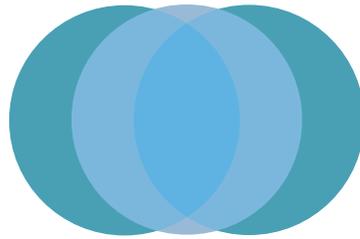


INTERNATIONAL SCIENTIFIC COOPERATION:
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AGREEMENT TO SUPPORT JOINT RESEARCH

Delfim Martins/PULSAR IMAGENS



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The agreement between FAPESP and the UK Research Councils (RCUK) aims to support joint research projects submitted by researchers in São Paulo and their colleagues in the United Kingdom. A unified selection process, with selection of reviewers done jointly by FAPESP and the appropriate Research Council, avoids exposing the proposals to a double jeopardy situation. The joint proposals compete with the normal stream of proposals analyzed at FAPESP and at the Research Councils.

Proposals are welcomed in any field of knowledge covered by FAPESP and by the seven UK Research Councils and submissions follow the RCUK deadlines.



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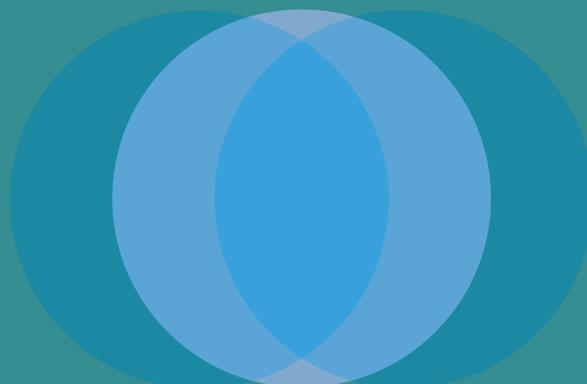
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TARGETED ANALYSIS OF MICROBIAL LIGNOCELLULOLYTIC SECRETOMES – A NEW APPROACH TO ENZYME DISCOVERY

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United Kingdom

PI: Neil Bruce (University of York)

Co-PI's: Simon McQueen-Mason, Peter Young (University of York)

FAPESP Process 2010/52362-5 | Term: Nov 2011 to Oct 2014

The long-term success of sustainable cellulosic ethanol production is dependent on the development of economical methods for processing plant biomass to exploit the energy rich polysaccharides in cellulose for fermentation. While the saccharification of lignocellulose remains a problem for industry, it is carried out effectively in the natural environment by microbial communities found in composting systems and soils. The major challenge in identifying the range of enzymes and other proteins used by communities of microorganisms during lignocellulose degradation lies in the complexity of the process itself. At present the vast majority of microbial biodiversity remains uncharacterised, because less than 1% of microorganisms in most environments are amenable to axenic cultivation, therefore, to date lignocellulose degradation has largely been studied in a few well characterised and culturable microorganisms. The research proposed here is concerned with discovering new enzymes and associated proteins for lignocellulose digestion from rotting cereal straw and sugar cane bagasse, and takes an integrated proteomics and metatranscriptomic approach for their identification. The innovative aspect to our proteomic approach arises from the fact that microbial cells cannot ingest pieces of undigested lignocellulose, but must first convert this material to simple sugars that can then be imported in to the cell, and this requires that they secrete the appropriate digestive enzymes. Thus, the majority of enzymes and accessory proteins involved in



Figure 1. Three-dimensional structure of the hydrolytic enzyme (cellulase)

lignocellulose mobilisation are distinguished from those involved in housekeeping activities by the fact that they are secreted. Combining the power of extracellular proteomics and metatranscriptomics will allow us to focus in on the proteins critical for lignocellulose deconstruction from microbial communities. This will greatly enhance our ability to identify completely new types of lignocellulose active proteins, both broadening our fundamental understanding of this process, as well as providing novel activities for research and industrial applications.

OBJECTIVES

From both a fundamental and industrial biotech viewpoint understanding the deconstruction of lignocellulose in soil and compost is of central importance. In the natural environments microbial communities can efficiently degrade or modify lignin to enable the effective enzymatic hydrolysis of the polysaccharides present in plant cell walls. The aim of this proposal is to use metatranscriptomics and proteomics to determine gene- and protein-centred details to determine new mechanisms and improved methods of lignocellulose deconstruction in mixed microbial communities from composting wheat straw and sugar cane bagasse. Exploring the digestion of lignocellulose by microbial communities using an integrated proteomics and metatranscriptomics has the potential to identify new approaches to lignocellulose utilisation along with new enzymes and intellectual property of benefit to the biofuel and biorefinery industries. Combining this potential with the power of high-throughput protein expression and top class analytical facilities in York and São Paulo will place the UK and Brazil in a strong position in this internationally competitive area.

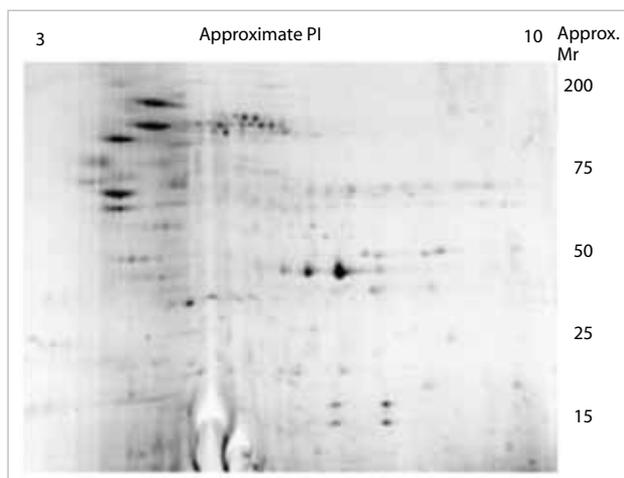


Figure 2. Two-dimensional electrophoresis of enzymes from decomposing wheat straw

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IMPACTS OF CLIMATE EXTREMES ON ECOSYSTEMS AND HUMAN HEALTH IN BRAZIL: PULSE-BRAZIL

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FAPESP Process 2011/51843-2 | Term: Apr 2012 to Mar 2015

The general aim of this RCUK-FAPESP joint proposal is to create the PULSE-Brazil system (where PULSE is Platform for Understanding Long-term Sustainability of Ecosystems) for analyzing, visualizing and understanding the interactions between climate, ecosystems and human health in Amazonia. PULSE-Brazil will enable stakeholders to explore the consequences of different policy options for adaptation and mitigation of environmental change in the Brazilian Amazon. Specifically, the objectives of PULSE-Brazil are to:

1. Support collaboration between UK Universities, the Met Office, FIOCRUZ, the Federal University of Minas Gerais, the National Institute for Space Research (INPE) – Brazil, Brazilian State Governments and the wider international community on topics related to the impact of climate extremes on ecosystem and human health and potential mitigation and adaptation strategies.
2. Develop and evaluate a spatially explicit database of recent climate extremes and their impacts on ecosystems and human health to establish the relationships between climatic variables and environmental and human health data.
3. Provide future climate change projections for Amazonia using state-of-the-art regional (Eta) and global climate models (MBSCG and UK Met Office-Hadley Centre models), covering a range of emission and land-use scenarios (through an associated Brazilian-funded project).
4. Develop a user-friendly GIS-based tool capable of integrating information of recent extremes and their impacts on ecosystems and human health with relevant physical climate variables and metrics from future climate projections, supporting

stakeholders to develop their own understanding of the interactions between climate, ecosystems and human health.

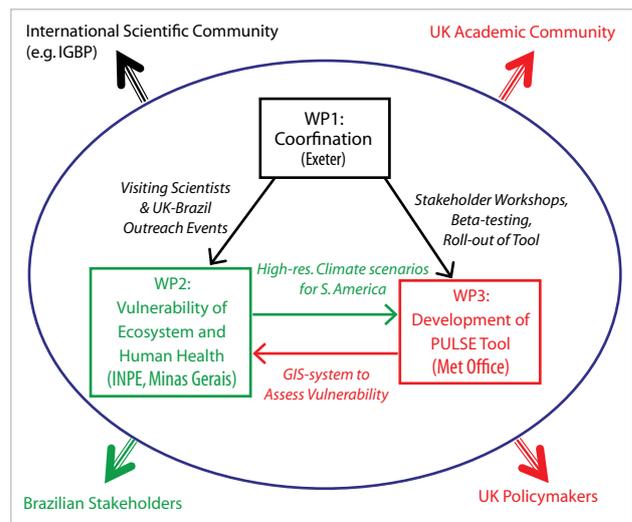


Figure 1. Conceptual model of PULSE-BRAZIL project

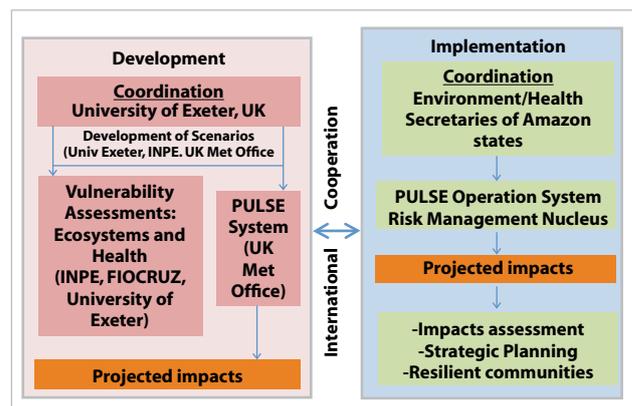


Figure 2. PULSE platform and integration of its components. This will be accomplished by an integrative cooperation between Brazil and UK partners, and governments from Amazonian states

OBJECTIVES

The PULSE-Brazil project consists of three inter-linked Work-packages (WPs – *Figure 1*):

Work-package 1 (WP1) will coordinate the exchange of scientists between the UK and Brazil, organise and run international conferences and stakeholder engagement activities, and manage the overall PULSE-Brazil project. The ultimate aim of this WP is to integrate the results and discussions between the cross-disciplinary research team and policymakers to propose strategies for mitigation and adaptation. (Leader: Luiz Aragão)

Work-package 2 (WP2) will focus on building the climate, environmental and human-health datasets for assessing the Impacts and Vulnerability to Climate Change in Brazil, based on state-of-the-art climate change projections from the regional Eta model and the MBSCG global model. The climate and environmental data will be delivered by INPE of Brazil, while the health data will be delivered by FIOCRUZ (Oswaldo Cruz Health Foundation). The climate part is funded by a related proposal to FAPESP-FRPGCC. (Leader: Jose Marengo)

Work-package 3 (WP3) will develop a user friendly decision-support system (PULSE) that will allow both academic and non-academic users to visualise the impacts of Climate Change on ecosystems and human health in the Brazilian Amazon, using relevant outputs from pre-existing model projections. This will be subcontracted to the UK Met Office. (Leader: Richard Betts)

At the heart of each WP will be scientific collaboration and stakeholder engagement at both national and international levels. *Figure 1* illustrates the interaction between the work-packages, and links to stakeholders and the wider scientific community.

PULSE-Brazil would interact with long-term programs such as LBA, and Brazilian initiatives such as the National Institute of Science and Technology for Climate Change, the FAPESP Research Programme on Global Climate change (FRPGCC) and the Brazilian Rede-Clima.

PULSE-Brazil would have a lasting positive impact

by greatly facilitate links between scientists in the UK and Brazil on global environmental change, by building capacity for the next generation of scientists and decision makers, and through the development of techniques to communicate scientific outcomes to stakeholders and the general public, using GIS-based systems.

CASE STUDIES

On the current developing phase of the project, case studies are key to identify the usefulness of the system and a “model state” for Amazonia. We are counting with the collaboration of the Environment Secretary of the Brazilian Amazonia state of Acre, a front-runner on environmental policies on the reduction of greenhouse gases as well as on risk management systems to react almost immediately to natural disasters, as the drought followed by forest fires in 2005 and 2010, and floods in 2009, 2011 and 2012.

The increased capacity for identifying areas of high risk of climate variability and change as well as the improved potential for mapping vulnerability, may help considerably to enhance our understanding of the spatial patterns of future environmental changes and its effects on health and ecosystems. Therefore, we expect that the PULSE platform can assist in the planning of government actions directed towards the increase of resiliency of Amazonian communities to climate change.

RELATED PUBLICATIONS

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AMELIORATION OF THE AUTONOMIC IMBALANCES OF OLD AGE WITH EXERCISE: EXPLORING THE MOLECULAR AND PHYSIOLOGICAL MECHANISMS

São Paulo, Brazil

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Co-PI: Vagner R. Antunes (ICB/USP)

United Kingdom

PI: David Murphy (School of Clinical Sciences/University of Bristol)
Co-PI: Julian Paton (School of Medical Sciences/University of Bristol)

FAPESP Process 2011/51410-9 | Term: May 2012 to Apr 2016

Lifespan augmentation, one of the most important medical advances in the last century, has not been accompanied by an improvement in the quality of life of elder people since autonomic balance to heart and vessels (an important neural mechanism controlling cardiovascular function – see scheme on *Figure 1*) declines with aging. Deficits in circulatory autonomic control (decreased vagal / increased sympathetic outflow, resulting in reduced dynamic flexibility and increased mortality) have been indicated as the common final pathway for different diseases such as hypertension, heart failure, stroke, obesity, diabetes, etc. Experimental evidence indicated that sympathetic / parasympathetic imbalance in adult hypertensive rats was accompanied by differential expression of several genes in brain autonomic areas. It is not known whether aging also interferes with gene expression in autonomic areas of hypertensive and normotensive individuals.

There are two approaches to treat frailty in old age: increased medical interventions or lifestyle changes. Accumulated evidence has shown that physical activity (a trivial lifestyle modification) improves autonomic control in normotensive and hypertensive animals, but our knowledge of the mechanisms underlying these changes is still scant. It is also unknown if training is able to modify/correct aging-induced deficits and how these changes would affect cardiovascular homeostasis. We hypothesized that the establishment/maintenance of autonomic imbalance (and consequent functional deficits) induced by aging/hypertension is associated with altered expression of a large number of genes in integrative autonomic areas of the brain, which can be corrected/modified by training.

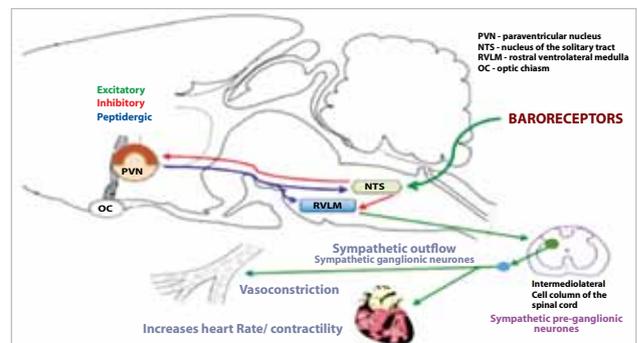


Figure 1. Scheme showing the neural regulation of autonomic output

To investigate the effects of aging, hypertension and training on gene expression, we sought to investigate and compare the effects of aerobic training on gene expression in the PVN, NTS and RVLM, in young (1 month) and old (12 months) SHR and WKY rats. We will relate these transcriptomic changes with sympathetic / parasympathetic outflow and cardiovascular variables. In order to identify putative networks and possible key hub genes, we also will carry out a detailed transcriptome analysis in SHR and WKY. The physiological function of these hub genes and their possible benefit in restoring a normal autonomic balance in hypertension and aged animals will be determined using virally mediated gene transfer *in vivo*.

OBJETIVES

The SHR is the best experimental model for neurogenic hypertension and exhibits a precocious autonomic imbalance. Previous studies from our laboratories in adult SHR showed marked sympathetic overactivity and depressed parasympathetic activity (1) and differential gene expression within brain areas involved in autonomic control (2,3), some of which had the ability to alter cardiovascular homeostasis when challenged by drugs or viral vectors (4). We also identified that low intensity aerobic training, as opposed to the sedentary lifestyle, improves autonomic control, increases vagal and reduces sympathetic activity blood pressure and heart rate (1,5). Training also changed neuronal plasticity/activity (1,6) and gene/protein expression of some neurotransmitters / neuromodulators as well as anti-inflammatory / pro-inflammatory cytokines within the NTS, PVN and RVLM (7-9, see Figure 2). By studying now young (1 month) and old (12 months) SHR and normotensive controls submitted to training or kept sedentary we will identify the effects of aging, hypertension and training and their association with autonomic control. We will identify putative gene networks within the brain governing cardiovascular autonomic control using transcriptomic analysis. We will test the physiological importance of identified hub genes using in vivo somatic gene transfer.

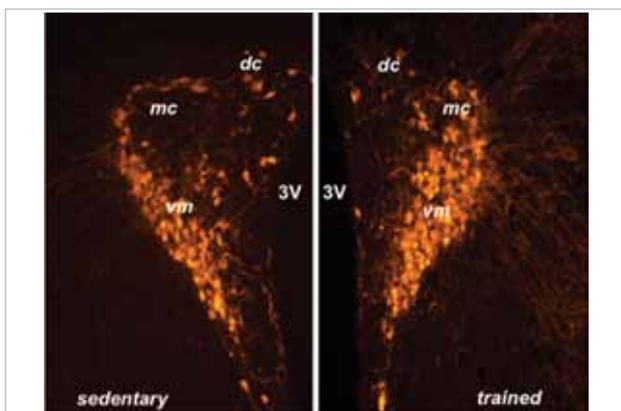


Figure 2. Immunohistochemistry of PVN oxytocinergic neurons in sedentary and trained rats. Note how the number of oxytocinergic neurons increases with training

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RESEARCH NETWORK FOR INVESTIGATING THE AMAZONIAN CARBON BUDGET FROM SPACE

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United Kingdom

PI: Hartmut Boesch (University of Leicester)
Co-PI's: Robert Parker (University of Leicester), Emanuel Gloor, Chris Wilson (University of Leeds), Paul Palmer, Siegfried Gonzi (University of Edinburg)

FAPESP Process 2011/51841-0 | Term: Apr 2012 to Mar 2015

The tropics are of key importance for the global carbon cycle and future climate mainly because tropical forests store large amounts of carbon and thus this carbon can potentially be released rapidly. Tropical ecosystems are also particularly precious ecosystems from a biodiversity perspective. The tropics are currently not only witnessing a changing climate, but are also subject to rapid external environmental change due to fast population growth and economic development causing extensive deforestation and urbanization. However we still do not even know with certainty whether the tropics are a net carbon source or sink.

Integral constraints on the state of tropical land regions are provided by greenhouse gas (GHG) balances (CO_2 , CH_4 , N_2O) of the troposphere over these regions. However for large parts of the tropics, notably Africa and Southeast Asia, comprehensive greenhouse gas observations are still lacking. For the Amazon region such measurements are being regularly measured by IPEN, lead by L. V. Gatti with aircraft at four locations since 2009 as part of the NERC AMAZONICA consortium project led by M. Gloor (University of Leeds) and by FAPESP grant led by H. R. Rocha (University of São Paulo) "Carbon tracker and water availability: Controls of land use and climate changes": A potential alternative to in-situ greenhouse gas observations are retrievals from satellite. Satellites are now observing these regions, however the accuracy of the retrievals remains highly uncertain and there is a pressing need to assess these properly.

The overarching objective of this project is to evaluate the feasibility of remotely sensing greenhouse gas concentrations for purpose of GHG flux monitoring



Figure 1. Map of existing and proposed aircraft sites. Currently routine aircraft observations are carried out at RBA, TAB, ALF and SAN. We will carry out flights at RBA until 8km height and at Salinópolis. Also show is the location of the existing ground-based column measurements at Paramaribo and the planned site at Manaus and the standard sampling pattern of GOSAT (red circles)

over Amazonia and eventually the tropics. This is to be achieved by joining space-based greenhouse gas observations efforts and community with the ongoing joint UK/Brazilian atmospheric GHG observation program (Surface/aircraft) by a team of leading experts from the UK and Brazil in all relevant areas such as satellite remote sensing, in-situ observations, transport and inverse modeling. If the feasibility of remote sensing of greenhouse gas concentrations is confirmed over the Amazon basin it can then be expanded to the rest of tropical land regions.

OBJECTIVES

Our specific objectives are:

1. Establish a network of Brazilian and UK researchers from relevant key areas (*in situ* observations, remote sensing and carbon cycle science) expanding on existing collaborations between UK and Brazilian institutions.
2. Adapt the necessary modeling and retrieval tools for combining *in situ* and remotely sensed greenhouse gas data based on the tools that have been developed for NERC NCEO and the AMAZONICA project.
3. Conduct a pilot study based on intensive on-ground and airborne measurements and GHG satellite observations (CO₂ and CH₄ columns from GOSAT and CO from MOPITT and IASI) to establish the consistency of remote sensing based greenhouse gas measurements over the Amazon with the *in-situ* measurements from the AMAZONICA project and new ground-based column observations and establish the accuracy of the remotely sensed data.
4. Develop a medium- to longer-term strategy based on the initial pilot study and consultation with the UK and Brazilian research community for greenhouse gas monitoring from space.
5. Evaluate possibilities to extend the approach pan-tropically.

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ROLE OF THE ENDOSOMAL SORTING MACHINERY IN CONTROLLING AMPA RECEPTOR TRAFFICKING

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PI: Sonia A. L. Correa (School of Life Sciences/University of Warwick)

FAPESP Process 2012/50147-5 | Term: May 2012 to Apr 2013

As the worldwide population is continuing to live longer, the number of people diagnosed with dementia and other neurodegenerative diseases has been increasing dramatically. Therefore, it is important that we improve our understanding of healthy cognitive ageing and this knowledge will help to provide insight on possible targets to help improve health and well-being across the lifespan. Alzheimer's disease (AD) is the leading cause of dementia, and recent estimates suggest that there are currently 37 million people who suffer from the disease. Patients suffering from AD experience progressive loss of cognitive functions. Interestingly, this decline has a direct link with synapse loss in specific areas of the brain and therefore dramatic deficits in synaptic transmission. Thus, understanding the molecular mechanisms underlying modulation in synaptic transmission has become very timely, as it will provide insights into normal and abnormal synaptic mechanisms and thus healthy ageing.

Changes in the amount and subunit composition of AMPA-type glutamate receptors (AMPA) at

synapses influence the strength of excitatory synaptic transmission in the brain. AMPAR density at postsynaptic sites is thought to be determined by a combination of constitutive and signal-regulated protein trafficking pathways that comprise of polarized sorting from the trans-Golgi network to somatodendritic membranes, endocytosis, endosomal recycling and lysosomal targeting. Findings from several studies indicate that dynamic control of AMPAR trafficking events provides efficient means to regulate synaptic plasticity. However little is known about how this control is achieved in a selective manner. The general aim of this project is to identify and characterize novel protein-protein interactions in the endocytic/recycling pathways, or the cell surface, modulating GluA1 and GluA2 levels at synaptic sites during synaptic plasticity. To this end, we will employ a combination of proteomics, mass spectroscopy techniques and functional assays using dissociated hippocampal neurons.

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CELLULAR AND REGULATORY BASIS FOR EARLY PLANT ORGAN GROWTH

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A central problem in Biology is to understand how genes cause organs to grow to a specific shape and size. Plants are convenient to address this question because their overall growth results primarily from the increase in cell numbers and increase in the size of individual cells. In addition, understanding organ growth in plants offers a clear path to practical use through the rational manipulation of crop growth and yield. A major bottleneck for understanding plant growth, however, is that although we know several genes that control the overall size and shape of organs, we do not understand what processes these genes control within cells to result in a net effect on the total size and shape of organs.

We aim to answer this question, by studying the early stages of floral organ development in the model species, *Arabidopsis thaliana*. Unprecedented opportunities to address the question above arise from two recent developments. One is the establishment of methods that allow quantitative, 3D analysis of cell geometry and cell division in growing organs. Using these methods, the UK partner in this project has recently found that a key regulator of organ growth, called *JAGGED (JAG)*, has an unanticipated role in co-ordinating cell volume with cell division in developing organs. The second is the development of techniques for detection of all genes controlled by a given regulatory gene, at well-defined stages of organ formation, which can reveal the repertoire of cellular functions that are controlled by a regulatory gene. Our Brazilian and Dutch partners have been developing these methods and applying them to understand the role of genes that control floral organ development.

Taking advantage of the complementary expertise, resources and biological interest of the partners involved in this project, we will extend both approaches



Flower of a wild-type Arabidopsis thaliana plant.

to a key set of genes that control plant organ growth: *JAGGED (JAG)*, *AINTEGUMENTA (ANT)* and *CIN-TCP* genes. We will test whether the co-ordination between cell size and cell division is a key feature of targeted by these genes at the early stages of organ growth. We will also test whether these genes target specific steps in cell division and clarify how the activities of these regulatory genes are combined during organ growth. Finally, we will identify the sets of genes controlled by *JAG* and *CIN-TCP* genes in the early stages of organ development which will show to what extent the function of these genes overlap, and reveal the key cellular functions targeted by these genes to determine how the organs grow.

OBJECTIVES

Work on this project is due to start in the second semester of 2012. Our work will benefit academics and industrial researchers working on the improvement of crop growth and yield. Computer modeling of plant growth is a very active research area at the moment and one of its main aims is to reveal the rules by which regulatory genes govern both localized and overall growth. A major limitation for making these models realistic and experimentally testable, however, is that we do not understand what cellular parameters (such as cell cycle progression or increase in cell mass) are growth limiting and targeted by growth regulators during normal development. Our project will directly benefit the field by addressing this important knowledge gap. In addition to essential knowledge on the control of plant organ growth, we will produce technical advances in quantitative imaging and image analysis with the potential to be adopted and widely used by the research community. Finally, by revealing which cellular processes are growth-limiting during normal development, we will facilitate the selection of candidate genes for improving crop growth and yield by conventional or transgenic approaches.

RELATED PUBLICATIONS

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Quantitative analysis of cell growth and cell cycle: virtual section of 3D image of wt floral bud with combined segmentation (individual cells marked in random colours) and EdU labeling (cells with newly made DNA show white nuclei).

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NETWORK FOR INVESTIGATION OF AMAZONIAN ATMOSPHERIC COMPOSITION AND IMPACTS ON CLIMATE – BUNIAACIC

São Paulo, Brazil

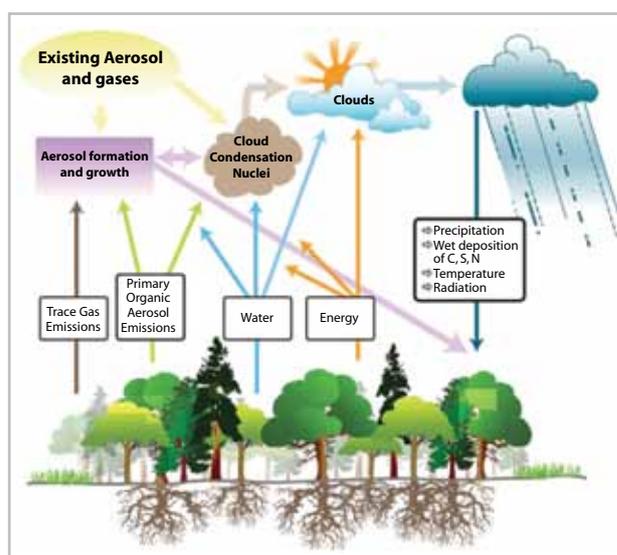
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The overarching goal of the BUNIAACIC proposal is to establish a coherent strategy for UK involvement in Amazonian atmospheric research by building a strong working relationship with the foremost Brazilian research groups in this area. By forming strong linkages with ongoing activities, in particular the FAPESP AEROCLIMA Thematic Grant number 08/58100-2, (titled: AEROCLIMA - Direct and indirect effects of aerosols on climate in Amazonia and Pantanal) a broad range of potential collaborative opportunities will be available for exploitation over a range of timescales both within and beyond the lifetime of the initial BUNIAACIC programme. Immediate short-timescale material objectives by which the collaboration will be able to contribute include: i) skill development and knowledge exchange through training in instrument operation and data analysis for University of São Paulo Aerosol Mass Spectrometry (AMS) operators, hence ii) enhancement of long-term aerosol property data delivery through online particle composition measurements iii) evaluation of the performance of the long-term monitoring instrument through comparison with intensive measurement by additional instrumentation iv) intensive measurements of additional aerosol properties for direct linkage between aerosol composition and optical/microphysical properties v) quantification of the impact of measured biogenic secondary organic aerosol (BSOA) and biogenic primary organic aerosol (BPOA) on climatically important behaviour related to their potential to impact on direct and indirect radiative forcing Strategic planning and infrastructure development objectives that the BUNIAACIC programme will address include: vi) construction of a White Paper outlining the recommended strategic methodology for UK participation in Amazonian atmospheric research vii)



The Amazon basin has strong coupling between terrestrial ecosystem and the climatic system including the hydrologic cycle: The linkages among carbon cycle, aerosol life cycle, and cloud life cycle need to be understood and quantified by the BUNIAACIC FAPESP-RCUK project.



appropriate planning for follow-up activities to address the research strategy on appropriate timescales, likely to include preparation of a consortium proposal. A UK office for collaboration on Amazonian atmospheric research will be established at the University of Manchester. The long-term particulate monitoring programme within AEROCLIMA will be expanded to include online aerosol composition measurements at the pristine rainforest site.

OBJECTIVES

The BUNIAACIC FAPESP-RCUK project is expected to provide the links between forest emissions, aerosol concentrations, radiation balance and ecosystem effects. Direct research areas that the BUNIAACIC collaboration will aim to address include the quantification of long term variability in aerosol composition, particularly of organic aerosol (OA), investigating the substantial seasonal trends in composition and transitions between sources. The biomass burning (BB) contribution to primary and secondary aerosol loading and variation in primary biological aerosol particles (PBAP) and hence of their potential contribution to ice nuclei (IN), will also be directly addressed. Broader objectives to which a UK network will be able to contribute include the long term variability in anthropogenic and biogenic VOCs including seasonal trends and transitions between sources. BVOC (isoprene, monoterpene and sesquiterpene) emission quantification and hence linkage to biogenic secondary organic aerosol (BSOA) precursor variability are also accessible to research expertise within the Brazilian and UK groups that will be accessed by the network. The key atmospheric chemistry measurement and modeling will be used in the investigation of oxidizing capacity through radical measurement (investigating potential discrepancies such as missing radical reactivity) will also be drawn into the network. It can be envisaged that such efforts can contribute to broader linkages through ecosystem response to anthropogenic atmospheric perturbations. Groups with appropriate expertise and interests will be engaged as the network develops, with particular attention paid to expanding the network to include larger-scale modelers with an emphasis on climate impact prediction and Earth System response.

RELATED PUBLICATIONS

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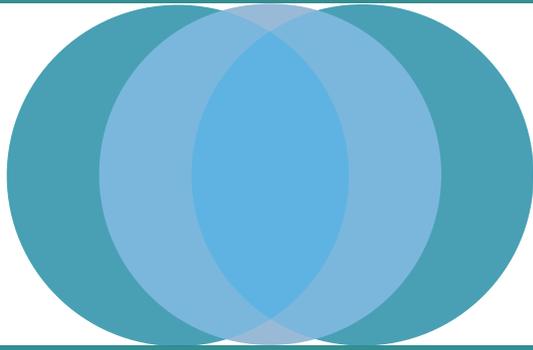
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