCIENTIFIC APPROACH

The Immunophysiology lab explores the role of cross-talk between neurons and the immune system in the prevention and resolution of disease. To that end, the team mainly focuses on mucosal barriers*. such as the intestine and the lung. These organs are in permanent contact with the external environment and have a complex and dense network of neuronal and immune cells. This combination of features makes these organs an optimal site to reveal how the neural and immune systems work together to preserve health.

Using this approach, the lab has recently revealed a surprising role of the neural network that surrounds these organs: immune regulation. The team discovered that while the immune system is the one that actively fights infection, the neurons are the ones that are in charge of detecting the invasion and setting the immune response in motion. These findings may have tremendous potential in the design of novel therapeutic approaches to disease as they pinpoint new selective targets that can be harnessed in allergy, inflammation, obesity and cancer.

Henrique Veiga-Fernandes talks about a new grant and its implication to the lab.

"In 2018, I received the Allen Distinguished Investigator award. This selection was motivated by our work on how the immune and nervous systems interact in our body to protect us from infections. With this award, our team will develop new techniques that will enable us to measure how those interactions occur."

* Mucosal barriers

Even though our digestive organs and our lungs are inside our bodies, they are in fact "external" in the sense that they are continuous with the external world. To separate the "inside" from the "outside", the body has barriers composed of specialised cells. These barriers allow the influx of nutrients and water and prevent the entrance of bacteria and toxins. The barrier cells also generate the mucosa which lines the organs and protects them from damage.

Research Associates

Senior researchers who manage independent projects in association with particular labs at CR.





Rita Fior

CANCER DEVELOPMENT & INNATE IMMUNE EVASION

Tumour cells employ mechanisms that circumvent the immune response. By doing so, tumours manage to grow and achieve further metastasis. Dr Fior's research combines live imaging, genetic and chemical tools to study the process of innate immune evasion and intra-tumoral clonal interactions using the zebrafish-larvae xenograft model. Understanding the process of innate immune rejection/ evasion may lead to new avenues of anti-cancer therapies based on modulating conserved innate immune mechanisms.

Team: Vanda Póvoa – PhD Stud. Associated with: Telomeres, Ageing & Cancer lab

Ruth Diez del Corral

DEVELOPMENT OF NEURAL CIRCUITS

The nervous system is composed of a large variety of neuronal and glial cell types that connect to create functional circuits. These circuits perform multiple functions, such as basic survival mechanisms (e.g. breathing) and behavioural responses to internal and external stimuli. The research of Dr Diez del Corral focuses on understanding how neural circuits are formed during development by using the zebrafish larva as an animal model.

Team: João Martins – MSc Stud. Associated with: Vision to Action & Collective Behaviour labs

Eran Lottem

5-HT AND DECISION MAKING

Serotonin (5-HT) is a central neuromodulator implicated in the regulation of many processes, and its dysregulation can contribute to altered perception as well as pathological conditions such as depression and obsessive-compulsive disorder. Using theory-driven experimental approaches, combined with electrophysiological, optical and genetic techniques in mice, Dr Lottem's research explores 5-HT's function in decision-making and learning.

Associated with: Systems Neuroscience lab

Claudia Feierstein

NEURAL CIRCUITS FOR VISUOMOTOR BEHAVIOUR

How does our brain use information to select appropriate behaviour? Dr Feierstein's research approaches this question by using custom-built microscopes and high-speed behavioural tracking to record neuronal activity in the entire brain of zebrafish larvae while closely monitoring their behaviour. By combining imaging, behavioural analysis, and manipulation of activity, she aims to understand the processing occurring in different brain areas and how they contribute to behaviour.

Associated with: Vision to Action lab

Adjunct Labs

In addition to the nineteen research labs, four adjunct labs, which work in complementary areas are also associated with CR.

Within the Champalimaud Centre for the Unknown

Neuropsychiatry

The Neuropsychiatry Unit started in 2013 as an interface between the Champalimaud Clinical Centre and the Champalimaud Neuroscience Programme. The team is dedicated to clinical care and translational research in mental and behavioural health, focusing on areas that are close to research interests in neuroscience under development at Champalimaud Research. At the Unit, psychiatrists and psychologists delivering care at the Clinical Centre work with other clinical and non-clinical researchers to deepen knowledge about neuropsychiatric disorders and their treatment.

Principal investigator: Albino Oliveira-Maia

Telomeres, Ageing & Cancer

The Telomeres, Ageing and Cancer lab conducts basic and clinical research. On the basic level, the lab asks how the shortening of telomeres structures that secure the end of chromosomes and protect them from deterioration—is involved in cancer. On the clinical level, the team is developing a method that will use zebrafish as "avatars" to determine the right type of chemotherapy for individual patients.

Principal investigator: Miguel Godinho-Ferreira

↓ A cuttlefish participates in a robotic hunting assay for Cephalopods, an Intelligent Systems Project.



Outside the Champalimaud Centre for the Unknown

Intelligent Systems

The goal of the Intelligent Systems lab is to identify the general principles of brain function that support intelligent behaviour and to implement them in machines. Specifically, they focus on how the brain constructs a representation of the environment: How is this representation learned? How is it encoded in the activity of neural networks? How is it used to control adaptive behaviour?

Principal investigator: Adam Kampff Affiliation: The Sainsbury Wellcome Centre, University College London

kampff-lab.org

Social NeuroEndocrinology

The main research interest of the Social NeuroEndocrinology lab is the integrative study of social behaviour that combines the study of proximate causes (gene modules, hormones, neural circuits, cognitive processes) and ultimate effects (evolutionary consequences). In particular, the team is interested in understanding how brain and behaviour can be shaped by the social environment, and how the cognitive, neural and genetic mechanisms underlying plasticity in the expression of social behaviour have evolved.

Principal investigator: Rui Oliveira Affiliation: Instituto Superior de Psicologia Aplicada & Instituto Gulbenkian de Ciência

oliveiralab.org

Publications Highlights

In 2018, CR investigators published 52 research articles in peer-reviewed journals. These publications mirror the expanding scope of the programme, featuring novel insights in diverse fields of biology.



Body movements just need a "puff" of dopamine to get started

A new study in mice by the Neurobiology of Action lab suggests that a burst of dopamine levels at the beginning of a movement only. as opposed to all the time, is what gets us going. This may have important implications for treating Parkinson's disease.

da Silva JA, Tecuapetla F, Paixão V, Costa RM (2018). Dopamine neuron activity before action initiation gates and invigorates future movements. Nature. DOI:10.1038/nature25457.

Run Faster Learn Better

While trying to figure out how connections between neurons change with experience to give rise to learning, the Neural Circuits and Behaviour Lab accidentally stumbled upon an important finding: the existence of a strong link between walking speed and learning speed in mice.

Albergaria C, Silva NT, Pritchett DL, Carey MR (2018). Locomotor activity modulates associative learning in mouse cerebellum. Nat Neurosci. DOI:10.1038/s41593-018-0129-x.







Serotonin speeds learning

Why do treatments with antidepressants like Prozac seem to work better when combined with behavioral therapies, which promote the learning of positive behaviors by the depressed patient? A new study by the Systems Neuroscience lab suggests a possible explanation.

ligaya K, Fonseca MS, Murakami M, Mainen ZF, Dayan P (2018). An effect of serotonergic stimulation on learning rates for rewards apparent after long intertrial intervals. Nat Commun.DOI:10.1038/s41467-018-04840-2.

52 research articles published in 2018

309

The total number of research articles published by CR investigators since the establishment of the programme

How the brain decides what to do in the face of danger

Fight, flee, or freeze; when faced with a threat, everyone, from mice to humans, is certain to choose one of these three strategies. Though critical for survival, we are still at a loss as to how the brain chooses which strategy to apply in any given instance. Now, in a new study by the Behavioural Neuroscience lab and the Innate Behaviour lab, begins to unravel the mystery.

Zacarias R, Namiki S, Card GM, Vasconcelos ML, Moita MA (2018). Speed dependent descending control of freezing behavior in Drosophila melanogaster. Nat Commun. DOI:10.1038/s41467-018-05875-1.



Publications Highlights

Losing neurons can sometimes not be that bad

Current thinking about Alzheimer's disease is that neuronal cell death in the brain is to blame for the cognitive havoc caused by the disease. But a new study by the Cell Fitness lab and the Stem Cells and Regeneration lab suggests that neuronal death in Alzheimer's patients may be a protective reaction against the disease. This could lead to a complete rethinking of therapeutical approaches to Alzheimer's disease.

Coelho DS, Schwartz S, Merino MM, Hauert B, Topfel B, Tieche C, Rhiner C, Moreno E (2018). Culling Less Fit Neurons Protects against Amyloid-β-Induced Brain Damage and Cognitive and Motor Decline. Cell Reports. DOI:10.1016/j. celrep.2018.11.098.





Scientists discover hidden structure of enigmatic "backwards" neural connections

The long-standing mystery of the organisation of "backwards" connections in the visual system has been solved. The Cortical Circuits lab, discovered that they tell the brain where not to look. These results could have deep implications for the field of machine vision.

Marques T, Nguyen J, Fioreze G, Petreanu L (2018). The functional organization of cortical feedback inputs to primary visual cortex. Nat Neurosci. DOI:10.1038/s41593-018-0135-z.



Fruit-fly hunger games: taste neurons in control

According to new findings by the Behaviour and Metabolism lab, right at the tip of the fruit fly's tongue sit two sets of taste neurons that have now been found to be crucial for the insect to develop a craving for protein.

Steck K, Walker SJ, Itskov PM, Baltazar C, Moreira JM, Ribeiro C (2018). Internal amino acid state modulates yeast taste neurons to support protein homeostasis in Drosophila. Elife. DOI:10.7554/eLife.31625.

A better view of brain connectivity

Novel findings by the Neuroplasticity and Neural Activity lab suggest that compared with current functional Magnetic Resonance Imaging (fMRI) methods, diffusion-weighted fMRI (dfMRI) signals better represent the underlying neural activity. These advances may have significant implications towards a more specific and accurate mapping of neural activity in the global brain in-vivo.

Nunes D, Ianus A, Shemesh N (2018). Layer-specific connectivity revealed by diffusion-weighted functional MRI in the rat thalamocortical pathway. Neuroimage. doi: 10.1016/j.neuroimage.2018.09.050



zebrafish movements Motor behaviour could be formed from a range of continuous possible movements. But it could also

Scientists reveal the "lego

pieces" that form complex

continuous possible movements. But it could also be constituted by sequences of distinct, discrete movement types. New results by the Vision to Action lab suggest that the latter is the case, at least for zebrafish larvae.

Marques JC, Lackner S, Félix R, Orger MB (2018). Structure of the Zebrafish Locomotor Repertoire Revealed with Unsupervised Behavioral Clustering. Curr Biol. DOI:10.1016/j. cub.2017.12.002.

Publications List

RESEARCH ARTICLES

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SCIENCE COMMUNICATION

Maria Vicente, Ana Pereira, Raquel Gomes, Gil Costa, Marta Moita and Catarina Ramos. (2018). Shhhh... Danger is Out There. Frontiers for Young Minds.

External Funding Highlights

During 2018, nearly all research groups received external financial research support, securing competitive funds from a plethora of public and private, national, European and overseas funding entities.

The European Commission Horizon 2020 Framework Programme constituted more than 50% of the total sum of competitive external funding.

18.1^M

CR investigators were awarded competitive external research funds with the sum of about 18.1 million euros. Of these, 95% were secured through competitive calls and 78% were awarded by public funding entities. **European Commission**



funding entities Fundação para a Ciência e Tecnologia (FCT) National **Public** 19% **Brain and Behavior Research Foundation** International **Breast Cancer Now European Foundation for the Study of Diabetes Private Federation of European Biochemical Societies** 18.2% la Caixa Foundation **Paul G. Allen Family Foundation Volkswagen Foundation** International Public **European Molecular Biology Organization Human Frontier Science Program** 2% Fundação Calouste Gulbenkian **National private** Fundação Bial 0.2%

External Funding Highlights

GRANTS

2M€

EUROPEAN COMMISSION - H2020 ERC CONSOLIDATOR GRANTS

Marta Moita Behavioural Neuroscience lab

460K € "LA CAIXA" FOUNDATION - HEALTH RESEARCH 2017

Carlos Ribeiro Behaviour and Metabolism lab

520K €

Michael Orger Vision to Action lab **1.3M€**

PAUL G. ALLEN FAMILY FOUNDATION – ALLEN DISTINGUISHED INVESTIGATORS PROGRAM

Henrique Veiga-Fernandes Immunophysiology lab

500K €

- HEALTH RESEARCH 2017

Leopoldo Petreanu Cortical Circuits lab

2.5M € EUROPEAN COMMISSION - H2020 WIDENING PROGRAMME

ERA Chair QuantOCancer Champalimaud Research

FELLOWSHIPS

EUROPEAN COMMISSION - H2020 MSCA-IF-EUROPEAN STANDARD

Camille Mazo Cortical Circuits lab

Constanze Lenschow Neuroethology lab

Roel Klein Wolterink Immunophysiology lab

EUROPEAN MOLECULAR BIOLOGY ORGANIZATION - EMBO INSTALLATION GRANT

Bruno Costa-Silva Systems Oncology lab HUMAN FRONTIER SCIENCE PROGRAM – HFSP POSTDOCTORAL FELLOWSHIPS

Camille Mazo Cortical Circuits la

Constanze Lenschow Neuroethology lab

FEDERATION OF EUROPEAN BIOCHEMICAL SOCIETIES – FEBS LONG-TERM

Ana Queiros Cell Fitness lab

Grants

1.4M €

16.7M €

Fellowships

Values are rounded to the nearest bulk number

Competitive Funding List

GRANTS

American Portuguese Biomedical Research Fund

Erythrocyte surveillance – the immune system looking within? Rita Fior – Rsch. Assoc

Brain and Behavior Research Foundation -NARSAD Young Investigator Grants

From neuronal firing to behaviour — breaking down the 5-HT chain events Romain Ligneul — Systems Neuroscience

Brest Cancer Now — Catalyst Programme

Bosutinib effects in premetastatic niche formation and lung metastasis in breast cancer. Brung Costa-Silva

European Commission — H2020 ERC Consolidator Grants

— 2017 call

Basal ganglia circuit mechanisms underlying dynamic cognitive behaviour.

Whole-brain circuits controlling visuomotor behaviour. Michael Orger

Hypothalamic circuits for the selection of defensive and mating behaviour in females. Susana Lima

— 2018 call

Actively frozen — contextual modulation of freezing and its neuronal basis (A-Fro). Marta Moita

European Commission — H2020 ERC Proof of Concept Grants

Behaviour phenotyping using inertial sensors (WEAR). Rui Costa

European Commission – H2020 MSCA-ITN-ETN

Zebrafish neuroscience interdisciplinary training hub (ZENITH). Michael Orger European Commission - H2020 Widening Programme

Leveraging the unique organismic approach to health and disease of the Champalimaud Foundation through the inception of a quantitative biomedicine research programme focused on cancer. ERA Chair QuantOCancer

European Foundation for the Study of Diabetes — Lilly Young Investigator Research Award

Erythrocyte surveillance — the immune system looking within? Roksana Pirzgalska — Immunophysiology

Fundação Bial – Funding for Scientific Research 2018/2019

Dissecting dynamical components of complex decision-making using a computer game-based task. Gautam Agarwal – Systems Neuroscience

Fundação Calouste Gulbenkian -Academias Gulbenkian do Conhecimento

Neuronautas — novos exploradores do cérebro Catarina Ramos — Science Communication, CR

Fundação para a Ciência e Tecnologia -2017 SR&TD Projects

— With the participation of the Champalimaud Foundation

Ongenetic and transgenerational effects of oxytocin-like peptides on social behaviour – an eco-evo-devo approach using zebrafish as a model. Bruno Costa-Silva & Michael Orger

Stratification of chronic metabolic diseases exosomes derived from the hepatic-intestinal axis. Bruno Costa-Silva

Diffuse large B-cell lymphoma blood-based proteome signatures.

Early exposure to mycotoxins and potential health impact. Manuela Ferreira – Immunophysiology

> — Coordinated by the Champalimaud Foundation

Spatial attention – dissecting the cortical and subcortical circuitry during rapid routing of sensory information. Bassam Atallah – Systems Neuroscience

The role of metastatic microenvironment in Multiple Myeloma extramedullary disease (EMphAsIS – Extramedullary MyelomA mIcroenvironment Study). Bruno Costa-Silva

Microbiome, nutrients and the brain – identification of the molecular mechanisms underlying the impact of essential amino-acids and of the microbiome on brain function. Carlos Ribeiro

Molecular mechanisms of neural stem cell activation following brain injury in drosophila. Christa Rhiner

Robustness and energy efficiency in spiking neural networks. Christian Machens & Alfonso Renart

Odors and memory: neural mechanisms for encoding contextual information in olfactory cortex. Cindy Poo – Systems Neuroscience

Serotonergic Control of Decision-Making and Impulsivity. Eran Lottem – Systems Neuroscience

Circadian regulation of lymphoid innate cells. Henrique Veiga-Fernandes

Cortical circuits for sensory expectations. Leopoldo Petreanu

Communication during courtship: the role of extending the ovipositor. Luísa Vasconcelos Function of dietary retinoids in natural intraepithelial lymphocytes and intestinal immunity at the early stage of life.

Manuela Ferreira — Immunophysiology

Neural mechanism of value based decision making of staying or leaving – deciding when to initiate locomotion to move to the next reward location. Masayoshi Murakami – Systems Neuroscience

The nature of error signals in the cerebellum during locomotive learning. Megan Carey

Mechanisms of operant conditioning in the whole brain of the zebrafish larvae – cells, circuits and behaviour. Michael Orger

"la Caixa" Foundation – Health Research 2017

Identifying and testing the metabolites generated by two psychoactive gut bacteria to alter brain function and behaviour. Carlos Ribeiro

Optical dissection of cortical circuits for sensory expectations. Leopoldo Petreanu

Liga Portuguesa Contra o Cancro — Núcleo Regional do Sul (LPCC) — Terry-Fox

Molecular mechanisms of innate immune evasion and rejection.

Rita Fior — Rsch. Assoc

Paul G. Allen Family Foundation — Allen Distinguished Investigators Program

Deciphering peripheral neuroimmune architecture by intercellular labelling. Henrique Veiga-Fernandes

Wellcome Trust — In collaboration with University College London

International Brain Laboratory. Zachary Mainen

Volkswagen Foundation – Life

How spontaneous behaviour emerges from brain-wide neural network dynamics.

ogy Michael Orger

g FELLOWSHIPS

European Commission - H2020 MSCA-IF-European Standard

Do cortical feedback connections store statistical knowledge of the environment? Camille Mazo – Cortical Circuits

Anatomical and functional characterization of the neural circuits controlling ejaculation (SEG) Constanze Lenschow – Neuroethology

Tracing of pulmonary neuroimmune networks.

Immunophysiology

Federation of European Biochemical Societies — FEBS Long-Term fellowships

Regulation of "fitness fingerprints" mediated cell competition. Ana Queiros – Cell Fitness

Fundação para a Ciência e Tecnologia (FCT) — Doctoral Fellowships

Unraveling the role of the BSM in ejaculation and micturition in mice. Ana Mendes – Neuroethology

Network mechanisms of multimodal cue integration for self-movement estimation. André Marques – Sensorimotor Integration

Forward models in the cerebellum for mouse motor adaptation. Diogo Duarte – Neural Circuits & Behaviour

Plasticity in the rodent auditory system. Frederico Severo – Neural Plasticity & Neural Activity

Whole-brain mechanisms of operant learning in zebrafish cells, circuits and behavior. Joaquim Contradancas — Vision to Action The mechanisms of sound localisation behaviour in the rat. Mafalda Valente – Circuits Dynamics & Computation

Signatures and consequences of distributional reinforcement learning. Margarida Sousa – Learning

Molecular mechanisms of neural stem cell activation following brain injury in drosophila. Mariana Santos – Stem Cells & Regeneration

Cell competition in drosophila's organs – the effects of suboptimal cells accumulation and an insight into the winnerloser communication in a competition scenario. Mariana Reis – Cell Fitness

Identifying the control mechanism for pursuing behavior in drosophila. Miguel Paço – Sensorimotor Integration

Fulbright / Luso-American Development Foundation Study / Research Award

The impact of diet and the microbiome on brain function via lncRNAs. Brittany Petros – Cortical Circuits

Human Frontier Science Program – HFSP Postdoctoral Fellowships

Do cortical feedback connections store statistical knowledge of the environment? Camille Mazo – Cortical Circuits

Anatomical and functional characterization of the neural circuits controlling ejaculation. Constanze Lenschow – Neuroethology

AWARDS

Associação Viver a Ciência - Prémio Crioestaminal, Honorable Mention

Molecular mechanisms of innate immune evasion and recognition. Rita Fior – Rsch. Assoc

Data in this chapter refers to the total funding awarded to CR in 2018 through competitive research calls (according to information collected at the beginning of the production of the report in January, 2019). These funds will be executed throughout the expected duration of the projects.



Education

Since the beginning, CR has regarded educating scientists as one of its main objectives. To this end, the CR has been dedicating considerable efforts to the development and implementation of outstanding educational programmes, advanced courses and workshops. Among these, two main endeavours are the International Neuroscience Doctoral Programme and the CAJAL Advanced Training Courses.

← Lagoa de Óbidos at Foz do Arelho: a nice view from the CR Student Retreat.

International Neuroscience **Doctoral Programme - INDP**

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. INDP students come from all over the world and from a range of backgrounds. including the life sciences, physics, psychology, mathematics and computational sciences.

During the first year of this four-year programme, students attend courses that cover basic topics in contemporary biology and neuroscience. The courses have a strong practical component, which includes a variety of experimental preparations. During this year, students also perform laboratory 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. Students are followed by a thesis committee which monitors their progress and provides input throughout their graduate education. The INDP is an accredited programme and degrees are granted by one of our two academic partners, Universidade Nova de Lisboa and the Instituto Superior de Psicologia Aplicada.

PhD students enjoy a vibrant academic environment at the Champalimaud Foundation, with a weekly schedule of both internal and guest seminars, as well as access to a wide range of meetings and workshops. INDP students also have the opportunity and funding to organise their own advanced courses, as well as an annual retreat.

Director: Joe Paton Education Committee: Eugenia Chiappe & Joe Paton **Coordinator: Thiago Carvalho** Managers: Simone Zacarias & Maria **Teresa Dias**







Elena Hindinge Frederico Severo 12 Kristin Fischer 13 Kcénia Bougrova Joaquim Contradanças Ana Rita Mendes Teresa Serradas Duarte 17 Nuno Rito **Matheus Farias** 19 Solène Sautory

11

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15

16

18

André Marques

Margarida Sousa

Tiago Quendera

Filipe Rodrigues

Ana Mafalda Valente

Mirjam Heinemans

Miguel Paço

Diogo Duarte

Lucas Martins

CAJAL Advanced Neuroscience Training Programme

The CAJAL Advanced Neuroscience Training Programme consists of 6 yearly courses, 2 held at the Champalimaud Centre for the Unknown in Lisbon and 4 in 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 USA for decades.

CAJAL Advanced Course — Behaviour of Neural Systems

Quantitative studies of behaviour are fundamental in our effort to understand brain function and malfunction. Recently, the techniques for studying behaviour, along with those for monitoring and manipulating neural activity, have progressed rapidly. Therefore, this summer course was structured to provide promising young scientists with a comprehensive introduction to state-of-the-art techniques in quantitative behavioural analysis. This 3-week course was a practical "hands-on" introduction to advanced methods in behavioural tracking and analysis that covered sufficient background such that all participants would be able to establish these techniques in their home laboratories.

July 15, 2018–August 4, 2018

Course Directors:

Gonzalo de Polavieja — CR, Portugal Benjamin de Bivort — Harvard University, USA Megan Carey — CR, Portugal Greg Stephens — VU University Amsterdam, The Netherlands



↑ A moment of connection at the beginning of the course.

CAJAL Advanced Neuroscience Training Programme



↑ Students have access to software and hardware, and freedom to experiment.

→ The course environment allows for moments of focus and quiet research.



CAJAL Advanced Course – Computational Neuroscience

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 an essential tool to cut through the vast complexity of neurobiological systems and their many interacting elements.

The course teaches the central ideas, methods, and practices of modern computational neuroscience through a combination of lectures and hands-on project work. During the course's mornings, distinguished international faculty deliver lectures on topics across the entire breadth of experimental and computational neuroscience.

For the remainder of the time, students work on research projects in teams of 2 to 3 people under the close supervision of expert tutors and faculty.

Research projects are proposed by faculty before the course and include the modelling of neurons, neural systems, and behaviour, the analysis of state-of-the-art neural data (behavioural data, multi-electrode recordings, calcium imaging data, connectomics data, etc.), and the development of theories to explain experimental observations.

August 7–10, 2018 – Pre-school August 12, 2018–September 1, 2018 – Full Course

Course Directors: Jakob Macke – Research Center Caesar, Germany Christian Machens – CR, Portugal Joe Paton – CR, Portugal

→ Small automata built as training for robotics and behaviour cathegorisation.



Theses List

DOCTORAL

Andreia Cruz

If you say freeze, I may freeze with you — How learning through self experience determines the meaning of the behavior of others

Thesis Advisor: Marta Moita — Behavioural Neuroscience

Asma Motiwala

Internal representations for time based decisions

Thesis Advisors: Christian Machens — Theoretical Neuroscience Joe Paton — Learning

João Semedo

Inter-area communication in the brain — a population-level approach

Thesis Advisors: Christian Machens – Theoretical Neuroscience Byron Yu – Carnegie Mellon University

Joaquim Alves da Silva

Exploring the role of substantia nigra dopaminergic neurons in the initiation of self-paced actions

Thesis Advisor: Rui Costa — Neurobiology of Action lab

Rita Domingues

Sensing and Transcriptional requirements of Innate Lymphoid Cells

Thesis Advisor: Henrique Veiga-Fernandes — Immunophysiology

Samuel Viana Meyler

Insights into perceptual ambiguity and inference in art — a practice based approach derived from the corporeal form

Thesis Advisors: Zach Mainen — Systems Neuroscience Jose Pedro Serra — Faculdade de Letras da Universidade de Lisboa

Sílvia Madeira

Environmental sensing by immune cells

Thesis Advisor: Henrique Veiga-Fernandes — Immunophysiology

Simone Lackner

How larval zebrafish respond to changes in illumination

Thesis Advisor: Michael Orger — Vision to Action

Tiago Marques

Mechanisms of Visual Perception in the Mouse Visual Cortex

Thesis Advisor: Leopoldo Petreanu — Cortical Circuits

MASTER'S

Ana Logrado

Zebrafish xenografts as a model for chemo and radiosensitivity evaluation of BRCA2 mutated tumors

Thesis Advisor: Rita Fior — Cancer Development & Innate Immune Evasion

Beatriz Belbut

The spatial structure of surround modulation in mouse visual cortex

Thesis Advisor: Leopoldo Petreanu — Cortical Circuits

Catarina Costa

The role of fu2 in Flower-dependent cell competition events

Thesis Advisor: Eduardo Moreno — Cell Fitnes

Cátia Almeida

Bevacizumab: more than an anti-angiogenic drug

Thesis Advisor: Rita Fior — Cancer Development & Innate Immune Evasion

Francisca Fernandes

Investigation of the mouse visual pathway via high-field functional MRI

Thesis Advisor: Noam Shemesh — Neuroplasticity and Neural Activity

Hugo Bettencourt

Investigating climbing fiber activity during locomotor learning

Thesis Advisor: Megan Carey — Neural Circuits and Behaviour

João Martins

Ontogenesis of visual processing circuits in the zebrafish: analysis of specific neuronal subpopulations in development

Thesis Advisor: Ruth Diez del Corral

Mafalda Antunes Ferreira

Functional characterization of tumour-derived exosomes in the zebrafish xenograft model

Thesis Advisor: Bruno Costa-Silva — Systems Oncology

Margarida Pexirra

Manipulations of striatal temperature cause dose dependent changes in duration judgments

Thesis Advisor: Joe Paton – Learning

Margarida Brotas

The role of ovipositor extrusion during courtship in female drosophila melanogaster

Thesis Advisor: Maria Luísa Vasconcelos - Innate Behaviour

Mariana Velez

Generation of new transgenic zebrafish lines for studying neuronal circuits underlying behavior in zebrafish

Thesis Advisor: Ana Catarina Certal & Ana Raquel Tomás - MTT Platform

Marta Maciel

Mapping the neural circuitry underlying spatial and temporal locomotor adaptation

Thesis Advisor: Megan Carey - Neural Circuits and Behaviour

Pedro Durão

The role of fu2 gene in cell competition in Drosophila melanogaster

Thesis Advisor: Eduardo Moreno — Cell Fitness

Rita Figueiredo

Impact of the metabolic program of germline cells on feeding behaviour

Thesis Advisor: Carlos Ribeiro — Behaviour and Metabolism

Sandra Martins Rebocho

Development of a new ultra-fast freezing procedure for zebrafish sperm cryopreservation

Thesis Advisor: Ana Catarina Certal - Fish Platform

Susana Ferreira

Optimization of Neoadjuvant Radiotherapy for zebrafish-avatars — towards personalized medicine

Thesis Advisor: Ana Catarina Certal - Fish Platform

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Events

To complement researchrelated activities, CR also organises scientific events on a regular basis. In 2018, the long list of events included, in addition to the annual Champalimaud Symposium, a weekly colloquia series and various international scientific meetings. What follows are a few highlighted events.

> → CR Symposium participants on a guided tour in Lisbon.



Events Highlights

7th Champalimaud Research Symposium -Quantitative Approaches

The goal of the 2018 Champalimaud Research Symposium was to gather experts from a diversity of fields—such as biology, physics, statistics, computer science and engineering—in order to identify key theoretical frameworks to describe animal behaviour and neuroscience and to showcase recent advancements in these fields achieved using quantitative approaches.

The symposium attracted a lot of attention and was the best attended Champalimaud Research Symposium to date. Triggered both by the content of the presentations, and especially by the lively group discussion sessions, there were several interesting debates on key topics such as how to tackle the high-dimensional nature of data in biology, the impact of artificial intelligence on neuroscience, and the challenges of relating neural activity and animal behaviour. All considered, the organisers felt the symposium achieved its goals of bringing together researchers across disciplines and forging new links between Champalimaud Research and scientists around the world.

Speakers:

Haim Sompolinsky (Keynote Speaker) – Hebrew University Albert-László Barabasi – Northeastern University Anne Churchland — Cold Spring Harbour Laboratory Barbara Webb - University of Edinburgh Christian Machens - Champalimaud Centre for the Unknown Florian Engert – Harvard University Josh McDermott – Massachusetts Institute of Technology Maria Neimark Geffen — University of Pennsylvania Mark Humphries - University of Nottingham Mark Transtrum – Brigham Young University Matthew Botvinick - DeepMind & University College London Megan Carey — Champalimaud Centre for the Unknown Rainer Friedrich - Friedrich Miescher Institute for Biomedical Research Stuart Geman - Brown University Surya Ganguli - Stanford University Tim Behrens – University of Oxford

> ↓ Talk at the Champalimaud Centre for the Unknown auditorium.



Chairs: Alfonso Renart Michael Orger





↑ Sharing data visualisations at the poster session of the event.

↓ The symposium begins with a reception at the amphitheatre.



CR ANNUAL REPORT | 2018

Events Highlights

Zebrafish Facility Management Workshop

This workshop aimed to strengthen the ever-expanding, worldwide network of zebrafish aquaculture supporting zebrafish research. With an international panel of 11 world experts in the field, this was a great opportunity for zebrafish facility managers, technicians and researchers involved in facility management, to sit together and discuss recent developments, current opportunities and personal experiences within the field.

The Fish Platform organised the first edition of this international Workshop. The event was fully sold out, counting more than 80 participants arriving from 18 different countries on-site, and about 20 more who joined via live streaming.

October 29-30, 2018

Organisers: Ana Catarina Certal – CF Claire Allen – University of Sheffield, UK João Cruz – CONGENTO

Advanced Course in Image Analysis

The advanced Course in Image Analysis provided both in-house and external microscopy users with extensive training on how to perform high-level analysis of images they acquire using microscopy techniques. The course was taught by specialists from the ABBE platform, Instituto Gulbenkian de Ciência, and the Scientific Volume Imaging Company from the Netherlands.

September 25, 2018 – Part 1: Image fundamentals and visualisation

November 20–22, 2018 – Part 2: Advanced image processing and analysis

Local organisers: Davide Accardi Rebecca Saleeb

↓ Observing zebrafish swimming around in their container.





European Society for Magnetic Resonance in Medicine and Biology Meeting

This course was intended for Magnetic Resonance (MR) physicists, other scientists and PhD students who already have experience in basic MR methods and knowledge of MR excitation and acquisition principles, and who wished to extend their knowledge on diffusionweighted imaging. This advanced course provided a detailed introduction into the field of diffusion measurements, which covers the physical principles of diffusion in heterogeneous media, measurement techniques and applications to the investigation of the cellular structure of living tissues.

September 03-05, 2018

Programme director: Felix Breuer — Research Center Magnetic Resonance Bavaria, Germany Course organiser: Valerij G. Kiselev — University of Freiburg Medical Center, Germany Local organiser: Noam Shemesh ← Colourised MRI image of a human brain.

Science Careers Workshop Series

The Science Careers Workshop Series was established with the goal of raising awareness amongst PhD students and postdoctoral researchers regarding the breadth of possible science careers, both in and outside of the academia, and help them develop skills required for these career paths. 2018 workshop topics included, among others, grant writing, career development, careers at the interface of science and data science networking session.

The series is supported by CR's Kickstarter initiative, in which CR labs divert resources to finance projects that are considered to be beneficial to the CR community. It was organised in collaboration between CR investigators and CR's Science Communication Office.

Multiple dates throughout 2018

Local organisers: Catarina Ramos Clara Ferreira João Afonso Silvana Araújo

Events Agenda

11 JAN

COLLOOUIUM Decoding the brain serotonergic system - from breathing to behaviour

Speaker: Susan Dymecki — Harvard Medical School USA

18 JAN

COLLOOUIUM Neural circuits for goal-directed sensorimotor transformation

Speaker: Carl Petersen – Ecole polytechnique fédérale de Lausanne, Switzerland

1 FEB

COLLOOUIUM Who wins and who loses in social competitions? A key role for mitochondrial function in the nucleus

Speaker: Carmen Sandi – Ecole polytechnique fédérale de Lausanne, Switzerland

8 FEB

COLLOOUTUM Deciphering anatomy and function of an inter-hemispheric neural circuit in the zebrafish optic tectum

Speaker: Filippo del Bene – Institut Curie, France

16 FEB

SCIENCE CAREERS WORKSHOP Grant writing

Instructors: Pre-award Unit; Constanze Lenschow; David Reato; Manuela Ferreira; Romain Ligneul; Susana Lima; Bruno Costa-Silva

5-6 MAR

SCIENCE CAREERS WORKSHOP Career development

Instructor: Sarah Blackford

15 MAR

COLLOOUTUM Cortical dynamics drive continuous recombination of cell assemblies in mouse auditory cortex

Speaker:

Simon Rumpel – University Medical Center of the Johannes Gutenberg University Mainz, Germany

13 APR

SCIENCE CAREERS WORKSHOP Careers at the interface of science

Instructor: Margarida Trindade Networking with: Cristina Oliveira – FCSH, UNL Sandra Aresta – CIBIO-InBIO Catarina Ramos – CR

Ana Paula Elias — CR Isabel Campos — CR

COLLOQUIUM The high-gain state of visual cortex a gateway to adult plasticity

Speaker: 7 JUN Michael Stryker – University of California, San Francisco, USA

19 APR

Ciência, Portugal

26 APR

COLLOQUIUM

from Drosophila

Hospital, Norway

Speaker:

3 MAY

Speaker:

Switzerland

10 MAY

COLLOQUIUM

Speaker:

France

COLLOQUIUM

Speaker:

16 APR

COLLOQUIUM Cell competition in the thymus and Leukemia

Vera Martins – Instituto Gulbenkian de

Autophagy and tumorigenesis, lessons

Tor Erik Rusten – Oslo University

Olfactory evolution in Drosophilids -

Dynamic synapses are a substrates for

David DiGregorio – Institut Pasteur,

temporal coding and learning

from receptors to behaviours

14 JUN

Speaker:

Miguel Maravall –

University of Sussex, UK

13 MAY

Data science

Instructors:

Unplugged

24 MAY

COLLOQUIUM

Technology, USA

Sneaker:

SCIENCE CAREERS WORKSHOP

Saghir Bashir; Andreia Carlos;

All are members of Data Science

Faces — a neural rosetta stone

Doris Tsao – California Institute of

Inês Teixeira; Raquel Ribeiro; Hugo Lopes

COLLOOUIUM The visual adaptations and behavioural strategies that allow miniature flies to detect and catch fleeting prey

Exploring tactile sequence recognition

Speaker: Paloma T. Gonzalez-Bellido – University of Cambridge, UK

19-22 JUN

CRANNUAL RETREAT

Retreat committee: Alex Azinheira; Ana Vieira; Anna Hobbiss; Catarina Bras Pereira; Christa Rhiner; Megan Carey; Francisco Romero; Patricia Correia; Tatiana Silva

26 JUN Richard Benton – University of Lausanne, SCIENCE CAREERS POP-UP TALK

> Speaker: Retsina Meyer

28 JUN

COLLOQUIUM Stability and flexibility in motor networks

Speaker: Michael Long -NYU School of Medicine, USA 5 JUL

COLLOQUIUM Biophysics of motor planning and shortterm memory

Speaker: Karel Svoboda – Janelia Research Campus, USA

15 JUL-4 AUG

CAJAL ADVANCED COURSE Behaviour of neural systems

Course Directors: Gonzalo de Polavieja — CR Beniamin de Bivort – Harvard Uni., USA Megan Carey – CR Greg Stephens – VU Uni. Amsterdam, The Netherlands

7–10 AUG & **12 AUG-1 SEP**

CAJAL ADVANCED COURSE Computational neuroscience

Course directors: Jakob Macke – Research Center Caesar, Germany; Christian Machens — CR Joe Paton – CR

3-5 SEP

EUROPEAN SOCIETY FOR MAGNETIC **RESONANCE IN MEDICINE AND** BIOLOGY MEETING

Programme directors: Felix Breuer — Research Center Magnetic Resonance Bavaria, German

Course organisers: Valerij G. Kiselev – University Medical Center Freiburg, Germany Noam Shemesh – CR

6 SEP

COLLOOUIUM Development of the Drosophila motion vision circuit

Speaker: Claude Desplan -New York University, USA

13 SEP

COLLOQUIUM Using virtual reality to identify neural circuits for vision in freely flying flies

Speaker: Andrew Straw – University of Freiburg, Germany

Severin Berger 23-26 OCT

CHAMPALIMAUD RESEARCH SYMPOSIUM Quantitative approaches to behaviour and neural systems

Symposium Chairs: Alfonso Renart; Michael Orger

COLLOQUIUM RNA regulation of the innate immune system

Jorge Henao-Mejia — University of

Towards a brain architecture for visual

20 SEP

Speaker:

24 SEP

COLLOOUIUM

Campus, USA

25 SEP

Speaker:

Pennsylvania, USA

behavior selection

Organisers: Ana Catarina Certal – CF Claire Allen – Uni. of Sheffield, UK João Cruz – CONGENTO

15 NOV

COLLOOUIUM Neural motion

Speaker: Gilles Laurent — Max Planck Institute for Brain Research, Germany

16-17 NOV

SCIENCE CAREERS WORKSHOP Project management

Instructor Christina Schütte

20-22 NOV

ADVANCED COURSE IN IMAGE ANALYSIS Part 2 – Advanced image processing and analysis

Organisers: Davide Accardi & Rebecca Saleeb – CF

29 NOV

COLLOOUIUM Neural computations and biophysics of collision avoidance

Speaker: Fabrizio Gabbiani – Baylor College of Medicine. USA

6 DEC

COLLOQUIUM Targeting dormant, disseminated tumor cells to prevent metastasis

Speaker: Cyrus Ghajar — Fred Hutchinson Cancer Research Center, USA

19 DEC

INDP REUNION & GRADUATION CEREMONY

Organisers: Irene Argudo Tiago Quendera Sòlene Sautory Gabriela Fioreze Miriam Heinemans Events and Education Units

29-30 OCT

ZEBRAFISH FACILITY MANAGEMENT WORKSHOP

Gwyneth Card — Janelia Research

ADVANCED COURSE IN IMAGE ANALYSIS Part 1 – Image fundamentals and visualisation

Organisers: Davide Accardi & Rebecca Saleeb – CF

29 SEP & 20 OCT

SCIENCE CAREERS WORKSHOP Poster design

Instructor: Gil Costa – CR SciCom Office

Columbia University, USA

School of Medicine, USA

ANNUAL STUDENTS' RETREAT

Fundação Inatel in Foz do Arelho

Allan Mancoo: André Marques:

Maria Bettencourt: Nuno Rito:

Basma Husain; Carolina Rodrigues;

17-18 OCT

Retreat committee:

Immune system - the seventh sense

Jonathan Kipnis – University of Virginia

4 OCT

15 OCT

COLLOOUIUM

Speaker:

Location:

COLLOQUIUM The neurobiology of decision making -

the best laid plans of mice and primates Speaker: Michael Shadlen —



Culture

As the CR community grows, its culture evolves with it. In the last few years, CR members introduced several new initiatives, as well as carried on with long-lasting, successful activities, such as the annual retreat, thereby continuously enriching the social and scientific life at CR.

← Mathematical formulas and personal items come together in one of the CR offices.

Culture Highlights

CISS - Champalimaud Internal Seminar Series

Each week, two CR researchers deliver a 25-minute presentation about 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.

↓ Custom-built prototype of

the Light Field Microscope

acquired as part of the CR

Kickstarter

The CR Kickstarter is a new internal funding mechanism designed to promote internal collaborative projects and the development of shared ideas and resources. In this initiative, which has been successfully running at CR since 2016, a portion of each lab's budget is allocated to projects proposed in this system. Anyone may propose projects, which must involve, or benefit, a group wider than one lab, along with a minimum required budget. If the project can gain enough support and meets the eligibility requirements, it will be funded.

In 2018, 18 new projects received support from the CR community that addressed a range of needs. These include projects dedicated to developing analysis and behavioural software, purchasing technical equipment and producing various types of educational events.

Organisers: Pedro Garcia da Silva Marta Moita Zachary Mainen

Monthly Charity Bake Sale

The monthly charity bake sale started in 2017 by a group of CR members dubbed "The Baking Lab", who decided to channel their love of baking towards charity. Besides the long list of dedicated bakers who rotate between events, other volunteers also contribute with juice, coffee and tea that benefactors receive for free to accompany their afternoon pastry.

In 2018, the group organised 11 events to support both national and international charities.

Organisers: Irene Argudo Márcia Matos Victòria Brugada

Charities: Get Shit Done Team Os Francisquinhos Casa da Alegria Ajuda de Berço NoMeioDoNada Acreditar Casa do Gil Kerala Salvador Uniao Zoofila Bom Samaritano

↓ Cake samples from one of the bake sales.

Culture Highlights

↑ Vines are one of the crops that grow at the retreat location, they also have great nectarines.

CR Annual Retreat

The Annual Retreat is a major event that gathers all CR members in a remote location for a period of four days. The retreat serves the purpose of familiarising individual scientists with each other's work while creating a sense of community. It combines scientific events, such as poster sessions, with creative cultural and social activities. As the CR continues to grow in numbers and scope of research, these events, now more than ever, serve as an important means of maintaining the scientific culture of collaboration and cooperation at CR.

June 19–22, 2018

Location: Vila Galé Clube de Campo, Alentejo

Retreat Committee: Alex Azinheira Ana Vieira Anna Hobbiss Catarina Brás Pereira Christa Rhiner Megan Carey Francisco Romero Patrícia Correia Tatiana Silva

↑ Sharing ideas and research at the retreat poster session.

↓ At night people gather at the tent to watch performances and presentations.

Science Communication & Outreach

One of CR's stated goals is to share knowledge not only within the scientific community but also with the community at large. Many CR researchers, at all career stages, adopt this vision and choose to organise and participate in various outreach activities, both at and outside of the CCU.

> → The Science Communication office displays its stand at the CR Symposium.

Scicom & Outreach Highlights

The Champalimaud Centre for the Unknown is one of the first "Academias Gulbenkian do Conhecimento"

This new programme of the Gulbenkian Foundation targets children and young people up to 25 years of age, intending to create novel approaches that will equip the participants to successfully navigate our rapidly changing world. The application to the programme was a competitive one, with 589 project applications from all across Portugal that resulted in the selection of only 34 projects.

Neuronautas, the project designed by a group of science communicators and scientists at the Champalimaud Foundation, will endeavour to develop communication, problem-solving and creative-thinking skills in high-school students by engaging them in a pioneering fieldwork programme in neuroscience. Throughout a series of training sessions at the Champalimaud Centre for the Unknown, followed by a neuroscience boot camp, that will take place in 2019, participants will learn how to make observations of animal behaviour, and how to measure those quantitatively and qualitatively by using opensource hardware and software tools.

Exploring sensory experiences at ERC^2 public event

Held at the Pavilhão do Conhecimento - Ciência Viva centre in Lisbon, this public event was part of the ERC = Science², a European project financed by the European Research Council, whose main goal is to promote researchers and their projects. In this immersive multisensory food experience, a special dinner menu challenged all five senses, while arousing emotions and memories.

Our scientists, namely CR Group Leaders Eugenia Chiappe and Carlos Ribeiro, as well as CR Associated Researcher Rui Oliveira, engaged with the audience and explored various topics such as the relationship between our senses and emotions and how losing one of the five senses may enhance others.

> ↓ People temporarily deprived of selected senses having dinner at the atrium of Pavilhão do Conhecimento.

Travels to the Unknown

Travels to the Unknown (Viagens ao Desconhecido) is a new educational initiative where students explore the science done at Champalimaud Research labs through participatory stories that can be used in the classroom. The goal of this initiative is to help teachers develop in students the skills essential for being a proactively informed citizen and possibly even a future scientist. Through these stories, students get to explore and reflect on the different steps of the scientific process and learn about scientific careers.

In 2018, the first two participatory stories were developed—"FEAR" (Medo), based on the work of the Behavioural Neuroscience lab and "Sweet or Savory" (Doce ou Salgado), based on the work of the Behaviour and Metabolism lab. Teacher guides were created and a teacher-training session was offered in partnership with the Centro de Formação Ciência Viva. The feedback received through surveys was very positive and some teachers have already implemented the stories in their classroom.

Currently, additional materials are being developed and the construction of an interactive, instructive website is underway.

← "Fear" story pack from Travels to the Unknown.

"Shhhh... danger is out there" — The first CR publication in the Frontiers for Young Minds

Frontiers for Young Minds (FYM) is an online journal by the academic publisher Frontiers that aims to bring real science to kids. The articles are written by scientists and reviewed and edited by kids and teenagers. In 2018, the article titled "Shhhh... danger is out there", written in collaboration between the scientists and members of the SciCom team, was published in FYM. This article was based on an original scientific article published by the Behavioural Neuroscience lab.

"Curiosity and the Unknown" — a public open-lab event

During this year's Science & Technology week, and to celebrate the National Day of the Scientific Culture. Champalimaud Research scientists welcomed visitors and hosted guided tours to several labs at the Champalimaud Centre for the Unknown. In these guided tours, the public had the opportunity to directly interact with scientists, ask questions about their research projects and about science in general. In parallel to the guided tours, the public, around 140 people of all ages, also had the opportunity to engage in informal conversations with young researchers. Conversation topics spanned diverse themes such as scientific career paths, to personal hobbies, to best and worst experiences in the lab.

Outreach Events

68 **CR** members helped

VOLUNTEERS

| Adinda Wens |
|-----------------------|
| Ana Gonçalves |
| Ana Paula Dias |
| Ana Queirós |
| Andreia Cruz |
| André Marques |
| Anna Hobbiss |
| Antonia Grone |
| António Rapos |
| Baylor Branger |
| Bruna Costa |
| Bruno Ceña |
| Carlos Ribeiro |
| Celso Matos |
| Clara Ferreira |
| Cristina Afonso |
| Cátia Almeida |

people

reached

Célia Baltazar Danbee Kim Daniela Domingues Daniel Nunes Ece Sonmez **Edite Figueiras** Elisa Figueiras **Eugenia Chiappe** Filipe Carvalho **Filipe Rodrigues** Gabriela Ribeiro Gautam Agarwal **Goncalo Lopes** Hedi Young **Hugo Cachitas Hugo Marques** Inês Ferreira

Irene Argudo Javier Peréz Caramé Juan Castineiras Lucas Martins Margarida Anjos Marta Iglesias Marta Moita Megan Carey Nuno Loureiro Oihane Horno Pedro Garcia da Silva Radhika Raian **Ricardo Matias** Rita Saraiva

Inês Soeiro

Nuno Rito

Rita Fior

Roberto Medina Rodrigo Dias Rui Oliveira Simone Zacarias Susana Ferreira Susana Lima Tatiana Silva Teresa Dias Thabelo Khoboko Thiago Carvalho Tiago Monteiro Tiago Quendera Vanda Póvoa Victoria Brugada Vitor Paixão Wynne Stagnaro Zita Santos

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7 Events for adults and

()

general public

15 **Events** outside the CCU

Events at the CCU

(•)

2

Events for

scientists

| JAN | FEB | MAR | APR | MAY | JUN |
|-----|--------|-------------|------|-----|------|
| | •• ••• | • • • • • • | •• | | |
| JUL | AUG | SEP | ост | NOV | DEC |
| • | | • • •• | • •• | •• | •• • |

JAN

18 | School visit FEB

- 02 | School visit
- 06 | School visit
- 20 | School visit
- 24 Round table
- 30| School visit

MAR

01 | Workshop "Viagens ao Desconhecido - Travels to the Unknown" 09 | ERC^2 Workshop 09 | ERC^2 Interactive Talk 10 | ERC^2 Dinner

12 | Brain Awareness

Week | Skype 12 | Visit to school 12 | School visit

JUN

13 | Brain Awareness Week | Skype conversation

conversation

16 | Brain Awareness JUL Week | Skype 02 to 06 | Workshop conversation Ocupação Científica 16 | Brain Awareness de Jovens nas Férias – Week | Talk Ciência Viva 20 | School visit SFP 27 | School visit 12 | Ar Event: Science and cooking in the APR blender 21 | COGITO Festival 12 | School visit 24 | School visit 26 | Lab tours MAY

28 | European **Researchers' Night** 09 | Visit to school

11 | School visit OCT 14 and 15 | Pint of

Science | Talks

15 | School visit

30 | Visit to school

10 | Study Abroad in Scandinavia visit

19 | Kick off session of Academias Gulbenkian do Conhecimento

25 and 26 |Symposium Lab Tours

17 | Viagens ao Desconhecido: Professional Development for Teachers

NOV

24 | Curiosity and the Unknown

DEC

5 | School visit from students who were awarded a prize for best project on justice and corruption proposed by Tribunal de Contas

7 | Conference "Clubes de Ciência"

12 | School visit

12 | Conference "1° Encontro internacional mente, cérebro e educação"

21 Events for schools students and teachers

>4000

berg

Events for graduate and undergraduate students

97

Champalimaud Research Support Units

| 1 2 25 | 3 4 5 24 | 6 7 7 23 | 3 10 9 22 | 12 1. 11 13 21 | ⁴ 15 20 | 18 17 19 |
|-----------|----------------|----------------|-----------------|----------------------|-----------------------|----------------|
| 26 | 27 | 28 | 29 | 30 | 31 | 32 |

Sona venancio Lauren Noblet Tatiana Freitas Vesna Petojevic Diogo Matias Margarida Nunes Henrique Moreira Joaquim Teixeira António Raposo Laura Ward Bruno Ceña Inés Bonifácio Ana Casaca Ana Gerschenfeld Pedro Alves Vanda Vicente João Cruz Catarina Ramos Teresa Carona

not in photo

21 Inês Soeiro
22 Rita Saraiva
23 Ryan Herbert
24 Joana Lamego
25 Raquel Gonçalves
26 Filipa Cardoso
27 Mariana Santa-Marta
28 Cátia Feliciano
29 Marta Correia
30 Simone Zacarias
31 Liad Hollender
32 Maria Teresa Dias Alexandre Azinheira * Gil Costa * Francisco Semedo * Telma Carrilho * Thiago Carvalho * Pedro Garcia da Silva * Patrícia Correia * Raquel Gomes * The CR Support Units (CRSU) provide all administrative, financial and operational assistance to the CR community. Accompanying the evolution and growth of CR, the support provided to CR's scientists also continuously grows in organisation and capacities. The CRSU team aims to provide all science administration, management and communication support to boost the work of scientists, maximising the focus on research.

Support Units List

Director of Research Support

Ryan Herbert

Direction Support Team

The Direction Support Team receives, delegates and implements direct instructions from the Research Direction Team and the Director of Research Support. This team also serves as a primary contact point for any problem-solving needs within CR, being able to advise on the resources available to the CR community.

Executive coordinator: Inês Soeiro **Operations manager: Cátia Feliciano** Financial manager: Joaquim Teixeira

Education and Courses

This unit runs mainly through the Teaching Lab and Classroom, the hubs of our PhD programme and all courses happening at CR. The team deals with the organisation and daily management of INDP classes, CAJAL courses and external teaching weeks (GABBA, IGC, MIT, etc.). The organisation of the Teaching Lab space and materials is another main function of this unit, as well as supporting the INDP recruiting process.

Graduate programme managers: Maria Teresa Dias & Simone Zacarias

> ↓ The Teaching Lab provides a sandbox environment for testing and devoloping research hardware and software.

events are kept in display along the seminar room wall.

Events

The Events unit supports scientific events organised by CR. From the large annual events like the CR Retreat and Symposium to our weekly CISS and Colloquium, the team will be able to help you with all eventrelated details, from conception and planning to logistical details such as travel and accommodation, venue set-up, catering and event management. This unit also supports the Faculty's events and other ad-hoc events such as Ar events and other outreach initiatives. The team also consolidates the management of all communal AV equipment, as well as expertise in videography and photography.

Coordinator: Patrícia Correia Events organiser: Ana Casaca Events assistant: Pedro Alves AV technician: Alexandre Azinheira

↑ Posters from past AR

Human Resources & **Fellows Support Office**

Every person that joins CR needs to go through HR. Whether it's a PI or an Intern or simply a guest, HR needs to be notified with as much notice as possible. They will advise on all the necessary procedures for everyone's correct registration as a CR member: contracts, social security, medical insurance, visas, CCU cards, language classes at CCU, etc. HR also supports all CR recruiting, including the INDP recruiting process.

HR liaison: Teresa Carona

Support Units List

← The office of the Preaward team faces garden beds where, sometimes, seagulls raise their chicks.

Lab Administration

Every lab is assigned a Lab admin but their role in the labs might vary slightly depending on whether the labs have a Lab manager (whose role is decided by the PIs). This team deals with administrative support for the labs, including budget management and execution, anything regarding the purchases of the lab and travel arrangements, among others. For that, they will coordinate with other CR support units and CF departments (OSP post-award, logistics, accounting, IT, maintenance) as well as external agents like the suppliers, shipping companies and customs.

Coordinator: Raquel Gonçalves

Lab administrators: Vesna Petojevic Telma Carrilho Lauren Noblet António Raposo Rita Saraiva Ana Margarida Nunes

Pre-award

The Pre-award team supports CF Research in all stages of the submission of research applications to external funding: from the identification of putative funding opportunities to the validation of the expression of interest by the CF Research Direction Team, up to the negotiation of successfully funded applications. We offer different types of support, from basic administrative support to non-scientific writing/proposal reviewing or even supporting proposal development itself.

Coordinator: Joana Lamego

Grants managers: Mariana Santa-Marta Filipa Cardoso Bruno Ceña

Post-award

The CF's OSP - Post-award will be able to give help and support in issues related to grant reporting (financial and scientific), grant administration and cost eligibility. The CF's OSP -Post-award also aims to function as a facilitator, creating a bridge between the CR Scientific Community and the more bureaucratic aspects of grant management. Support to post-award is also provided by a resident team from Verbochave, Consultoria Lda. comprised by Carina Quintal, Inês Bonifácio, Gonçalo Pardal, Henrique Moreira and Pedro Monteiro.

Coordinator & Financial manager: Joaquim Teixeira

Grants officer: Francisco Semedo Project managers: João Cruz & Laura Ward

Science Communication

Science Communication is responsible for disseminating information on the activities and ongoing or emerging objectives of the Champalimaud Research 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 and 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 organization of scientific meetings. The team is also able to support the CR community in their scientific endeavours, with in-house scientific design and illustration.

Coordinator: Catarina Ramos

Science writers: Liad Hollender & Ana Gerschenfeld Science education and outreach officer: Raquel Gomes Graphic and editorial designer: Marta Correia Science graphic designer: Gil Costa Multimedia producer: Alexandre Azinheira

→ Students participate in a "Travels to the Unknown" event, using stories to explore and understand how scientific research can be done.

Scientific and Technological Platforms

The Scientific and Technological Platforms of the Champalimaud Centre for the Unknown carry out technical -scientific and specialised support work for the activities of research groups and clinicians. They operate in a wide range of areas, from the development of sophisticated technologies in animal models, imaging tools, hardware and software, to resource management and research infrastructures.

 1
 Leonor Morgado
 13
 Sérgio Casimi

 2
 Anna Pezzarossa III
 14
 Inês Oliveira

 3
 Rita Torre
 15
 Eduardo Andre

 4
 Carlos Silva
 16
 Filipe Carvalho

 5
 Soraia Rodrigues
 17
 Artur Silva

 6
 Erineu Silva
 18
 Mariana Velez

 7
 Ana Carolina Cabrera I
 19
 Seidy Semedo

 8
 Andreia Madalena
 20
 Luís Teixeira I

 9
 Mariana Sampaio I
 21
 João Baúto

 10
 Inês Marques
 22
 Paulo Carriço

 11
 Fernando Santos
 23
 Dario Bento

 12
 Suana Dias
 24
 Hugo Cachitas

• not in photo I affiliated with CONGENTO II affiliated with BioData III affiliated with PPBI 25 Joana Monteiro 26 Ana Cunha I 27 Laurent Lachaud 28 Sofia Silva 29 Liliana Costa 30 Ricardo Ribeiro II 31 Isabel Campos 32 Ana Catarina Certal 33 Leonor Gomes 34 Bruno Novais 35 Inês Antunes 36 Maria José Vito María Inês Romano
 Madalena Martins
 Jhosaba Abreu
 Davide Accardi
 Pedro García Silva
 Ana Raquel Tomás
 Dolores Bonaparte
 Ana Rita Pereira *I
 Catarina Craveiro *
 Cláudio Macedo *
 João Pereira *

Wilcilaya Pontes * Wilma Sobral * Ana Reis * I Teresa Gomes * I Zichiena Zovo * Pedro Garcia da Silva * Tânia Vinagre * Ana Rita Almeida * Sandra Martins * Ana Vieira * Patrick Teca *

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Platforms Highlights

← A set of images acquired from a three-dimensional object, can be stacked to produce a two-dimensional projection of the original object from different angles.

Advanced BioImaging and BioOptics Experimental Platform

In 2018, the ABBE platform has become a hub for light-sheet fluorescence microscopy, an imaging approach named "Method of the Year 2014" by the journal Nature Methods. This technique provides fast, six-dimensional imaging of large samples at low excitation power. As photo-bleaching and photo-toxicity are minimal, this method allows experimenters to perform studies on topics such as tissue regeneration, neurogenesis, or cancer treatments, which require imaging over multiple days.

Fish Platform

The coordinator of the Fish Platform, Ana Catarina Certal, acted as President of the 2018 Executive Board of the Zebrafish Husbandry Association, an international nonprofit organisation promoting and developing zebrafish husbandry standards through education, collaboration, and publication.

↑ Detail from Harp's Sound Card built by the Scientific Hardware Platform.

Scientific Hardware Platform

One of the product-lines developed by the Scientific Hardware Platform is called Harp. This is a family of devices that provide an efficient, intuitive and user-friendly implementation, within an environment of high-performance tools. Following enthusiastic feedback by users within the CCU, in 2018 the platform began providing Harp products to external users as well. So far, a total of 194 devices have been built and are currently being distributed across eleven laboratories located in nine different institutions worldwide, such as Columbia University in the U.S., Max Plank Institute in Germany, UCL in UK, and the The Hebrew University in Israel.

Platforms List

← Some of the experimental microscopy setups at CR are curated and assembled by the ABBE platform.

Advanced Bioimaging and Biooptics Experimental Platform (ABBE)

In 2017, the Optical Imaging and Microscopy Platform was re-launched as the Advanced BioImaging and BioOptics Experimental (ABBE) platform. ABBE includes a team of experts apt to support users with all stages of the experimental process from design to analysis. and implements state-of-the-art techniques that facilitate a multi-scale research approach which spans imaging protein interactions to whole organisms. This platform forms a bridge between the clinical and basic research at the CCU by introducing methods across fields.

In addition to the newly implemented improvements, ABBE maintains its high standards and performance by carrying out its own research on method optimization and collaborates with other Champalimaud Foundation platforms to customize the sample preparation and imaging workflow to the needs of the users.

Coordinator: Pedro Garcia da Silva Group head: Davide Accardi **Technician: Leonor Morgado** Senior tech: Anna Pezzarossa

Fish Platform

The Fish Platform applies rigorous health and welfare standards in the housing and breeding of zebrafish, the second most used animal model in biomedical research. It works closely with CR's Molecular and Transgenic Tools Platform to provide advanced research services such as transgenic zebrafish. The Platform also collaborates with other CR Platforms and external institutions to develop new protocols and technologies, which are then communicated via peer-reviewed publications and presentations at international meetings. Also, it participates in the development of an integrated database for zebrafish facilities and new automation solutions for zebrafish husbandry. The Platform is also part of CONGENTO, where it plays a pivotal role by delivering zebrafish services and providing facility management consulting to both the national and international research communities.

Coordinator: Ana Catarina Certal Senior technician: Joana Monteiro **Platform manager: Sandra Martins**

Ana Carolina Cabrera Rita Almeida Seidy Semedo

Technicians:

Mariana Sampaio Fernando A. Santos

Scientific Software

The Scientific Software Platform aims to support high-level scientific research by providing high-quality software support and ensuring the performance of CR computational infrastructures. With educational backgrounds in Software. Electrical and Physics Engineering. the Platform's team members have a broad range of skills and knowledge in areas such as computer vision, image processing, machine learning, hardware control, graphics, web, data management and systems administration. In 2017, the team focused on the development of the PvBpod and Pvthon Video Annotator for behavioural analysis, and on the improvement of the data flow pipeline. The later improvement was achieved with the construction of a high performance computational and storage cluster and by the installation of an internal highspeed network to connect the data acquisition equipment to the computational resources.

Coordinator: Pedro Garcia da Silva Group head: Ricardo Ribeiro Cloud specialist: Joao Baúto Data manager: Hugo Cachitas Software developer: Luís Teixeira

Glasswash & Media Preparation (GMP)

The GlassWash and Media Preparation Platform provides clean and sterilised labware such as glass, plastics and instruments to investigators and laboratories. This Platform also prepares high quality tissue culture and bacteriological media required for standard research protocols.

Coordinator: Tânia Vinagre Group head: Maria José Vito

Technicians: Patrick Teca Maria Madalena Martins Soraia Rodrigues Jhosaba Abreu

Histopathology

The Histopathology Platform provides specialized services to all the scientific community and aims to offer a personalized service tailored to each of its users' objectives. For that purpose, the Histopathology Platform currently has available the following services: tissue sectioning, using vibratomes, cryostats and sliding microtomes; special histochemistry stains which allow to distinguish different tissue components and morphology; immunohistochemistry techniques in slides, free-floating and whole mounting methods that allow to identify and quantify the presence of specific tissue's antigens/proteins; brain clearing techniques, with the purpose of getting completely transparent samples, allowing the observations of whole mounting.

Coordinator: Tânia Vinagre Group head: Ana Santos

Technicians: Susana Dias Sérgio Casimiro

Inês Marques Maria Inês Romano

Flow Cytometry

The Flow Cytometry Platform was established in April 2017 with the mission to provide both to the Champalimaud community and to external groups, technical and scientific advice regarding the use of flow cytometric technologies. These include collaboration on design, data acquisition, analysis and interpretation. The Flow Cytometry Platform is one of the founders of the FLxFlow - a Portuguese network for Flow Cytometry, which aims to bring together core Flow Facilities in the Lisbon area with the goal of enabling the access of scientists to cutting edge applications.

Coordinator:

Pedro Garcia Da Silva Group head: Ana Vieira

Platforms List

Rodent Platform

The Rodent Platform supports experimentation conducted under CF Research Programmes. In addition to normal husbandry routines, the platform supports specialised services such as colony management, line genotyping, transgenic generation, rederivation and assisted reproduction techniques. To ensure the application of suitable and humane techniques, the platform complies with international best practices as well as national and European legislation and guidelines for animal accommodation, care and experimentation. Importantly, animal care and use is carefully supervised and monitored by the internal Animal Welfare Body, the Vivarium technicians and the attending veterinarian.

To ensure that all procedures are performed according to the 3Rs (Replacement, Reduction and Refinement): alternatives to animals are used whenever possible, the number of animals is minimised, and any discomfort or pain possibly experienced by the animal are minimised and weighed against the potential benefits for science.

Coordinator – Isabel Campos Veterinarian – Dolores Bonaparte

| Technicians: |
|-------------------|
| Ana Rita Pereira |
| Andreia Madalena |
| Carlos Silva |
| Catarina Craveiro |
| Cláudio Macedo |
| Eduardo André |
| Erineo Silva |
| |

João Pereira Mariana Velez Natacha Leonardo Rita Torres Wilcilaya Pontes Wilma Sobral Bruno Novais Leonor Gomes ↓ The hardware available for experimentation and development ranges from simple Arduino boards to complex research setups.

Scientific Hardware

The goal of the Scientific Hardware Development Platform is to facilitate research at the individual, group and programme level, by proving the full pipeline of experimental hardware development: from requirement specification and analysis, to design, development, implementation, validation procedures and testing execution. It also provides diverse services, including 3D printing and the day-to-day support and management of the Electronic and the Mechanical Workshops

Coordinator: Pedro Garcia da Silva Group head: Filipe Carvalho Technician: Dario Bento

Hardware developers: Artur Silva Paulo Carrico.

Molecular and Transgenic Tools (MTT)

The Molecular and Transgenic Tools Platform (MTTP) performs complex transgenic and gene editing projects. It assists users in all stages from the conceptual design to the final animal delivery by providing support in molecular biology techniques from basic services such as the production of competent bacterial cells or primer design, to complex cloning of knock-out and knock-in constructs to generate new cellular, zebrafish, fly or mouse models. The MTTP also encompasses a viralvector production service and has several collaborations for continuous development and implementation of new viral systems. The Platform acts as a hub of shared resources and expertise not only for the CR but also for the national and international research communities by providing services through CONGENTO.

Coordinator: Ana Catarina Certal

Senior Research Technicians: Ana Raquel Tomás & Ana Cunha Technician: Sara Mateus

Fly Platform

The Fly Platform is a multi-room facility central to all researchers using Drosophila as a model system. This Platform offers stateof-the-art conditions for Drosophila breeding, maintenance and manipulation, supporting researchers in establishing, applying and developing advanced genetic methods.

The Platform has dedicated staff to ensure the proper functioning of shared equipment that also provides technical services to all users. Importantly, the highly-trained Platform team will perform high-quality, standardised and reproducible routine protocols and specialised, technically demanding services, difficult to carry out in individual labs and often outsourced.

Coordinator: Isabel Campos Senior technician: Liliana Costa

Technicians:Ana Rita PereiraSofia SilvaAna ReisTeresa GomesCatarina CraveiroZichiena Zovo

→ The fly facility faces the river and is full of useful Drosophila diagrams.

Team

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Designer & Illustrator Diogo Matias

Managing editor Catarina Ramos

Art director & Photographer Alexandre Azinheira

Photography advisor Tor Stensola

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Proofreader Teresa Fernandes

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Other info

Group photos in this document were taken in early 2019 and therefore include team members of both 2018 and 2019.

CC Champalimaud Foundation

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