University of Amsterdam

The Swammerdam Institute for Life Sciences

Annual Report 2009

Faculty of Science

Contents

1. Preface by the director

The Swammerdam Institute for Life Sciences: developments in 2009

In 2009 for the whole of SILS there were several important developments. In the spring/summer of the year 9 out of the 12 research groups relocated to the new FNWI building. In this new building (completion in summer 2010) all research institutes of the FNWI, as well as the faculty and the teaching organization will be housed together. This will definitely lead to more extensive sharing of knowledge and facilities between the various researchers. State of the art laboratory facilities are now available to SILS personnel, and the initial feedback on these premises was very good. However, the relocation to the new building also had some downsides. There were delays up to 8 months in various areas due to technical problems. This will inevitably lead to a negative short term effect on research output.
The two major bachelor studies in the Life Sciences, Psychobiology and Biomedical Sciences showed an impressive increase in new students (an increase of 59% and 103% respectively). Despite this major increase in teaching obligations, SILS staff managed to cope with this influx during 2009.
In the fall off 2009 the Scientific Advisory Board (SAB) visited the Institute to perform the mid-term review over the period 2006- 2008. The outcome of this review was encouraging. For all four clusters, overall quality and productivity of research was rated very good to excellent. This was an improvement over the rating SILS received during the external review over the period 2000 – 2005. The SAB pointed to the fact that with the increasing number of students it would be difficult to maintain the high research standards. In addition, the FNWI and also SILS are confronted with serious budget cuts, and prudent financial management over the coming years is necessary to continue to support the research at SILS. In that light it is important to note that an increased influx of students, both in the BSc and especially in the MSc could largely counteract the negative budgets forecasts.

Research groups within the Swammerdam Institute for Life Sciences

The Living Cell

Molecular Microbial Physiology	Prof.dr. K.J. Hellingwerf
Molecular Biology and Microbial Food Safety	Prof.dr. S. Brul
Structure and Functional Organisation of the Cell Nucleus	Prof.dr. R. van Driel
Epigenetic Regulation of Gene Expression	Prof.dr. A.P. Otte
Molecular Cytology	Prof.dr. Th.W.J. Gadella

Plant Signalling

Plant Physiology	Prof.dr. M.A. Haring
Plant-Pathogen Interaction	Prof.dr. B.J.C. Cornelissen

SILS Center for NeuroScience

Animal Physiology and Cognitive Neuroscience	Prof.dr.C.M.A. Pennartz
Cellular and Systems Neurobiology	Prof.dr. W.J. Wadman
Hormonal Regulation of Signal Transduction in the Brain	Prof.dr. M. Joëls

Life Science Technologies

Mass Spectrometry of Biomacromolecules	Prof.dr. C.G. de Koster
BioSystems Data Analysis	Prof.dr. A.K. Smilde
Micro Array Department and Integrated Bioinformatics Unit	Dr. T.M. Breit

Research Cluster

The Living Cell

Molecular Microbial Physiology

Chairholder: Prof. dr. K.J. Hellingwerf

Prof. dr. J. Hugenholtz	Professor
Prof. dr. M.J. Teixeira de Mattos	Professor

Introduction

The general aim of the research in the Molecular Microbial Physiology Group (MMPG) is to discover the properties that allow living (microbial) cells to catalyze a large array of concurrent chemical fluxes and information flows. From these processes and in particular their mutual interactions 'life', with its typical characteristics such as: adaptation to the environment, reproduction, and evolution, has emerged. Microorganisms are particularly successful in this respect as can be concluded from the fact that they inhabit even the most extreme and variable ecosystems known to exist on this earth (and possibly even beyond); they can grow at very high rates, and can even adapt/evolve genetically.
Our work focuses on various aspects of this complex process, like (i) the details of intra-molecular signal-generation in (photo) receptor proteins, (ii) signal transfer between subsequent components in a signal transduction chain, (iii) the regulatory function of modulated gene expression, (iv) the generation of new metabolic capacities through the methods of synthetic biology and (v) the functional integration of these processes in the physiology of a range of micro-organisms, relevant for food and health, etc. By combining theoretical (*i.e.* computational) and experimental approaches, insight is obtained into basic principles that underlie functional interactions in (information) flux-carrying macromolecular networks, and accordingly into a ***bio***chemical ***system*** that sustains microbial (*i.e.* cellular) ***life***.

Research Highlights

- Our approach for analysing the physiological function and significance of the branched nature of the respiratory chain of *Escherichia coli* has gained further momentum by the publication on the role of cytochrome bdII oxidase. Quantitative analysis has shown that this terminal oxidase does not contribute to the build-up of a proton motive force, i.e. to energy conservation. Nevertheless, the electron flux through this oxidase is significant. A further step has been set in unravelling the complex signal perception of the major regulator of respiration and fermentation in *E. coli*, the so-called ArcBA two-component-regulatory system: We have shown that the redox state of both the ubiquinone and the menaquinone pool play a role in activating this system.

- As part of the SysMO-LAB project, we compared the physiological response of three quite different lactic acid bacteria – *Lactococcus lactis*, *Enterococcus faecalis* and *Streptococcus pyogenes* – in the chemostat to pulses in glucose, to changes in environmental pH, and to deletion of the gene encoding the enzyme lactate dehydrogenase. Although the three lactic acid bacteria operate the same homolactic catabolism, clearly different responses were observed upon the described modulations. With the metabolic models that were developed for each lactic acid bacterium by the different partners within the SysMO-LAB project, these differences will be explained in the coming year via the underlying regulatory mechanisms.
- In our "photofermentation" research, aimed to generate a system for the production of solar biofuel, 'proof of principle' has been provided for the production of two different biofuel substrates. Additional fermentation pathways, composed of oxygen-resistant enzymes from various bacteria and yeasts, are being assembled for insertion into the genome of *Synechocystis* sp. PCC6803.
- Two independent approaches have provided evidence that the transient (*i.e.* picosecond) ground state intermediate that is formed in parallel to the pathway towards signaling state formation in PYP, has a structure with single- rather than double-bond isomerization. Through site-directed mutagenesis the yields of signaling state and transient ground state were modulated in a way that can be rationalized through Molecular Dynamics modeling.
- Photoactivation of the general stress response in *Bacillus subtilis* with red light, via RsbP/Q of the energy-branch of the upstream signaling pathway, has been characterized in detail through a publication in the Journal of Bacteriology.

Other Highlights

- The FES program "Towards BioSolar Cells", in which MMPG actively participates, has been granted with a total sum of 45 MEu. Prof. Hellingwerf has been appointed as coordinator of the central theme in this program: Photosynthesis at the cellular level
- Prof Teixeira de Mattos has been elected by Executive Board of the European Federation of Biotechnology as Chair of the Scientific Committee of the 15th European Congress on Biotechnology (September 2012, Istanbul)
- The two projects in the MMP Group that were granted in the framework of the transnational SYSMO call were very positively evaluated and acquired funding for a second period.
- A patent was filed on the use of a modified *E. coli* strain, lacking all oxidase activity, as a platform for the optimization of fermentation pathways under aerobic conditions, e.g. through directed evolution.

Research aims for the coming year

- In our photofermentation research additional metabolic fermentation pathways will be tested with respect to functionality in the cyanobacterium *Synechocystis*. Whenever relevant, initial tests of selected heterologous pathways will be performed in *Escherichia coli* MB43 in the absence and presence of oxygen. Pathway expression will be optimized through gene-amplification strategies.
- To deepen the systems-biology understanding of photoreceptor functioning in bacteria, we will extend our studies to a structure-driven site-directed mutagenesis study of the role of YtvA. These studies will include mutant proteins with altered microscopic rate constants for signaling state formation to test bottom-up systems biology models of the process. In addition, jointly with our colleagues from Newcastle, we will try to reconstitute light-activation of the stressosome of *B. subtilis in vitro*.
- The observed differences in physiological behaviour of the three homofermentative lactic acid bacteria will be explained using the newly developed metabolic models. The comparative Systems Biology approach will be expanded through the SysMO-LAB-2 project, that was granted at the end of 2009. This project will focus more on species- and strain differences regarding regulatory networks and the interaction between amino acid metabolism on the one hand and the primary carbon- and energy metabolism on the other hand.
- The aim of SUMO-2 is to formulate a mathematical model of the entire catabolic network of *E. coli*. Whereas in SUMO-1 the focus was on the respiratory chain, we will now include a glucose transport-, glycolysis- and TCA cycle module. The common denominators in these modules are NAD(H) and AD(T)P. Dr Bruggeman (CWI) will play a active part in connecting these modules to respiration, jointly with our SUMO partners.

Molecular Biology and Microbial Food Safety

Chairholder: Prof. dr. S. Brul

Dr. J.C. van der Spek	Assistant Professor
Dr. G.J. Smits	Assistant Professor
Dr. F.M. Klis	Senior scientist (former Associate Professor)
Dr. B. Ter Kuile	Researcher Dutch Food & Drug Authority (VWA)
Dr. J.P.P.M. Smelt	Senior researcher (former Unilever scientist)

Introduction

Our group aims at a fundamental understanding of **stress response** of **micro-organisms** in relation to **infection** and **infection prevention**. We focus on food and medical antimicrobial treatments and agents used in the human as well as animal health sector. Model studies are performed in the single cell model yeast *Saccharomyces cerevisiae*, pathogenic *Candida albicans* as well as the prokaryotic spoilage and pathogenic bacteria *Bacillus subtilis* and *Escherichia coli*. The group is a member of the Netherlands Institute for Systems Biology (NISB). Results are quantified and analysed using a number of modelling tools including proteomics, micro-array and functional data analysis software. We have long standing contacts with food safety and medical groups including the food and pharma industry focussing on applied studies. The Scientific Advisory Board of SILS judged at the mid-term review of SILS that we have made compared to the previous formal research assessment of 2000-2005 a (required) major leap forward and are now at a very good to excellent level of research quality and viability.

Future Prospects & Societal impact

Spin-off of the studies is on important societal aspects. Firstly we contribute to improved food quality (in particular lower salt and sugar levels) at continued food safety in collaboration with the Dutch Food Safety Authority (Havelaar et al., 2009). Secondly, the group has delivered with PhD student Alex Ter Beek a screening method for new food preservatives to Unilever. Through consultancy of prof. Brul this was implemented for screening in the Chinese (Shanghai) lab. Thirdly, we are key players in a large European project on vaccine development against an important group of infectious diseases caused by *Candida albicans*. In both areas patents were filed and / or patent options discussed. Thus, in crucial societal fields the group is well placed and externally acknowledged for contributing to the areas of food security and resistance to infection. Furthermore, with the embedding in the 'Netherlands Centre for Systems Biology' the central basic research theme of molecular systems biology of stress response and cellular plasticity is strengthened and guaranteed for the future. We are partners in the application of the Science Council for a National Centre for Systems Biology.

Research Highlights

We succeeded in the expression of a pH sensitive green fluorescent protein (pHluorin) in the cytosol and the mitochondria of *Saccharomyces cerevisiae* cells. PHluorin was used to probe for the first time *in vivo* at seconds time scale the behaviour of the pHi in response to cellular and environmental stress. (Orij et al., 2009). The tool was extended to *B. subtilis* and used for antimicrobial screening (Unilever).

In 2009 our group was successful in the quantification of the *Candida albicans* cell wall proteome relevant to health and disease.Work in our group in collaboration with the de Koster group at SILS has focused on establishing microbial proteomics of the cell surface. We established the quantitative difference in the cell wall proteome upon exposure of *Candida albicans* cells to an environmental pH of 4 and one of 7. pH 4 is the normal pH of the vagina. An alkalinisation of the vaginal pH is associated with a pathological state and the development of Candida infection (discussed in Klis et al., 2009; see also Butler at al. 2009).

In our line of research on bacterial spore-formers we formulated a model for the molecular processes operative in weak organic acid stress resistance in *Bacillus subtilis* (Ter Beek, 2009, PhD thesis) as well as spore germination and outgrowth of the organism (Ter Beek et al., 2010 submitted). The gene-systems involved in sorbic-acid resistance have been patented together with Unilever.
The bacterial research-line focusing on antibiotic resistance development, directly linked to microbial food safety issues and run in close collaboration with the Dutch Food Safety Authority (VWA) was firmly established in 2009. The studies focused on the acquisition of resistance as a consequence of antibiotic exposure both in conditions where exchange of genetic material can take place as well as in monocultures. For all experiments we use *Escherichia coli* in combination with 3 antibiotics that all have a different working mechanism. Low levels of antibiotics pose an increased hazard for both transmission of resistance as well as the de novo development of resistance.

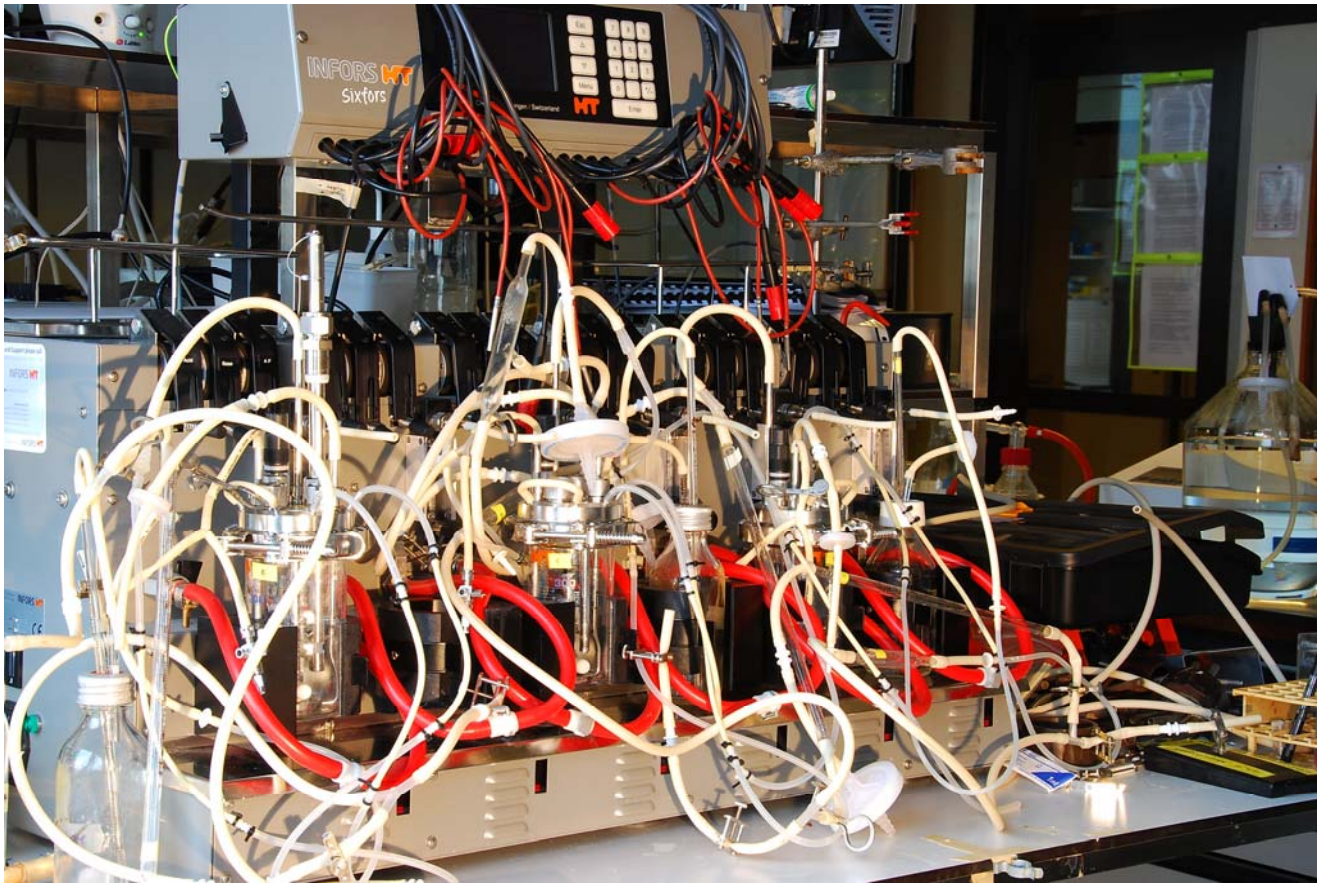
Other Highlights

S. Brul: FEMS representative of the Dutch Society for Microbiology as of 2009; Chair of the Dutch Institute for BioScience; Joined the editorial board of Elsevier's Food Microbiology; STW fellowship and FES funds in the field of microbial stability; member of the STW VICI committee and EU FP7 project reviews.

F.M. Klis: Editor Eukaryotic Cell, FEMS Yeast Research, Yeast..

Research aims for the coming year

- *Temperature and weak organic acid stress in yeast; the role of energy metabolism in generating efficient stress responses.* In the study of yeast energy metabolism and its role in stress response against environmental insult our group will focus on two aspects: (1) A mild thermal stress and (2) a stress with weak organic acid compounds. The latter is work that has a pendant in the Bacillus studies of the group as may be inferred from the information presented. Previous work on the glycolytic pathway of yeast cells cultured at elevated temperatures revealed that control of the response to such conditions mostly is distributed over the various levels of cellular organization (PhD student Jarne Postmus).
- *The role of the cell wall in virulence and related stress responses of medically relevant yeast (Candida).* Here we will continue our work on the detailed proteomic analysis of the Candida cell wall. This 'organelle' consists of an internal layer, which is responsible for its mechanical strength and an external protein coat, which is responsible for interactions with the environment. The latter is crucial for biofilm formation, adhesion to abiotic surfaces, recognition of host cells and general fitness.
- *The mechanisms of temperature resistance and weak organic acid stress response in Bacilli.* This research line includes a continuation of a long standing effort in the field of bacterial spore germination mechanisms and the acquisition of weak organic acid preservative resistance. Recent genome-wide expression data by Ter Beek show the induction of several genes that play a role in the elongation of fatty acid chains on glycerol-lipid units as well as on their iso or anti-iso branching (PhD Ter Beek., 2009). We will continue biochemical analysis of mutants that are perturbed in phospholipids biosynthesis.
- *The temperature stress resistance and germination / outgrowth capacity of damaged spores.* In 2010 we will reinforce this sub-project with two researchers (sponsored by ERASMUS MUNDUS). One will study the proteome of wild-type and laboratory strain derived Bacillus spores in collaboration with the proteomics group of the Institute. A second PhD candidate will work on single spore germination studies under supervision of a post-doctoral fellow. This new 4 year post-doctoral fellow-ship is supported by NWO-STW and started per January this year. The fellow will continue genome-wide and genetic analysis on the molecular modules involved in the regulation of bacterial spore germination.
- *The development of antibiotic resistance.* In 2010 we will round up the first period of this work. We will next focus on the identification of the molecular physiological basis of the resistance development.
  Write ~15 (collaborative) research articles.



Structure and Functional Organisation of the Cell Nucleus

Chairholder: Prof.dr. R. van Driel

Dr. P.F. Fransz	Assistant Professor
Dr. M.E. Stam	Assistant Professor
Dr. P.J. Verschure	Assistant Professor

Introduction

Nuclear Organisation Group (NOG)

The one-dimensional structure of the genome of an increasing number of eukaryotes has been fully sequenced. A major challenge is to understand how expression of its many thousands of genes is orchestrated. In the eukaryotic genome gene expression is controlled at three hierarchical levels. One is that of individual genes, involving cis-regulatory elements and trans-acting factors. Information at the second level is present as posttranslational modifications of histones, incorporated histone variants and DNA methylation patterns. The third level involves the dynamic

folding of the chromatin fibre, resulting in functional compartmentalisation of the nucleus.

Our aim is to unravel gene regulatory mechanisms at these three control levels. We concentrate on the dynamic structure of chromatin and the behaviour of chromatin-associated molecular machineries involved in gene activation, gene silencing and DNA repair. We combine structural studies, often on living cells, with molecular biological, biochemical and other methodologies and with predictive modelling. In particular, we analyse spatial folding and looping of chromatin in relation to transcriptional regulation. We develop synthetic in vivo systems to explore epigenetic control systems and analyse the in vivo kinetic behaviour of the nucleotide excision DNA repair system. We develop, in cooperation with several other groups, quantitative and predictive models that give insight into system properties and guide further experimentation.

Research Highlights

- Pernette Verschure and Frank Bruggeman focused on theory and models to understand design principles of epigenetic transcription control. Initial theoretical studies show that in eukaryotic systems a random multi-step assembly of the initiation complex has a large effect on the waiting time for transcription, but only a small effect on the noise in the waiting time. Furthermore, the number of steps in the transition from the permissive to the non-permissive transcription initiation state has a large effect on the RNA burst-size distribution. Interestingly, similar steady state RNA levels result from quite different parameters regimes: (i) the Poisson-regime, showing minimal burst-like behavior, and (ii) the RNA burst regime, for which a quasi steady-state is reached during the non-permissive of initiation.
- Maike Stam and colleagues published the first evidence of gene regulation by long-range interactions through chromatin looping in plants (maize). Also, they identified epiallele- and expression level-specific chromosomal looping and showed that the chromosome conformation capture (3C) technique identifies unknown regulatory sequences.
- Paul Fransz, in cooperation with others, carried out precise mapping with base pair accuracy of the breakpoints of a paracentric inversion that spans euchromatin and heterochromatin regions in chromosome arm 4S of Arabidopsis, giving insight into the process of an inversion event and the and epigenetic consequences of chromosomal rearrangements.
- Roel van Driel and colleagues developed and published, together with two theoretical groups, predictive quantitative kinetic models of the in vivo assembly of chromatin-associated DNA repair complexes and polymer models of chromatin folding in relation to genome function. Both type of models based on extensive in situ and in vivo measurements carried out by the NOG group in the past few years.

Other Highlights

Roel van Driel is director of the Netherlands Institute for Systems Biology (NISB) and the national NGI-funded research program Netherlands Consortium for Systems Biology (NCSB)

Research aims for the coming year

- *Verschure and colleagues*
  Our systems biology approach of engineered epigenetically toggled cell systems in mammalian cells, allowing quantitative in vivo measurements and computational modelling, will be expanded. We aim to combine state-of-the-art biological, biophysical and computational techniques (collaboration Dr van Noort, RUL, prof. Wuite, VU and Dr Bruggeman, NISB) (i) to resolve the composition, structure, mechanism and kinetics of epigenetic transcription regulation in vivo at the single gene level, including inherent stochastic variations, and (ii) to incorporate this knowledge into a refined numerical model for transcription regulation. Also, a national research line to understand epigenetic gene regulation in Huntington's disease from a combined systems biology and synthetic biology perspective will be initiated (collaboration with prof. Van Ommen, LUMC, Leiden and prof. Smilde, SILS, UvA).
- *Stam and colleagues*
  Building on the 3C technology developed in the past years we will elucidate the interplay between epigenetic regulation and long-range chromosomal interactions in gene regulation in higher eukaryotes, in particular in *Arabidopsis thaliana*. In this context we make use of the large collection of well-characterized Arabidopsis mutants known to affect chromatin structure. In our study on the role of chromatin structure in paramutation we aim at completing our analyses of mutants affecting paramutation. Results will provide insight into underlying mechanisms.
- *Fransz and colleagues*
  Aim is to assess relationships between chromosome folding and nuclear reprogramming and to investigate long-range chromosome interactions. Research will concentrate on 3-D chromosome studies in Arabidopsis, in collaboration with Stam c.s.
- *Van Driel and coworkers*
  The two research lines of the previous years are expanded: understanding large scale chromatin folding, the kinetics of in vivo assembly and the functioning of chromatin-associated protein complexes. In both cases we start from predictions made by the quantitative models we developed earlier.

Epigenetic Regulation of Gene Expression

Chairholder: Prof.dr A.P. Otte

Dr.Ir.J.A. Verhees Assistant Professor

Introduction

It is our aim to understand aspects of epigenetic regulation of gene expression. Research is focused on genomic elements that have a powerful, positive influence on promoter activity. These elements are employed to facilitate the production of therapeutic monoclonal antibodies in mammalian cell lines. Unfortunately, the increased protein expression levels have a negative influence on cell growth. Very high protein expression levels even force cells to stop growing at all, which is an undesirable phenomenon from a practical point of view. We attempt to understand this inverse relationship between protein expression levels and cell growth at a quantitative level. Furthermore, we develop inducible gene expression systems in which we can reversibly modulate protein expression levels and cell growth.

Research Highlights

We have identified novel genomic elements are initiation points for high levels of transcription. These elements are also defined by a higher histone acetylation status. They probably provide a more 'open' chromatin state in which a transfected gene that is flanked by these elements also becomes more open for transcription. In order to develop novel inducible expression systems in which we can reversibly modulate protein expression levels and cell growth, we devised a novel set of selection markers. These markers include the Zeocin resistance protein, as well as markers that restore the synthesis of essential metabolic components that normally lack from the cells.
Application of these markers warrants both high proteins expression levels as well as a high degree of stability of protein expression over prolonged periods of time.

Other Highlight

Director of a biotechnology company, CellaGenics, a spin-off company, emerging from SILS, FNWI and the UvA Holding in 2008. CellaGenics works in the research area of expression of therapeutic proteins and cell growth.

Future Prospects

In the coming year we focus on further developing expression systems in which protein expression, growth rates of the cells and secretion of the proteins can be coordinately modulated to achieve an optimal expression platform for therapeutic proteins. As such we aim to investigate and modulate in a comprehensive way

(i) the role of novel genomic elements in expression and stability of protein expression;
(ii) an inverse relationship between cell growth and protein expression levels.

Molecular Cytology

Chairholder: Prof.dr Th.W.J. Gadella

Dr. T. den Blaauwen	Assistant Professor
Dr. Ir. J. Goedhart	Assistant Professor
Dr. E. M. M. Manders	Assistant Professor
Dr.Ir.M.A.Hink	Assistant Professor

Introduction

Molecular Cytology & Centre for Advanced Microscopy (CAM):
Molecular Cytology is the study of the dynamic architecture of living cells. Our central theme is 'Self-organization and signalling in living cells'. Self-organization is the intrinsic property of matter to organize itself in a (dynamic) structure, whereas signalling implies the activity of gene-products to control a local activity which can alter the local cellular architecture (e.g. driving morphogenesis). In order to achieve a certain 3D architecture in cells, these two important mechanisms work in concert. At Molecular Cytology both mechanisms are studied with emphasis on membrane-related architecture of living cells using advanced microscopy tools. The main research areas are:

1) *Spatial organization of sub-cellular signalling* (group leaders prof. dr. T.W.J. Gadella, dr. J. Goedhart & dr. M.A. Hink). By employing genetic encoded fluorescent biosensors we analyze the in situ molecular interactions between signalling molecules (phospholipid-second messengers, receptors, G-proteins and effector molecules) & flow of information across and in the plane of the membrane of living mammalian cells. We aim to understand how cells can achieve and maintain a local signal in the membrane (e.g. in order to drive morphogenesis, or to define new cytoskeletal anchorage or vesicle-docking sites). The main pathways under study involve histamine/P2Y GPCR receptors, G-alfaQ to PLC activation triggering downstream calcium, kinase signalling and small GTPase (Rho/Rac/Cdc24) signalling. The close intertwining of several signalling cascades and our quantitative microscopy approach both necessitates and permits the generation of quantitative predictive modelling, which effectively will integrate this research line with Systems Biology approaches.

2) *Molecular dynamics of the bacterial cycle* (group leader dr. T. den Blaauwen). The morphology of rod shaped bacteria is achieved through two very dynamic synthetic complexes: the elongasome and the divisome. The elongasomes use the actin-like cytoskeleton MreB helix underneath the plasma membrane as tracking devise to elongate the cell envelope whereas the divisome is responsible for division and the synthesis of new cell poles. Cell division is directed by the FtsZ ring (a tubulin homolog), which exerts a small force on the bacterial envelope. The assembly and the dynamics of the elongasome and divisome are studied in vivo using immunofluorescence and fluorescence microscopy techniques (FRET, FRAP,

localization) and in vitro using state of the art biochemical and biophysical techniques. By aiming to obtain quantitative data, we hope to model the measured and observed interactions.

3) These research themes heavily depend on advanced microscopy technology organized within the *Centre for Advanced Microscopy* (CAM, 2004). The goal of CAM (em. prof. dr. G.J. Brakenhoff, prof. dr. T.W.J. Gadella, dr. E.M.M. Manders & dr. M. Hink) is to boost Life Sciences research using & developing (optical) microscopy techniques. Current most prominent developments are Controlled Light Exposure Microscopy (CLEM) (dr. Manders), multimode Fluorescence Lifetime Imaging Microscopy (FLIM) (dr. Gadella), Spinning disk & Total Internal Reflection & PALM-microscopy (dr. Hink, Manders & Gadella) & Fluorescence (cross) correlation microscopy (dr. Hink).

Research Highlights

The main achievement in 2009 was the successful move to the new science faculty building. The entire wetlab including cold room, centrifuges, molecular biology and cell culture facilities as well as all advanced microscopes were moved in April 2009 and were fully operational in September 2009.

Another achievement was the generation of mTurquoise: the brightest cyan fluorescent protein to date. This study will be published in Nature Methods in 2010.

Other Highlights

-Tanneke den Blaauwen received a four year FP7, EC, Collaborative project with coordinator Miguel Vicente (CSIC, Spain), "Exploiting Gram-negative cell division targets in the test tube to obtain antimicrobial compounds" Acronym "Divinocell" FP7-223431 (627 k€)

-Mark Hink & Dorus Gadella received a medium scale NWO-grant for the implementation of multimode FCS microscopy (392 k€)

-Dorus Gadella was appointed as national coordinator in setting up the ESFRI European Large Scale Infrastructure Program on EuroBioimaging. Here a pan-European distributed facility will be created for Advanced Light Microscopy.

Research aims for the coming year

- Implement a major Systems Biology research line on GPCR signaling
- To investigate the localization and function of PBP5 in regulation of the morphogenesis of E. coli.
- To investigate the interaction and function of PBP1A and PBP2 in regulation of length growth of E. coli.
- To develop a spectral FRET method for in situ protein-interaction studies in E. coli
- Implement PALM microscopy
- Application of CLEM in Neurobiology
- Implement multimodal FCS/FLCS/FLIM microscopy
- Found the Netherlands Centre for Advanced Microscopy

Research Cluster

Plant Signalling

Plant Physiology

Chairholder: Prof. dr. M.A. Haring

Dr.Ir.R.C. Schuurink	Associate Professor
Dr. T. Munnik	Associate Professor
Dr. C. Testerink	Assistant Professor

Introduction

The Plant Physiology group investigates plant signaling at the cellular level (phospholipids) and at the level of the whole plant (Volatiles). Our phospholipid signaling research is focused on the biological function of phosphatidic acid (PA) and polyphosphoinositides (PPIs). The latter are inositol-containing phospholipids, which are phosphorylated at the D3-, 4- or 5 position via specific PI (phosphatidylinositol) and PIP (phosphatidylinositolphosphate) kinases (i.e. PIK and PIPK). PA can be produced via activation of phospholipase D (PLD) or indirectly, via the combined action of phospholipase C (PLC) and diacylglycerol kinase (DGK). Knockout lines of individual *PIK* (11), *PIPK* (11), *PLC* (9), *DGK* (7) and *PLD* (12) genes in *Arabidopsis* plants, are used to elucidate their role in signaling and development. An important research goal is to elucidate how PA modulates protein function and downstream plant responses. To study the biochemistry of scent of Petunia flowers we investigate genes involved in volatile benzenoid and phenylpropanoid synthesis, emission and regulation, which we have discovered by microarray studies. Because plant volatiles that are important for interactions with insects are produced in leaf-hairs (trichomes) we are dissecting the metabolism of volatile terpenes in trichomes. Large scale sequencing of trichome-ESTs from wild and cultivated tomato plants has provided us with a wealth of candidate genes. Our aim is to engineer the production of these terpenoids in tomato trichomes in such a way that they become repellant for pest insects. Finally, we use Arabidopsis for transcriptomics and forward genetic screens to identify genes important in the response to the wound-induced C6-volatile *E*-2-hexenal and the subsequent hormonal signal GABA.

Research Highlights

Phospholipid research:

To analyze phospholipid signalling in vivo, we have been constructing various lipid biosensors, gene fusions of a specific lipid-binding domain and a fluorescent protein, which can be stably expressed in plant cells or whole plants and imaged under the confocal microscope. Currently, we have sensors for PI3P, PI4P, PI(4,5)P2, DAG and PS, expressed in Arabidopsis and tobacco BY-2 cells in various colors. In animal cells, it is now clear that PI(4,5)P2 is not only a substrate for PLC but also functions as a second messenger itself. In plants, concentrations are 30-100 fold lower and so far, osmotic stress was the only trigger known to increase PIP2. Recently, we discovered an unexpected novel agonist, i.e. heat stress. In non-stimulated cells, PIP2 concentrations are too low to reveal the lipid in the membrane so the biosensor predominantly resides in the cytosol (see Figure 1, panel 1a), but in response to heat stress, the biosensor quickly accumulates at the plasma membrane (panel 1b). Later, punctate structures in the cytosol appear (panel 1c), and finally, after about 30 min, the nuclear membrane becomes labelled (panel 1d,e).

Two genes involved in the generation of phosphatidic acid, AtPLDα1 and AtPLDδ, were found to be involved in wounding, salt stress tolerance and plant defence. Knock-out lines exhibited impaired wound-induced PA responses, with the severest effect in AtPLDα1/AtPLDδ double knock-out mutants. Mutants were also more sensitive to NaCl in the growth medium and to be required for full disease resistance against avirulent Pseudomonas, but not to virulent strains. Interestingly, several protein kinases were found to directly bind PA. These include SNF-1 related protein kinases (SnRKs) implicated in osmotic stress, and the MAPKKK homologue CTR1, which is a negative regulator of ethylene signalling. We have further characterized the two PA-binding SnRKs, which are part of a subfamily of ten members in Arabidopsis. Importantly, we have found that other, highly similar members of this subfamily do not have affinity for PA. Moreover, lipid-binding analysis of SnRK2.4 fragments has narrowed down the PA-binding site to a short stretch at the C-terminus of the protein. Genomic SnRK2.4-GFP fusions have been expressed under their own promoter to complement *snrk* knock-out plants and where found to show dynamic localization in cytosol/punctate structures and nucleus. In another research line, we also found changes in localization of two other protein kinases, PID and PDK, in response to salt treatment.

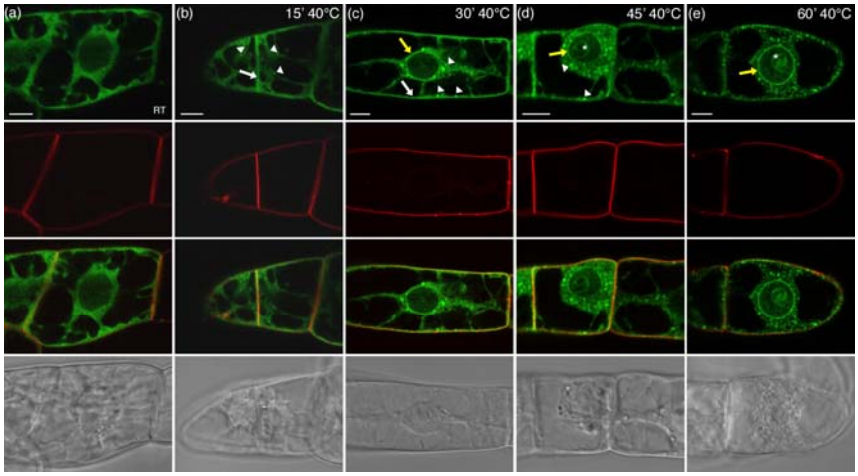
Plant volatiles research:

We have discovered that the plant volatile methylsalicylate (MeSA) is an important signal in plant defence. By knocking down the enzyme activity of salicylic acid methyl transferase (SAMT) and thus the production and emission of we could show that these plants no longer can "cry out for help" when they are attacked by herbivores. For other volatiles, terpenes, we could show that they are important repellants for whiteflies that are foraging on tomato plants. We started to dissect the regulation of terpene biosynthesis in tomato trichomes with the Massive Parallel Sequence technology of 454 Life Sciences (GS-Titanium) and the Genome Analyzer from Ilumina in collaboration with Keygene. This resulted in novel enzymes and transcription factors specific for these organs. We used the yeast-one-hybrid technology to identify transcription factors that bind to the trichome-specific box of

the Monoterpene synthase I promoter (MTS1) and have identified several candidates that are now subjected to further analyses. We continued to study the role of E-2-hexenal in Arabidopsis and its downstream component γ-aminobutyric acid (GABA). We have discovered that GABA down-regulates the type III secretion system of Pseudomonas syringae DC3000. Finally, after the identification of the ketoacylthiolase gene involved in floral benzenoid production in Petunia (see figure 2) we have been able to identify motifs in the promoter of the R2R3-MYB ODORANT1 (ODO1) that determine volatile production in non-fragrant and fragrant petunias. We are currently screening with the yeast-one-hybrid technology for transcription factors that can bind to it. It this way we aim to identify a regulatory factor upstream of ODO1.

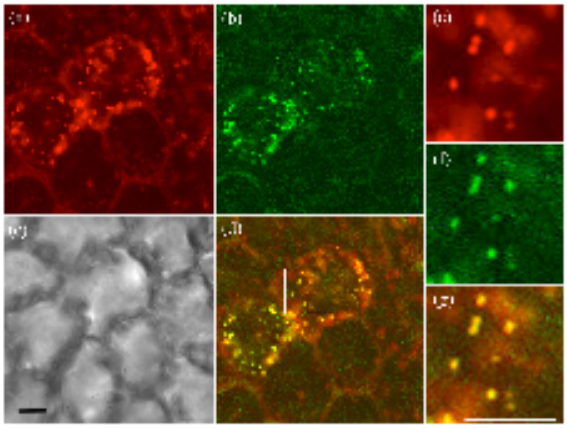
ILLUSTRATIONS:

FIGURE 1



Heat stress triggers PIP_2 at the plasma membrane, intracellular compartments and nuclear membrane. Tobacco BY-2 cells stably expressing the PIP_2 biosensor, YFP-$PH_{PLC\delta1}$, were incubated and imaged at room temperature (a) and 40°C after 15 (b), 30 (c), 45 (d) and 60 min (e). To reveal the plasma membrane, 2 μM FM4-64 was added immediately after treatment. YFP fluorescence is shown in green, FM4-64 in red, and DIC in grey. Arrowheads indicate YFP-$PH_{PLC\delta1}$-labelled punctate structures, white arrows show PM labelling, yellow arrows indicate nuclear envelope labelling, and asterix indicates the nucleolus. Bar = 10 μm. Adapted from Miskind et al. (2009). *Plant J.* **60**, 10-21.

FIGURE 2



In vivo peroxisomal targeting of PhKAT1, 3-ketoacyl-CoA thiolase, which is involved in the benzenoid biosynthetic pathway and the production of benzoic acid. The mCherry peroxisomal marker px-rk (a) and 35S:PhKAT1-GFP (b) were transiently co-expressed in *Petunia hybrida* Mitchell flowers. The merged and bright field images are shown in (d) and (c), respectively. (e,f,g) Magnification taken from the boxed area shown in (c). Confocal images were obtained with a Zeiss LSM 510 confocal laser scanning microscope. Co-localisation was seen several times in independent experiments. The scale bars represent 10 µm.

Other Highlights

Christa Testerink: STW grant within the STW Perspectief Program "Learning from Nature to Protect Crops" (430 k€)

Future Prospects

- Identification of the PA-binding site of the SnRK2, PID and PDK1 protein kinases
- To investigate the role of lipid signalling and protein kinases in the response of Arabidopsis roots to salt
- To establish and characterize knock-out mutants and non-PA-binding mutants for SnRK2
- To perform a proteome-wide membrane recruitment screen of salt-induced PA-binding proteins
- To explore natural variation in Arabidopsis accessions for salt tolerance

Plant-pathogen Interactions

Chairholder: Prof. dr. B.J.C. Cornelissen

Dr. Ing. F.L.W.Takken	Assistant Professor
Dr. M. Rep	Assistant Professor

Introduction

Plant–pathogen interactions result either in disease or in a successful resistance response of the plant that prevent further pathogen ingress. To reveal the molecular basis of susceptibility and resistance we focus on the interaction between the fungus *Fusarium oxysporum* and susceptible tomato (*Solanum esculentum*) as well as resistant plants that carry the I-2 resistance (R) gene. Besides I-2 we also study other (R) proteins. Our specific interests are basal and induced defence mechanisms of the host and virulence and avirulence factors of the pathogen.

The ability of a pathogen to colonise its host depends on 'general' pathogenicity genes as well as on specific, secreted 'effector' proteins. Effectors are called 'avirulence factors' when they are recognized by an R protein, and trigger disease resistance. For example disease resistance of tomato to strains of *F. oxysporum* producing the effector Avr2 (Avirulence factor 2) is mediated by the R protein I-2.

Our research aims at: 1) the identification and dissection of the protein complex(-es) involved in R protein mediated resistance. This work includes the functional analysis of individual complex-components and conformational changes in R proteins; 2) uncovering the role of pathogenicity genes and effector proteins (including avirulence factors) of *F. oxysporum* and identification of their targets in tomato.

Research Highlights

- Our earlier discovery that most of the genes coding for effectors reside on a single 'pathogenicity' chromosome and that this chromosome can be transferred to a non-pathogenic strain, turning it into a tomato pathogen, was combined with complementary results from whole genome sequence comparisons and the resulting paper was accepted by Nature (2010).

- Screens for plant proteins interacting with effectors were initiated, yielding a first set of candidates that interact with Avr2 (Six3), Six6 and Six8

- The *SIX2*, *SIX5* and *SIX6* genes were deleted in *Fusarium oxyporum* and *SIX6* was shown to contribute to virulence.

- *SIX2*, *SIX4* and *SIX6* were shown to suppress R-gene-mediated HR in leaves of *N. benthamiana,* whereas *SIX8* and *SIX10* enhance cell death triggered by the *Phytophthora infestans* protein Inf-1.

- Transient expression of *SIX2*, *SIX4*, *SIX6* and *SIX10* genes lacking the protein secretion signals indicates that these proteins exert their functions intracellularly, similar to Avr2.

- To study regulation of expression of effector genes, the first of a set of *AVR2* (*SIX3*) and *AVR3* (*SIX1*) promoter deletion mutants was generated, and strains

overexpressing the *SIX* gene regulator Sge1 were constructed to artificially activate these genes.

- Most R proteins are multi-domain proteins. Before we showed transcomplemention between the N-terminal CC-NB part and the C-terminal LRR domain of Mi-1. We now revealed transcomplemention and physical interactions between the N-terminal CC-domain and the C-terminal NB-LRR that can be abolished by specific mutations in either the CC or NB domain.
- One specific isoform of Hsp17 was found to interact with I-2. Silencing of this gene (partly) abolished Mi-1 and I-2 activity, probably by destabilizing R protein accumulation.
- Analysis of Arabidopsis plants in which SUMO (small ubiquitin-like modifier) isoforms were either silenced, knocked-out or over-expressed revealed that the different SUMO isoforms have non-redundant and specific functions in plant development and SA mediated plant defences.
- Silencing of the SA methyltransferase in tomato was found to abolish methylsalicylate production and decrease disease symptom development upon *Fusarium* infection.

Other Highlights

Appreciation for our research by the scientific community was apparent by the invitations from high impact journals such as Science, Trends in Plant Science and Current Opinion in Plant Biology (the last two are ranked #1 and #2 in plant science) to contribute review papers.

Research aims for the coming year

With the awarding of a NWO-Vici grant to M. Rep, a new line of research will be initiated aimed at elucidation of the mechanism and evolutionary consequences of chromosome transfer between *Fusarium* strains. This project includes genome sequencing and identification of effectors and pathogenicity chromosomes in host specific forms of *F. oxysporum* additional to f.sp. *lycopersici*. Identification of plant proteins interacting with effectors of f.sp. *lycopersici* (Six and Avr proteins) will be continued, as well as identification of regulatory elements in promoters of the *AVR2* and *AVR3* genes. Since many of these effectors function inside host cells we will focus on the mechanism underlying translocating of these proteins from the xylem sap into the xylem-contact cells. For Avr2 deletion constructs will be made to define the minimal regions required for virulence and avirulence functions. Our nucleotide binding studies will be continued to relate nucleotide binding to intra- and intermolecular interactions in R proteins. Furthermore, the function of I-2-interacting proteins will be studied in relation to disease resistance in stably silenced transgenic plants. Finally, in collaboration with Harrold van den Burg we will further analyse the Arabidopsis SUMO lines to unravel the molecular basis of the defence phenotypes.

Research Cluster

SILS – Center for NeuroScience

Animal Physiology and Cognitive Neuroscience

Chairholder: Prof. dr. C.M.A. Pennartz

Dr. W.E.J.M. Ghijsen	Assistant Professor
Dr. F.P. Battaglia	Assistant Professor
Dr. S.M. Daselaar	Assistant Professor

Introduction

The group's global research aim is to elucidate how neuronal networks distributed across the prefrontal cortex, sensory neocortex, hippocampus and ventral striatum, cooperate in a number of cognitive processes, including learning and memory consolidation, perception and multisensory integration. This aim is pursued using a variety of techniques and at various aggregate levels, ranging from cellular to systems and behavioral levels. Most of the research focuses on the level of systems physiology. General research topics include:

- The consolidation of memorized information of recent experiences. A very promising candidate mechanism for mediating this process is spontaneous "off-line" reactivation of stored information. After an initial experience which is marked by highly specific firing patterns in brain structures involved in memory, a replay of these firing patterns can be observed, with preservation of temporally specific features such as the order in which brain cells fire. In particular, we pursue the relevance of this phenomenon for memory consolidation, and how the replay is being orchestrated amongst different brain areas, such as the hippocampus and ventral striatum. Technically, this project is carried out in animals by performing ensemble recordings using ´tetrode arrays´, and in humans by fMRI (functional magnetic resonance imaging) and TMS (transcranial magnetic stimulation) techniques.
- Using fMRI and TMS, we study how brain systems interact during encoding, storage and retrieval of information.
  As in our animal research, much of these interactions relate to the communication between the hippocampus and neocortical structures. A current focus here is to elucidate functions of the Default-Mode Network, comparing memory tasks to related cognitive functions such as attention to

external vs internal (memory-driven) inputs, mental imagery and memory reconstruction during retrieval.

- We are also studying memory consolidation problem from theoretical and computational viewpoints. We are developing new computational models of memory consolidation and the formation of semantic memories, by making use of concepts from computational linguistics and Bayesian inference.
- Another main question in the field of learning and memory is how networks of cells collectively learn to generate predictions about upcoming rewards, based on sensory cues that precede reward delivery. Learning-related changes in rhythmic neural activity and network coherence are highlighted. We also investigate which neurotransmitters and receptors influence the formation of neural representations of reward predictions. In addition, neural correlates of attention and flexible shifting of attention are studied with ensemble recording techniques.
- We investigate interrelationships between genes, learning and memory capacities as measured in behavior, and the systems physiology which forms the interface between gene expression and overt behavior. These interrelationships are studied in the context of spatial navigation, conditioned place preference and cognitive flexibility in targeted knockout mice, e.g. regionally restricted NMDA receptor deletions in hippocampus and deletions of the *Arc* gene, which is involved in synaptic plasticity. This research line has been supplemented with clinically relevant mouse models, e.g. of mental retardation.

We investigate how neural assemblies in the brain cooperate to generate conscious or unconscious multisensory representations, and how sensory inputs from different modalities are combined to achieve such integrated representations. Moreover, the impact of reward on visual representations is studied. This goal is being pursued by in vivo 2-photon-imaging of neural ensemble activity, gauged with Calcium-sensitive fluorescent dyes.

Research Highlights

- Joint ensemble recordings have been made from two brain structures simultaneously. These recordings are being made in a study on how animals learn to predict reward value based on discrete cues and locations in the environment. In a Y-maze task, we found that two connected brain structures, the hippocampus and ventral striatum, represent task-related information differently. Hippocampal representations concern environmental locations, but a switch of the environmental map can be achieved by a reward-predictive cue (i.e., a light preceding reward delivery). Ventral striatal neurons fire in relation to approach actions to reward sites in a way that is less spatially dependent. Also in this structure predictive cues cause a switch in representations, occurring concurrently with that in hippocampus.
- In examining the neural basis of reinforcement learning and attention switching, we found that the rat orbitofrontal cortex encodes information about the probability of a reward an animal expects after having perceived an olfactory cue associated with the reward. We discovered oscillatory activity in the theta-range (4-12 Hz) to which spikes are phase-locked, a phenomenon that correlates to

reward expectancy. In contrast, gamma oscillatory activity (40-80 Hz) correlates with suppression of movement-related activity, occurring in a task phase where the animal has learned to withhold a motor response during odor sampling. Furthermore, gamma oscillatory activity in the ventral striatum was identified and found to correlate with anticipation and delivery of reward, not movement suppression.

- We studied the interactions between the hippocampus and the prefrontal cortex in rats during performance of a decision making task, and during the subsequent sleep. During behavior, hippocampal/cortical coherence manifested itself in the form of oscillatory coherence and neural ensemble synchronization. During sleep, transient replay events were observed in the prefrontal cortex, simultaneously with hippocampal sharp wave/ripples.
- We studied the dynamics of medial prefrontal ensemble firing patterns when rats are exposed to attentional distracters and engage in attentional switching. Attentional performance was found to correlate to a high maintenance of prefrontal ensemble activity, in spite of distractor stimuli presented to the animal.
- We carried out an extensive set of experiments involving tetrode ensemble recordings in the hippocampus of control and NMDA receptor knockout mice, in a series of tasks, involving food search in a star-shape maze and running in a circular task, with the purpose of analyzing the activity of hippocampal place cells when the NMDA receptor, crucial for synaptic plasticity, is functionally impaired. This study sheds new light on the role of synaptic plasticity, mediated by these receptors, in the plasticity of spatial representations and mechanisms underlying spike timing relative to theta rhythms. Recordings in mouse models related to mental retardation and Arc-dependent memory deficits have begun.
- A 2-photon imaging setup was used to visualize the spatially ordered structure of neuronal population activity in the living mouse brain. We examined effects of appetitive conditioning on visual processing in area V1 by pairing moving grid patterns with different outcomes (reward or no reward). Our results indicate a broadening of tuning curves (i.e., a broadening of the cell´s sensitivity to visual motion direction), but only in a selective assembly of cells that is tuned to the reward-predicting visual stimulus (CS+).
- fMRI studies in healthy human subjects were carried in combination with monitoring of respiratory activity during performance of a memory task. These studies demonstrate a strong influence of breathing patterns on BOLD signals that have been previously attributed to cognitive processing. Thus, respiration should be taken into account as possible explanatory factor in a wide range of cognitive brain-imaging studies.
- fMRI studies in healthy human subjects were carried out to investigate the neural signatures of intransitive decision-making. This type of decision-making violates traditional neuroeconomic models, but frequently occurs in humans when they have to choose between alternatives composed of multiple attributes (e.g. amount of money gained, probability). These new findings ground the behavioral process of intransitivity to a network of brain areas.
- We developed a novel model of memory consolidation and semantic memory formation based on algorithms from computational linguistics, that we mapped onto biologically plausible neural dynamics. This model is able to reproduce many experimental data relative to semantic memory.

Other Highlights

1. The group published 5 papers in high-impact journals, viz. Plos Biology (2X; Huijbers et al.; Lansink et al.), Nature Neuroscience (1X, Peyrache et al, featured in Nature Reviews Neuroscience 10, 546-547.) and J. Neuroscience (2X; Van Duuren et al.; Pennartz et al.).

2. Several papers received extensive coverage in international newspapers, internet bulletins and national radio broadcasts and the paper by Huijbers et al. (2009; PLoS Biology) was selected for a video lab demonstration on display at several science musea in e.g. Vancouver, Chicago, New York and Cleveland).

3. Cyriel Pennartz was appointed board member of a committee of the Netherlands Organization for Scientific Research (NWO) for interdisciplinary projects (Medical, Chemical, Life and Exact Sciences).

4. Grants acquired: Midsize equipment grant from the Netherlands Organization for Scientific Research (NWO); Collaborative Grant from the Cognition Spearhead Program of the University of Amsterdam (postdoc fellowship).

5. Francesco Battaglia was invited speaker at the Physics@FOM conference, Veldhoven, Spring Hippocampal Research Conference, Verona, Italy, CNS (Computational Neurosience conference, Berlin, Germany, and gave an invited lecture at the Bernstein Center for Computational Neuroscience, Goettingen, Germany.

6. Agreement on Book contract with MIT Press (Pennartz).

7. Several international Symposia and workshops were organized and chaired, including "Corticostriatal interactions during learning and memory processing" at the Society for Neuroscience, Chicago. U.S.A. (Pennartz). Battaglia was invited speaker at the Spring Hippocampal Research Conference, Verona, Italy.

Future Prospects

- We aim to disrupt memory consolidation and extra-hippocampal replay by electrical intervention of hippocampal processing in rats. The results will be used to develop novel methods for intervening with anxiety and PTSD-like disorders.
- The *in vivo* 2-photon imaging technique, combined with bulk labelling of neurons with Calcium-indicator dyes, will permit us to study multimodal interactions in the population dynamics of sensory neurons in the rat neocortex. Visual processing will be compared across awake, anesthetized and sleep states in mice, and we further aim to study ensemble activity at high spatial resolution in a more evolved type of cortex, i.e. of ferrets.
- Furthermore, the role of Orbitofrontal NMDA receptors in mediating neural coding of reward expectancy will be elucidated.
- We aim to make further ensemble recordings from mutant mouse brains, yielding indications about the neural mechanisms of spatial memory, self-localization, short- and long-term consolidation. Recordings from several genetically modified mouse lines will be completed (e.g. Arc & FMR-1 genes). Ensemble recordings from mice with hippocampal NMDA-receptor deletions will be completed. This project will also be the test-bed for the development of a wireless electrophysiology recording system.
- We plan a new series of experiments investigating the interaction between the hippocampus and prefrontal cortex during sleep, by using Local Field Potential and Current Source Density Analysis methods.
- We are currently following up on our recent fMRI experiments using transcranial magnetic stimulation, which allows us to temporarily disrupt the brain regions that were active in the fMRI experiments. We are also examining the effects of physiological variables, such as respiration and heart rate, on the fMRI signal and their relation with cognitive performance.
- The question of how neural assemblies in the brain cooperate to generate multi-sensory (visual-tactile) representations will be pursued using ensemble recording techniques applied to several neocortical and hippocampal recording areas simultaneously. We will study how information from different sensory modalities is being integrated along the sensory neocortical-to-hippocampal hierarchy, using optogenetic techniques in combination with electrophysiology. Theoretical and modelling work on perception-memory interactions will be strengthened.
- Novel experiments will target how brain systems (in particular, the hippocampus) represent data on external agents relative to the representation of the organism´s own state.

Cellular and Systems Neurobiology

Chairholder: Prof.dr W.J. Wadman

Dr. J. A. van Hooft	Assistant Professor
Dr. J. A. Gorter	Assistant Professor
Dr. T. R. Werkman	Assistant Professor
Dr. N. L. M. Cappaert	Assistant Professor

Introduction

Excitability is still the most prominent property of the nervous system. How ion-channels are organized and quantitatively balanced in the neuronal membrane, how they lead to neuron specific firing patterns and how these can be modulated at different times scales (plasticity) belong to the most exciting problems in neuroscience that can now be solved in a multidisciplinary approach. Neurons communicate with each other through a variety of synapses. To provide minimal functionality neurons need to be combined in small circuits. We have organized our research around a few well defined topics in the realm of neuronal excitability. Our core approach is functional electrophysiological one (from patch-clamping to *in vivo*). State-of-the-art optical techniques (Ca-imaging, Voltage Sensitive Dyes) and various multi-contact electrode recordings allow the analysis of population activity. When needed, collaborations provide anatomical, immuno histochemical, molecular, genetic and behavioural expertise.

The first of our three major research lines studies the fundamental properties of the 5-HT3 receptor and tries to understand its functional role in local circuits and development. Molecular techniques produced mice in which the 5-HT3 receptor expressing neurons are labelled with GFP and can be studied efficiently. This has opened a wide range of possibilities to investigate the role of this receptor in functionally connected neurons and also its highly specific role in cortical column formation.

The second research line studies epilepsy e.g. seizure generation, epileptogenesis (micro-array technology) and pharmacoresistance. The latter topic we approach from two sides: a) (non-)penetration of druge sia the blood-brain-barrier and b) modification of drug targets, mainly sodium channels. These studies are of high clinical relevance and we strengthen them through a side appointment at the Academic Hospital in Ghent and intense collaboration with the epilepsy center in Heemstede (SEIN). The therapeutic potential of deep brain stimulation is investigated in patients and in animal models.

The third research line concentrates on specific pharmacological modulation of neuronal circuits. A new line that focuses on the role of the endocannabinoids system has been started. We support the activities of a spin-off company Sensocom.

Most of our experiments are supported by computer modeling, focusing on single cell excitability in relation to the direct chemical surrounding of the neuron as well as on the adaptive strategies for excitability that optimize the working range of active neurons. In the latter case we try to extrapolate the consequences of single cell strategies to larger neuronal networks. The combination of theoretical and experimental work has proven to be very fruitful in the scientific setting of SILS and the FNWI.

Research Highlights

Within the research line on epilepsy projects, both dealing with potential sources of pharmaco resistance came to a successful finish this year. The long standing study that concentrated on the role of the sodium channel in epilepsy and in pharmacoresistance has completed a large study where the responses of different sodium channel subunit types to the standard collection of anti-epileptic drugs was investigated with state-of-the-art patch clamp techniques. We observed considerable differences that open possibilities for therapeutic strategies. A new project subsidised by NEF has started to this aim. In a second project the role of the blood brain barrier, which under normal conditions forms an almost impassable barrier to the brain was investigated. Special proteins remove unwanted foreign objects that leak through the barrier and a lot of pharmaceuticals share this fate. However, in particularly during epilepsy, large leakage of the BBB may occur in particular during and after seizures.

On the other hand such events also up regulate the protein with the barrier function. Erwin van Vliet carefully investigated this delicate balance and also manipulated the proteins involved in order to understand their role. The challenge was also to find differences in transport into the brain for classical and new anti-epileptic drugs, which has potential therapeutic value. After successful defence of this thesis Erwin continued as a post-doc on this project.

The studies on homeostatic scaling of brain excitability were restarted with three new project lines: one that aims at revealing the molecular mechanisms behind the increase/decrease of HCN expression (in collaboration with prof. Tallie Baram in Irvine, CA) funded by NEF, one that aims at theoretical understanding on how such a mechanism can be incorporated in large networks without serious negative consequences for stability, learning and memory in such networks and one project that aims at applying this knowledge in therapeutic strategies in particular involving deep brain stimulation. The link with the clinic in Ghent proved to be very useful in this sense.

The use of Voltage Sensitive Dyes for parallel recording from large numbers of sites in (neuronal slice) networks has finally surpassed the level of technical developments and a first study that proves its use as a technique to understand functional connectivity between larger brain structures was published. We predict that this technique will be incorporated in many other research projects as it is the best way investigate synchronization in large neuronal populations (epilepsy) as

pilots show that it is quite possible to identify the cortical columnar organization (5-HT3 project) and as it might be the best way to determine the spatial extend of functional stimulation.

Finally the series of studies that used modelling, mainly at the cellular level, to understand the generation of epileptic seizures, spreading depression and the role of ion homeostasis in these events, was completed and finished with theses defences. In a new project on computational modelling we will investigate how the cellular knowledge can best be expanded to understand network behaviour.

Other Highlights

>>Yaov Noam received the Unilever research prize for this experimental work.

>>Taco Werkman acquired and started a large research grant in the context of the Top Institute Pharma and in collaboration with Solvay Pharmaceuticals.

>>Hans van Hooft acquired an ALW grant to further investigate the role of the 5-HT3 receptor in columnar cortical development.

>>Jan Gorter acquired a NEF grant to continue the studies on the role of inflammation in epileptogenesis.

Future Prospects

The almost complete renewal of the AIO crew in our group has lead to a considerable redefinition of the project lines, in light of current international developments. As all lines were very successful in acquiring external funding there was no reason to limit our efforts; the refocus on basis mechanisms of phenomena with strong clinical relevance (epileptogenesis, pharmaco resistance Deep Brain Stimulation, Cortical development, Cannabinoid modulation) will therefore be continued with fresh spirits. The fact that we are strongly supported by at least three industrial partners underscores the societal relevance of the questions we are dealing with.

Hormonal Regulation of Signal Transduction in the Brain

Chairholder: Prof.dr M. Joëls

Dr. P.J. Lucassen	Associate Professor
Dr. H. Krugers	Assistant Professor
Dr. H. Karst	Researcher

Introduction

Group Lucassen/Krugers (remaining members of the former group of Marian Joels)

Research of the group focuses on the effects of stress on the brain, in particular on structural and functional changes like neurogenesis and synaptic plasticity, and on the relevance of such changes for cognition and diseases like depression.

Current status; a period of transition
With the leave of Marian Joels to Utrecht, the teaching load has further increased and the remaining members of the group face several new challenges in terms of teaching and research. Despite this and the move of the lab and animal facility to the new building, the group has kept up a very good output in 2009, and managed to publish many high quality papers in a.o. J. Neurosci and Nature Rev Neurosci.

Research Highlights

Early life stress increases the risk for psychopathology in adult life. We tested if severely adverse early life stress reduces structural and functional plasticity in adult life. After maternal deprivation at postnatal day 3, reduced levels of adult hippocampal neurogenesis and an altered dendritic tree organization were found in adult animals. These structural changes were paralelled by impaired learning of a spatial task, but by improvements in network properties and emotional learning in a high-stress environment. This shows that adversity early in life does not always impair functionality but can even improve emotional forms of memory and thereby prepare the organism to perform optimally when exposed to stressful conditions in adulthood (Oomen et al., J Neurosci, in press 2010).

Other Highlights

The group has further improved visibility by organizing several master classes and scientific meetings, and by their membership of boards of CSCA, NEURAD, ISAO, ONWA, KNAW, NWO, Neurofederation. They further obtained external funding from the Alzheimer (ISAO) and Parkinson Foundation (IPF), Corcept and the KNAW. Group members further received numerous invitations to give lectures and write papers and act as reviewer for major journals like J Neuroscience, PNAS, Nature and Science.

Grants Obtained

- International Stichting Alzheimer Onderzoek, Euro 150.000,-
- Royal Academy of Science, Euro 30.000,-
- International Parkinson Foundation, Euro 138.000,-
- Extension of support from Corcept Inc (with M Joels), Euro 25.000,-
- Collaborative PhD project with Gothenburg University Sweden, Euro 200.000,-

Aims for the coming years

>>Further develop our research line into the consequences of stress during early life for structural plasticity and cognition at an adult age.
>>Extend these lines into models of diseases like depression, epilepsia and dementia.
>>Extend the research on neurogenesis in rodent models also to other brain areas like the amygdala and cortex and in a translational perspective, also to human brain.
>>Develop translational approaches to monitor and measure neurogenesis in the live human brain using MRS spectroscopy in relation to development and depression.
>>Incorporate and develop tools to manipulate adult neurogenesis in vivo using molecular and viral tools.

Research Cluster

Life Science Technologies

Mass Spectrometry of Biomacromolecules

Chairholder: Prof.dr. C.G. de Koster

Dr. L. de Jong Associate Professor
Dr. L.J. de Koning Assistant Professor

Introduction

Future progress in the life sciences will heavily depend on the integration of knowledge from the fields of chemistry, physics, mathematics, (bio)informatics and biology. Within the framework of the UVA priority area Systems Biology we developed together with prof Hellingwerf (SILS) and prof Brul (SILS) the research theme molecular systems biology of micro-organisms. Our molecular systems biology of micro-organisms programme demands, amidst others omics data such as transcriptomics and metabolomics (and their modeling), proteome wide quantitative insight in protein synthesis- and degradation rates, concentrations and resolution of the protein/macromolecule interaction networks of the cell. The participating groups focus at the cellular level on an analysis of response to environmental signals, be they from the extracellular or intracellular milieu, governing cell survival, growth, the formation of desired products as well as unwanted microbial growth in food products and microbial infection. Analyses are performed at the level of (i) whole cells, (ii) cellular compartments such as the yeast cell wall, mitochondria and the Bacillus spore coat and (iii) macromolecular protein complexes, including Bacillus RNA polymerase and the stressosome.

SILS Mass Spectrometry of Biomacromolecules focuses in the context of microbial proteomics on three research themes that adhere to the study of cellular response to external signals and that are crucial for our molecular systems biology ambition. We study (i) post-transcriptional regulation of gene expression by analyzing quantitatively protein synthesis and degradation rates. We develop (ii) new analytical strategies for the experimental evaluation of models of the 3-D structure of protein complexes. We aim at insight in (iii) adaptation of the cell surface proteome of fungi and bacteria. SILS-MS is developing advanced and innovative, mass spectrometry-based proteomics technology that is designed for these research areas. Our technology is not confined to the field of microbial proteomics and is widely applicable to molecular systems biology. Here, we have long term

collaborations with the SILS plant groups where we study fungal pathogen – plant interaction and identify target proteins upon stress.

Research Highlights

A mass spectrometric method is developed to identify and quantify several hundreds of newly synthesized proteins in *Escherichia coli* upon pulse labeling cells with the methionine analogue azido homoalanine (AZHAL). For the first 30 minutes after inoculation, a methionine-auxotrophic strain grows equally well on azhal as on methionine. Upon a pulse of 15 minutes and digestion of total protein, azhal-labeled peptides are isolated by a retention-time shift between two reversed phase chromatographic runs. The retention time shift is induced by a reaction selective for the azido group in labeled peptides using tris-(2-carboxy-ethyl)-phosphine. Selectively modified peptides are identified by LC-tandem MS. We identified 527 newly synthesized proteins. These proteins are representative of all major Gene Ontology categories.

A general method is developed to sequester peptides containing azides from complex peptide mixtures, aimed at facilitating mass spectrometric analysis to study different aspects of proteome dynamics. The enrichment method is based on covalent capture of azide-containing peptides by the azide-reactive cyclooctyne (ARCO) resin and is demonstrated for two different applications. Enrichment of peptides derived from cytochrome c treated with the azide-containing cross-linker bis(succinimidyl)-3-azidomethyl glutarate (BAMG) shows several cross-link containing peptides. Sequestration of peptides derived from an Escherichia coli proteome, pulse labeled with the bio-orthogonal amino acid azidohomoalanine as substitute for methionine, allows identification of numerous newly synthesized proteins. Furthermore, the method is found to be very specific, as after enrichment over 87% of all peptides contain (modified) azidohomoalanine.

Research aims for the coming year

Focal points in our MS research program are as mentioned above (i) systematic analysis of protein-protein interactions, (ii) post-transcriptional regulation of gene expression, and (iii) host-fungal pathogen interactions. In program (i) we will extent our cross-link methods to assess the structure of larger protein assemblies (> 300 kDa). We will map interaction sites of initiation and elongation factors that modulate the activity of RNA polymerase and we will quantitate cross-links formed during initiation and elongation in an effort to detect conformational changes. (ii) In collaboration with Prof. Hellingwerf and Prof. Teixeira de Mattos we will use our mass spectrometric AZHAL pulse labeling method to unravel the regulatory circuit underlying the transition of aerobic to (semi)-anaerobic metabolism in *E. coli* and metabolic labeling to study carbon catabolite repression in *E. coli*. Parallel to our diagonal chromatography approach we will develop selective and sensitive methods for sequestration of AZHAL containing peptides in total *E coli* cell lysates and capture of BAMG cross-linked peptides in complex biomatrices. (iii) The MS group will further explore the question how mass spectrometry in combination with novel purification strategies and bioinformatics tools can provide detailed quantitative

structural and functional information about cell wall proteins of Candida albicans and other fungi. In the framework of the EC FINSysB project we will focus on the quantitative cell wall protein composition of Candida albicans to identify new leads for novel anti-*Candida* vaccines, drugs and diagnostic markers. Furthermore, we will extent research line (iii) in collaboration with Prof. Brul to the functional characterization of spore coat proteins of *B. subtilus.* We will continue the productive collaborations with the groups of the SILS-plant cluster and our external national and international partners.

Biosystems Data Analysis

Chairholder: Prof.dr. A.K. Smilde

Dr. H.C.J..Hoefsloot	Associate Professor
Dr. J.A. Westerhuis	Assistant Professor
Prof. dr. A.H.C.van Kampen	Professor (0.2 fte)

Introduction

General goal
Developing and validating methods for organizing, summarizing and visualizing complex biological data.

The research is divided in three connected themes: Semantic Biosystems, Data Fusion and Networks & Dynamics. We apply our methods in diverse areas of systems biology focusing mainly on microbiology, nutrition and medical biology.

Semantic Biosystems (Antoine van Kampen)
Well-structured, accessible and integrated information is crucial for disciplines like genomics and systems biology. To support these disciplines, we develop novel information management approaches based on cutting edge Semantic Web standards in a framework that allows the construction of high quality domain-specific knowledge bases.

Data Fusion (Johan Westerhuis)
To understand the functionality of complex biological systems, different types of measurements have to be combined with systems information stored in a knowledge base. We develop data analysis methods that are able to find biologically relevant patterns in these data that on the one hand match the systems information and on the other hand generate new insights.

Networks & Dynamics (Huub Hoefsloot)
In a biological system molecules interact. These interactions, the network, causes the system to change over time. We develop methods to reverse engineer networks from

time-resolved functional genomics data. The networks can be metabolic networks, protein-protein interaction networks, gene-regulatory networks or association networks.

Research Highlights

General
Thanks to our involvement as core-partner in the Netherlands Metabolomics Centre we obtained a subsidy of 2.3 mln euros. This resulted in 5 postdoc and 2 PhD positions for the group. Moreover, we received funding from NISB (PhD student) and NBIC (PhD and postdoc).

Semantic Biosystems
Information management research is subject of lively research in bioinformatics and e-science and essential for genomics and systems biology. As part of the BioExpert project we develop a Semantic Web-based information management framework to enable the development of specific knowledge bases. The peroxisome knowledge base (PxKB) is a first example of this. A SKOS peroxisome vocabulary (PxVO) functions as a central information hub that connects various pieces of information. We setup a TripleStore that supports RDF Schema inferencing and querying. It contains the PxVO, manually curated concept maps and (subsets of) UniProtKB, GO, ChEBI, Mesh and PubMed. Curation was done by prof. Ronald Wanders (Genetic Metabolic Disease, AMC). We are now in a prime position to be one of the first dedicated linked data providers in life sciences in the world! Linked data comprises best practices for exposing, sharing and connecting pieces of data, information and knowledge on the Semantic Web using URIs and RDF. We developed initial versions of a concept map editor and browser. We started a collaboration with prof. Bwee-Tien Poll-Thé (Pediatric Neurology, AMC) and prof. Peter Barth (Pediatrics, AMC) to extend PxKB towards peroxisomal disorders. BioRange-II funding was acquired (PI Dr. Johan Westerhuis) to integrate phenol degradation knowledge base with grey statistical modelling.

Data Fusion
Thanks to the genomics era a wealth of information can be obtained from biological systems in the form of measurements of body fluids or tissue on the gene, protein and metabolite level. Furthermore, physiological parameters and environmental conditions can be quantified on a regular basis. In the field of human systems biology, we introduced nutrikinetics as a measure for bioconversion capacity of polyphenols in humans. By combining data from in-vitro models and a human intervention trial combined with a one-compartment nutrikinetic model strong and weak polyphenol metabolizers could be identified. In another project we analyzed flux distributions through reactions in a metabolic network of L. lactis for several environmental conditions. Variant and invariant reactions could be identified when the medium (rich – minimal) was varied as well as the growth condition between aerobic, anaerobic and aerobic respiratory (in the presence of oxygen under addition of haem, which aids the transport of oxygen into L.lactis).

Networks & Dynamics
In 2009, crossfit analysis was introduced. This is a novel method to characterize the dynamic variation of a biological system after a perturbation. This analysis was introduced for a plant example but it can be used for all types of living organism. It uses the idea to build global and local models for the different groups. These models are then compared in a systematic manner and biological conclusions are drawn. In collaboration with the LUMC, methods to built association networks between rapidly measured hormone levels in blood were developed. The essentia dynamics and regulation of such systems was captured and visualized in networks. These appeared to be highly relevant and interpretable. Papers are underway.

Research aims for the coming year

General
Filling in all vacancies.

Semantic Biosystems
We will further develop the BioExpert information management framework and the Peroxisome Knowledge Base. We will develop initial applications in the field of peroxisomal disorders, grey statistical models (BioRange-II) and systems biology (NCSB). In addition, we expect to increase the number of joint projects between the Bioinformatics Laboratory (AMC) and the BioSystems Data Analysis group.

Data Fusion
In the coming years we aim to develop new tools for grey model analysis in which systems information can be combined with several sources of systems data. We will build a knowledge base for the polyphenol degradation pathways in the human gut taking into account the gut bacteria that are present. This knowledge base will be used in a grey modeling approach to explore bioavailability of polyphenol catabolism in much more detail and can be used in a personalized nutrition framework.

Networks & Dynamics
In the next few years we are going to develop tools to analyze the interactions of bio-molecules and the changes of these interaction over time. For this we will use and adapt concepts for the analysis of covariation- and correlation matrices. Especially the changes in covariance and correlation over time will have our attention. Whereever possible, a priori knowledge of known parts of networks and network modules will be incorporated in the data analysis.

Micro Array Department and Integrative Bioinformatics Unit

Group leader: Dr. T.M. Breit

Dr.Ir.R.A.Wittink Project management "wet-lab"
Dr.M.J. Jonker Project management "dry-lab"

Introduction

MicroArray Department (MAD) & Integrative Bioinformatics Unit (IBU):

Microarray technology is a well-established tool in the analysis of genome-wide gene-expression studies. The ultimate goal of a microarray experiment is to simultaneously investigate the expression of all genes of a specific organism, in a cell type, during specific growth or stress conditions. This enables study of complex cellular mechanisms or identification and use biomarkers. Transcriptomics biomarkers are genes whose expression profile can be used for diagnostic purposes or to monitor and predict cellular processes. Because microarray experiments produce a vast amount of data, extensive bioinformatics infrastructure, methods and expertise are needed to cope with these data effectively. Microarray bioinformatics comprise data-handling (storage and exchange), data-preprocessing (normalization and validation), and data-analysis (clustering, biomarker selection, etc.).

The MAD-IBU consist of a microarray technology section (Wet-lab) with ~5 specialists that provide transcriptomics service & support and perform microarray technology R&D; a microarray data-analysis section (Dry-lab) with ~6 bioinformaticians that provide transcriptomics data analysis service & support and performs bioinformatics R&D; Together, the MAD operates as a transcriptomics technology and bioinformatics expertise centre and core facility for UvA scientists, as well as external academic and industrial customers. The MAD is an official Affymetrix Agilent Service Provider.

The focus of the Wet-lab R&D is to improve the microarray technology for transcriptomics with a strong focus on array controls and sample size reduction. We aim to eventually analyze all kinds of single cells by microarray technology. The focus of the Dry-lab is on the bioinformatics and e-bioscience methods, tools and infrastructure necessary to perform advanced transcriptomics data-analysis starting from array design until publication. Another important focal point for the whole group is design-for-experimentation. Performing well-designed range finding experiments should elucidate the role of time and space in microarray transcriptomics experiments. To this end, MAD-IBU participates in three nationwide projects: "BioRange", a nationwide bioinformatics NBIC research project; "BioAssist", a national bioinformatics NBIC support programme and "Virtual Lab for e-Science (VL-e)", the Dutch e-science project in the field of ICT infrastructure and methods.

Research Highlights
The Wet-lab:
Developed a microarray protocol for small-sample transcriptomics analysis on human skin.
Introduced a new microarray platform; NimbleGen/Roche.
Acquired a new, fully automated high-throughput microarray platform; Affymetrix, GeneTitan.
The Dry-lab:
Developed a complete microarray design pipeline from DNA sequence to probe.
Developed many necessary advanced microarray probe controls.
Performed many data-analysis experiments for biologists.

Other Highlights
The whole group further strengthened the strategic collaborations with several external research organisations: Laboratory for Health Protection Research, RIVM, (Bilthoven); Medical Microbiology, UMC (Utrecht); ACTA, VU-AMC (Amsterdam); Molecular Cell biology, UL, (Leiden).

Research aims for the coming year

- Analyze maternal RNAs in unfertilized Zebrafish and human eggs.
- Analyze the transcriptomics of the earliest stages of Zebrafish and human embryogenesis.
- Perform a hallmark time-axis microarray experiment on Zebrafish.
- Perform several range-finding experiments in the context of design-for-experimentation.
- Extend the MicroArray Problem Solving Environment for microarray data analysis and interpretation
- Become a central player in the national e-bioscience domain, such as the FNWI zwaartepunt e-science and the e-Science Research Centre.
- File at least 1 patent on microarray technology innovations.

Write > 15 (collaborative) research articles.

Management

Finance

The integrated results for 2009 show an operating shortage of 342 k€ where a negative result of 1049 k€ was budgeted. Revenues and costs over 2009 are difficult to compare directly with previous years. This is due to changes in the financial methodologies used by the UvA.

Year	2001	2002	2003	2004	2005	2006	2007	2008
University funding *	5838	6131	7364	8987	7577	13234	12795	13848
External funding	3852	3883	4474	6167	4515	4701	4952	5489
total revenues	9690	10014	11838	15154	12092	17935	17747	19337
Personnel costs	7096	7465	8919	9626	9122	12816	13918	14448
Bench fees	2236	2450	3310	4989	2729	5362	4138	5240
total costs	9332	9915	12229	14614	11851	18178	18056	19688
result	358	99	-391	540	241	-243	-309	-351

* All amounts are given in K Euro.

Figure: Graphic representation of revenues and costs of the Swammerdam Institute for Life Sciences, in k€, for the years 2001-2009. In 2006, the university changed to a new financial system in which budgets were increased and full costs were calculated.

	2009
university funding *	13580
external funding	5084
total revenues	18645
personnel costs	11191
bench fees and overheads	7795
total costs	18986
result	-342

In 2009 several financial changes were implemented. Reallocation of financial resources within the university led to budget cuts in the Faculty of Science. In 2009, SILS received 429 k€ less university funding. Of this 429 k€ reduction, 318 k€ was a direct result of these budget cuts. The remaining budget (12.448 k€) was split in two parts: 2565 k€ (costs for education) and 9883 k€ (for all remaining costs).

After this, the "allocation model" was implemented. In the allocation model, institutes earn part of their budget based on parameters such as number of PhD degrees, amount of acquired external funding and number of master degrees. The allocation model was introduced in such a way that the budget of 9883 k€ itself was not altered.

The acquired part of this budget was 3456 k€. The remaining 6427 k€ is referred to as "basic" university funding. Acquired budget can in- or decrease, based on how successful the institute operates. The basic budget is supposed to be stable. But if future budget cuts are unavoidable, these budget cuts are possibly a percentage of the basic budgets of the institutes.

Year	2008		2009		2009		2009		2010
		step 1		step 2		step 3		step 4	
University funding	12851	→	12448	→	9883	→	6427	→	5989
Acquired budget	0		0		0	→	3456	→	3999
Education	0		0	→	2565		2565		2565
Total	12851		12448		12448		12448		12553

Figure: changes in university funding and overview of financial methodology changes implemented in 2009.
Step 1: from 2008 → 2009: budget cut 429 k€.
Step 2: 12.448 k€ of university funding is split in 2565 k€ for education and 9883 for remaining costs.
Step 3: the 9883 k€ remainder is spilt in an acquired budget (3437 k€) and 6446 k€ basic budget.
Step 4: basic university funding is cut , but the acquired budget increased (due to e.g. more PhD diploma's)

Funding

The funding system of Dutch universities distinguishes three different kinds of funding resources. These are referred to as so called "funding sources" and are numbered one to three. Resources originating from the university itself are referred to as the first funding source. External funding is divided into funding from the Netherlands Organization for Scientific Research (second funding source) and money originating from all other resources such as EU and contract research (third funding source).

	2003	**2004**	**2005**	**2006**	**2007**	**2008**	**2009**
Revenues	7793	8987	7577	13234	12795	13848	13580
Costs	8291	8902	7357	13580	13259	14115	13845
Result	-498	85	220	-346	-464	-306	-265

Figure 1: representation of income and costs in the 1st funding source, in k€, for the years 2003-2009.

	2003	**2004**	**2005**	**2006**	**2007**	**2008**	**2009**
Revenues	2279	2303	2160	2032	2299	2434	1821
Costs	2279	2303	2160	2048	2226	2436	1713
Result	0	0	0	-16	73	-2	108

Figure 2: representation of income and costs in the 2nd funding source, in k€, for the years 2003-2009.

	2003	**2004**	**2005**	**2006**	**2007**	**2008**	**2009**
Revenues	1766	3864	2355	2669	2653	3055	3244
Costs	1659	3409	2334	2550	2571	3097	3429
Result	107	455	21	119	82	-42	-185

Figure 3: representation of income and costs in the 3rd funding source, in k€, for the years 2003-2009.

Figure 1 shows that in 2006, first funding source income and costs increased by almost 6000 k€ compared to 2005. This increase is the result of the introduction of a new university wide full-cost financial system. Essentially, overhead costs that were not calculated in previous years such as housing and computer infrastructure were calculated to the institute as of 01-01-2006. Simultaneously budgets were increased.

Funding from the Dutch Organization for Scientific Research (2nd funding source) remains decreased in 2009. Third funding source income slightly increased in the past years. The numbers of 2004 profited from two major incidental incomes and explain the increase numbers of 2004. The first incidental revenue in 2004 existed of 1045 k€ that SILS received for its role as coordinator of an EU program. This was transferred directly to other partners in this program. The second was a 404 k€ result of the successful sales of a spin-off company.

Personnel

The university aims at a more equal division of males and females in the staff at all levels. At the level of PhD students the male: female ratio is about 40:60 at SILS. At the post doctoral level this is 80:20. About 70% of the assistant professors is male. In 2009, professor Marian Joels, SILS' only female full professor, moved to the University of Utrecht. Age wise our staff is spread over the full range from starting PhD, to people who are (close to) retiring.

Infrastructure

In 2009, the Swammerdam Institute for Life Sciences still was divided over two locations In the early summer of 2009, the first part of the institute moved to this new location. Start-up problems caused significant delay for several research lines. SILS tried to minimize the effects on the careers of several researchers with a temporary appointment by extending the duration of their contracts. Positive parts of the new building are the brand new labs in a beautiful building. In 2010, the rest of the institute's employees will be united in the new building.

Appendix 1
Research Cluster The Living Cell

Molecular Microbial Physiology

Key publications

Angermayr, S.A., Hellingwerf, K.J., Lindblad, P. and Teixeira de Mattos, M.J. (2009) Energy biotechnology with cyanobacteria. *Curr Opin Biotechnol.* 20(3): 257-263.

Avila Perez, M., Vreede, J., Tang Y., Bende, O., Losi, A., Gartner, W., Hellingwerf, K.J. (2009) In vivo mutational analysis of YTVA from *bacillus subtilis*: Mechanism of light-activation of the general stress response. *J. Biol. Chem.* 284, 24958-64.

Bekker M, de Vries S, Ter Beek A, Hellingwerf KJ and Teixeira de Mattos MJ (2009) Respiration of *Escherichia coli* can be fully uncoupled via the non-electrogenic terminal cytochrome bd-II oxidase. *J Bacteriol.* 191(17):5510-5517.

PhD Thesis

Bekker, M. (2009, November 05). Respiratory electron transfer in *Escherichia coli*: components, energetics and regulation. UvA Universiteit van Amsterdam (150 pag.). Prom./coprom.: prof.dr. K.J. Hellingwerf & prof.dr. M.J. Teixeira De Mattos.

Patent application

M. Bekker, M.J. Teixeira de Mattos & K.J. Hellingwerf (2009) A Gram-negative bacterium, its generation and its use to test oxygen sensitivity of metabolic pathways -- P6024762EP

Academic publications (refereed)

Alexandre, M.T.A., Domratcheva, T., Bonetti, C., Wilderen, L.J.G.W., Grondelle, R. van, Groot, M.L., Hellingwerf, K.J. & Kennis, J.T.M. (2009). Primary reactions of the LOV2 domain of phototropin studied with ultrafast mid-infrared spectroscopy and quantum chemistry. *Biophys. J.*, 97(1), 227-237.

Alexandre, M.T.A., Grondelle, R. van, Hellingwerf, K.J. & Kennis, J.T.M. (2009). Conformational heterogeneity and propagation of structural changes in

the LOV2/Jα domain from Avena sativa phototropin 1 as recorded by temperature-dependent FTIR spectroscopy. *Biophys. J.*, 97(1), 238-247.

Angermayr, S.A., Hellingwerf, K.J., Lindblad, P. & Teixeira De Mattos, M.J. (2009). Energy biotechnology with cyanobacteria. *Curr. opin. biotechnol.*, 20(3), 257-263.

Avila Perez, M.E., Vreede, J., Tang, Y., Bende, O., Losi, A., Gartner, W. & Hellingwerf, K.J. (2009). In vivo mutational analysis of YTVA from Bacillus subtilis: Mechanism of light-activation of the general stress response. *J. Biol. Chem.*, 284(37), 24958-24964.

Bekker, M., Vries, S. de, Beek, A.S. ter, Hellingwerf, K.J. & Teixeira De Mattos, M.J. (2009). Respiration of Escherichia coli can be fully uncoupled via the non-electrogenic terminal cytochrome bd-II oxidase. *J. Bacteriol.*, 191(17), 5510-5517.

Cate, J.M. ten, Klis, F.M., Pereira-Cenci, T., Crielaard, W. & Groot, P.W.J. de (2009). Molecular and cellular mechanisms that lead to Candida biofilm formation. *J. Dent. Res.,* 88(2), 105-115.

Deng, D.M., Hoogenkamp, M.A., Cate, J.M. ten & Crielaard, W. (2009). Novel metabolic activity indicator in Streptococcus mutans biofilms. *J. Microbiol. Methods,* 77(1), 67-71.

Deng, D.M., Urch, J.E., Cate, J.M. ten, Rao, V.A., Aalten, D.M.F. van & Crielaard, W. (2009). Streptococcus mutans SMU.623c codes for a functional, metal-dependent polysaccharide deacetylase that modulates interactions with salivary agglutinin. *J. Bacteriol.*, 191(1), 394-402.

Hellingwerf, K.J. & Teixeira De Mattos, M.J. (2009). Alternative routes to biofuels: Light-driven biofuel formation from CO2 and water based on the 'photanol' approach. *J. Biotechnol.*, 142(1), 87-90.

Hendriks, J.C. & Hellingwerf, K.J. (2009). pH Dependence of the Photoactive Yellow Protein Photocycle Recovery Reaction Reveals a New Late Photocycle Intermediate with a Deprotonated Chromophore. *J. Biol. Chem.*, 284, 5277-5288.

Hoff, W.D., Horst, M.A. van der, Nudel, B.C. & Hellingwerf, K.J. (2009). Prokaryotic phototaxis. *Methods Mol. Biol.*, 571, 25-49.

Horst, M.A. van der, Stalcup, P.P., Kaledhondar, S., Kumauchi, M., Hara, M., Xie, A., Hellingwerf, K.J. & Hoff, W.D. (2009). Locked chromphore analogs reveal that photoactive yellow protein regulates biofilm formation in the deep sea bacterium *Idiomarina loihiensis*. *J. Am. Chem. Soc.*, 131(47), 17443-17451.

Kramer, G., Sprenger, R.R., Back, J.W., Dekker, H.L., Nessen, M.A., Maarseveen, J.H. van, Koning, L.J. de, Hellingwerf, K.J., Jong, L. de & Koster,

C.G. de (2009). Identification and quantitation of newly synthesized proteins in Escherichia coli by enrichment of azidohomoalanine-labeled peptides with diagonal chromatography. *Mol Cell Proteomics,* 8(7), 1599-1611.

Levering, J., Fiedler, T., Bekker, M., Hugenholtz, J., Kreikemeyer, B. & Kummer, U. (2009). Modelling the glycolytic pathway in *Streptococcus pyogenes. Int. J. Med. Microbiol.*, 299(suppl.46), 19.

Rupenyan, A., Stokkum, I.H, Arents, J.C., Grondelle, R. van, Hellingwerf, K.J. & Groot, M. de (2009). Reaction pathways of photoexcited retinal in proteorhodopsin studied by pump-dump-probe spectroscopy. *J. Phys. Chem., B*, 113(50), 16251-16256.

Rzeznicka, I.I., Wurpel, G.W.H., Bonn, M., Horst, M.A. van der, Hellingwerf, K.J., Matsunaga, S., Yamada, T. & Kawai, M. (2009). Observation of photoactive yellow protein anchored to a modified Au(111) surface by scanning tunneling microscopy. *Chem. phys. lett.*, 472(1-3), 113-117.

Martijn Bekker, Svetlana Alexeeva, Wouter Laan, Gary Sawers, Joost Teixeira de Mattos and Klaas Hellingwerf (2009) The ArcBA two-component system of *Escherichia coli* is regulated by the redox state of both the ubiquinone and the menaquinone pool. *J. Bacteriol.* 192(3): 746-754.

Avila-Pérez M, van der Steen JB, Kort R, Hellingwerf KJ (2009) Red light activates the sigma-B mediated general stress-response of *Bacillus subtilis* via the energy branch of the upstream signaling cascade. *J Bacteriol.* 192(3): 755-762.

Brooijmans, R.J.W., de Vos, W.M., and Hugenholtz. J. (2009) Electron transport chains of lactic acid bacteria – walking on crutches is part of their lifestyle. *F1000 Biology Reports* 1:34

Brooijmans, R.J.W., de Vos, W.M., and Hugenholtz, J. (2009) Lactobacillus plantarum WCFS1 electron transport chains. Applied and Environmental *Microbiology* 75: 3580-3585

Pastink, M.I., Teusink, B., Hols, P., Visser, S., de Vos, W.M. and Hugenholtz, J. (2009) Genome-scale model of *Streptococcus thermophilus* LMG18311 for metabolic comparison of lactic acid bacteria. *Applied and Environmental Microbiology* 75: 3627-3633

Santos F., Teusink, B., Molenaar, D., van Heck, M., Wels, M., Sieuwerts, S., de Vos, W.M., and Hugenholtz, J. (2009) Effect of amino acid availability on vitamin B12 production in Lactobacillus reuteri. *Applied and Environmental Microbiology* 75: 3930-3936

Brooijmans, R.J.W., Smit, B., Santos, F., van Riel, J., de Vos, W.M., and Hugenholtz, J. (2009) Heme and menaquinone induced electron transport in lactic acid bacteria. *Microbial Cell Factory* 8: 28-35

Santos, F., Teusink, B., de Vos, W.M., and Hugenholtz. J. (2009) The evidence that pseudovitamin B(12) is biologically active in mammals is still lacking - a comment on Molina et al.'s (2009) experimental design. *Journal Applied Microbiology* 107: 1763

Snoep JL, Mrwebi M, Schuurmans JM, Rohwer JM, Teixeira de Mattos MJ (2009) Control of specific growth rate in *Saccharomyces cerevisiae*. *Microbiology*155(5): 1699-707.

Maleki-Dizaji S, Holcombe M, Rolfe MD, Fisher P Green J, Poole RK, Graham AI (2009) SYSMO-SUMO consortium. *On line Journal on Bioinformatics* 10(1): 51-59

Invited lectures

Hellingwerf, K.J. (2009, June 29). 'Tactic' responses in bacteria to blue light. Düsseldorf, Germany, XVth International Conference on Photobiology.

Hellingwerf, K.J. (2009, April 22). 'Tactic' responses of bacteria to (blue) light. Papendal, the Netherlands, NVVM Meeting.

Hellingwerf, K.J. (2009, April 27). Biophysics and biochemistry of photoperception. Amsterdam, the Netherlands, VU University Amsterdam.

Hellingwerf, K.J. (2009, November 02). Duurzame productie van energie (brandstof). Amsterdam, the Netherlands, UvA VU Gemeente Amsterdam 'Kennis voor de Stad'.

Hellingwerf, K.J. (2009, October 14). Lifting photosynthesis out of the stone age. Noordwijkerhout, the Netherlands, 5th NISB Symposium.

Hellingwerf, K.J. (2009, March 18). Molecular microbial photophysiology. Buenos Aires, Argentina, Leloir Institute.

–

Hellingwerf, K.J. (2009, August 26). Molecular microbial physiology. Turin, Italy, KP7-satellite Meeting.

Hellingwerf, K.J. (2009, July 14). Photosensory proteins as vehicles to bridge computational biophysics and systems biology to initiate the field of synthetic biology. Freiburg, Germany, University of Freiburg.

Hellingwerf, K.J. (2009, November 06). Systems biology of photosynthesis. Amsterdam, the Netherlands, NISB.

Hellingwerf, K.J. (2009, March 31). The "Photanol" process: Cyanobacteria for simple solar fuel. Leiden, the Netherlands, Lorentz Center Workshop.

Hellingwerf, K.J. (2009, June 22). The archetype photochemistry relevant for biological signal transmission: E/Z isomerization.12. Düsseldorf, Germany, XVth Int.Conference on Photobiology.

Hellingwerf, K.J. (2009, November 20). The Photanol approach: Developing a third-generation biofuel production system. Delft, the Netherlands, Het Technologisch Gezelschap.

LeBlanc, J.G., Sybesma, W., Starrenburg, M., Sesma, F., de Vos, W.M., Savoy de Giori, G., and Hugenholtz, J. (2009) Supplementation with engineered Lactococcus lactis improves the folate status in deficient rats. Nutrition Epub November 18th

Maischberger, T., Mierau, I., Peterbauer, C.K., Hugenholtz, J. and Haltrich, D. (2010) High-Level Expression of Lactobacillus beta-Galactosidases in Lactococcus lactis Using the Food-Grade, Nisin-Controlled Expression System NICE. Journal of Agriculture and Food Chemistry Epub January 10th 2010

Book Chapter

Hendriks, J., Horst, M.A. van der, Chua, T.K., Ávila Pérez, M., Wilderen, L.J. van, Alexandre, M.T.A., Groot, M.-L., Kennis, J.T.M. & Hellingwerf, K.J. (2009). Photoreceptor proteins from purple bacteria. In C.N. Hunter, F. Daldal, M.C. Thurnauer & J.T. Beatty (Eds.), The purple phototrophic bacteria (Advances in photosynthesis and respiration, 28) (pp. 811-837). Dordrecht: Springer.

Membership editorial board

Teixeira De Mattos, M.J. (Ed.). (2009). FEMS Yeast Res..

Molecular Biology and Microbial Food Safety

Key Publications

Klis, F.M., Sosinska, G.J., de Groot, P.W. and **Brul, S**. 2009 Covalently linked cell wall proteins of *Candida albicans* and their role in fitness and virulence. *FEMS Yeast Research* 9: 1013-1028.

Orij, R., Postmus, J., TerBeek, A., Brul, S. and Smits, G.J. 2009. In vivo measurement of cytosolic and mitochondrial pH using a pH-sensitive GFP derivative in *Saccharomyces cerevisiae* reveals a relation between intracellular pH and growth. *Microbiol.* 155: 268-278.

Schuurmans, M.J., Hayali, A.S.N., Koenders, B.B. and Ter Kuile, B.H. 2009. Variations in MIC value caused by differences in experimental protocol. J. Microbiological Methods, 79, 44-47.

Hornstra, L., TerBeek, A., Smelt, J.P., Kallemeijn, W. and Brul, S. 2009. On the origin of heterogeneity in (preservation) resistance of *Bacillus* spores; input for a 'systems' analysis approach of bacterial spore outgrowth. Int. J. Food Microbiol. 134, 9-15.

PhD Thesis

Beek, A.S. ter (2009, June 04). Weak organic acid stress in Bacillus subtilis. UvA Universiteit van Amsterdam (204 pag.). Prom./coprom.: prof.dr. S. Brul & prof.dr. K.J. Hellingwerf.

Patent application

Beek, A.S. ter, Brul, S. and Vaart, M van der. Screening method for a preservative. no EP 1935984.

Academic publications (refereed)

Butler, G., Rasmussen, M.D., Lin, M.F., Groot, P.W.J. de, Klis, F.M. & Cuomo, C.A. (2009). Evolution of pathogenicity and sexual reproduction in eight Candida genomes. *Nature*, 459(7247), 657-662.

Cate, J.M. ten, Klis, F.M., Pereira-Cenci, T., Crielaard, W. & Groot, P.W.J. de (2009). Molecular and cellular mechanisms that lead to Candida biofilm formation. *J. Dent. Res.*, 88(2), 105-115.

Groot, P.W.J. de, Brandt, B.W., Horiuchi, H., Ram, A.F.J., Koster, C.G. de & Klis, F.M. (2009). Comprehensive genomic analysis of cell wall genes in *Aspergillus nidulans. Fungal Genet. Biol.*, 46(1), S72-S81.

Hornstra, L.M., Beek, A.S. ter, Smelt, J.P.P.M., Kallemeijn, W.W. & Brul, S. (2009). On the origin of heterogeneity in (preservation) resistance of Bacillus spores: Input for a 'systems' analysis approach of bacterial spore outgrowth. *Int. J. Food Microbiol.*, 134(1-2), 9-15.

Klis, F.M., Sosinska, G.J., Groot, P.W.J. de & Brul, S. (2009). Covalently linked cell wall proteins of *Candida albicans* and their role in fitness and virulence. *FEMS Yeast Res.*, 9(7), 1013-1028.

Moreno-Ruiz, E., Ortu, G., Groot, P.W.J. de, Cottier, F., Loussert, C., Prévost, M.C., Koster, C. de, Klis, F.M., Goyard, S. & d'Enfert, C. (2009). The

GPI-modified proteins Pga59 and Pga62 of *Candida albicans* are required for cell wall integrity. *Microbiology,* 155(6), 2004-2020.

Oomes, S.J.C.M., Jonker, M.J., Wittink, F.R.A., Hehenkamp, J.O., Breit, T.M. & Brul, S. (2009). The effect of calcium on the transcriptome of sporulating B.subtilis cells. *Int. J. Food Microbiol.*, 133, 234-242.

Orij, P.J., Postmus, J., Beek, A.S. ter, Brul, S. & Smits, G.J. (2009). In vivo measurement of cytosolic and mitochondrial pH using a pH-sensitive GFP derivative in *Saccharomyces cerevisiae* reveals a relation between intracellular pH and growth. *Microbiology*, 155(Pt1), 268-278.

Shen, T., Bos, A.P. & Brul, S. (2009). Assessing freeze–thaw and high pressure low temperature induced damage to Bacillus subtilis cells with flow cytometry. *Innov. Food Sci. and Emerg. Technol.*, 10(1), 9-15.

Wortman, J.R., Gilsenan, J.M., Joardar, V., Deegan, J., Clutterbuck, J., Andersen, M.R., Archer, D., Bencina, M., Braus, G., Coutinho, P., Döhren, H. von, Doonan, J., Driessen, A.J., Durek, P., Espeso, E., Fekete, E., Flipphi, M., Estrada, C.G., Geysens, S., Goldman, G., Groot, P.W.J. de, Hansen, K., Harris, S.D., Heinekamp, T., Helmstaedt, K., Henrissat, B., Hofmann, G., Homan, T., Horio, T., Horiuchi, H., James, S., Jones, M., Karaffa, L., Karányi, Z., Kato, M., Keller, N., Kelly, D.E., Kiel, J.A., Kim, J.M., Klei, I.J. van der, Klis, F.M., Kovalchuk, A., Kraševec, N., Kubicek, C.P., Liu, B., MacCabe, A., Meyer, V., Mirabito, P., Miskei, M., Mos, M., Mullins, J., Nelson, D.R., Nielsen, J., Oakley, B.R., Osmani, S.A., Pakula, T., Paszewski, A., Paulsen, I., Pilsyk, S., Pócsi, I., Punt, P.J., Ram, A.F.J., Ren, Q., Robellet, X., Robson, G., Seiboth, B., Solingen, P. van, Specht, T., Sun, J., Taheri-Talesh, N., Takeshita, N., Ussery, D., Kuyk, P.A. van, Visser, H., Vondervoort, P.J. van, Vries, R.P. de, Walton, J., Xiang, X., Xiong, Y., Zeng, A.P., Brandt, B.W., Cornell, M.J., Hondel, C.A. van den, Visser, J., Oliver, S.G. & Turner, G. (2009). The 2008 update of the *Aspergillus nidulans* genome annotation: A community effort. *Fungal Genet. Biol.,* 46(1), S2-S13.

Orij, P.J., Urbanus, M.L., Vizeacoumar, F.J., Dyk, N. van, Boone, C., Giaever, G., Nislow, C., Brul, S. & Smits, G.J. (2009). Genome-wide analysis of pH homeostasis using a pH sensitive GFP. Antonie van Leeuwenhoek, 95(suppl.1), 71-71.

Van Zuijlen, A., Periago, P.M., Amézquita, A., Palop, A., Brul, S. and Fernández, P.S. 2009. Characterization of Bacillus sporothermodurans IC4 spores; putative indicator microorganism for optimization of thermal processes in food sterilization. *Food Research International, Epub ahead of print.* Doi:10.1016/j.foodres.2009.11.011.

Klis, F.M., Brul, S. and de Groot, P.W.J. 2009. Covalently linked wall proteins in ascomycetous fungi. *Yeast, Epub ahead of print.* Doi:10.1002/yea.1747.

Havelaar, A.H., Brul, S., Jong, A. de, Jong, R. de, Zwietering, M.H. and TerKuile, B.H. 2009. Future challenges to microbial food safety. *Int. J. Food Microbiol. Epub ahead of print.* Doi: 10.1016/ j.ijfoodmicro.2009.10.015.

Schuurmans, M.J., Hayali, A.S.N., Koenders, B.B. and Ter Kuile, B.H. 2009. Variations in MIC value caused by differences in experimental protocol. *J. Microbiological Methods*, 79, 44-47.

Non refereed publication

Zuijlen, A.C.M. van, Oomes, S.J.C.M., Vos, P. & Brul, S. (2009). Detecting bacterial spores in soup manufacturing. *New food*, 3, 21-24.

Book Chapter

Gonzalez, M., Groot, P.W.J. de & Klis, F.M. (2009). Glycoconjugate structure and function in fungal cell walls. In A.P. Moran, O. Holst, P.J. Brennan & M. von Itzstein (Eds.), Microbial Glycobiology (pp. -chapter 10). London: Academic Press.

Invited lectures

Brul, S. (2009, January 01). Applying systems biology approaches to microbial food preservation. Norwich, UK, Institute for Food Research.

Brul, S. (2009, September 07). Applying systems biology to generate models of mcirobial behaviour in foods. Washington, USA, 6th International Congress on Predictive Microbiology in Foods.

Brul, S. (2009, November 03). Bacterial spores in food manufacturing: their presence, characterisation and outgrwowth analysis. As, Norway, Norwegian Food Industry.

Brul, S. (2009, January 01). Nog invullen! Norwich, UK, Inst. of Food Research.

Brul, S. (2009, June 15). On the origin of heterogeneity in preservation resistance of Bacillus spores: advanced from a 'systems' analysis of bacterial spore occurrence and outgrowth. Quimper, France, SPORE 2009: International Conference on Bacterial Spores.

Klis, F.M. (2009, April 20). An in vitro model for mucosal infections of Candida albicans reveals the dynamics of its cell wall proteome. Arnhem, the Netherlands, Dutch Soc.for (Medical) Microbiology: Spring Meeting.

Klis, F.M. (2009, March 08). An in vitro model for mucosal infections reveals the dynamics of the cell wall proteome of the clinical fungus Candida albicans. Bochum, Germany, Ver. für Allgemeine und Angewandte Mikrobiologie.

Klis, F.M. (2009, August 30). Covalently linked fungal cell wall proteins. Warsaw, Poland, IV International Conference on Molecular Mechanisms in Fungal Cell Wall Biogenesis.

Klis, F.M. (2009, October 09). Quantitative analysis of fungal wall proteins. Düsseldorf , Germany, FINSysB Course.

Membership Editorial board

Brul, S. (Ed.). (2009). Innov. Food Sci. and Emerg. Technol..

Brul, S. (Ed.). (2009). Journal of Biomedicine & Biotechnology.

Klis, F.M. (Ed.). (2009). Eukaryotic Cell.

Klis, F.M. (Ed.). (2009). FEMS Yeast Res..

Klis, F.M. (Ed.). (2009). Yeast.

Structure and Functional Organisation of the Cell Nucleus

Key Publications

Louwers, M., E. Splinter, R. van Driel, W. de Laat, and M. Stam. 2009. Studying physical chromatin interactions in plants using Chromosome Conformation Capture (3C). Nat Protoc. 4:1216-29.

Luijsterburg, M., G. Von Bornstaedt, A. Gourdin, A. Politi, M. Moné, D. Warmerdam, J. Goedhart, W. Vermeulen, R. Van Driel, and T. Höfer. 2010. Stochastic and Reversible Assembly of a Multiprotein DNA Repair Complex Ensures Accurate Target Site Recognition and Efficient Repair. J Cell Biol. 189:445-63.

Luijsterburg, M.S., C. Dinant, H. Lans, J. Stap, E. Wiernasz, S. Lagerwerf, D.O. Warmerdam, M. Lindh, M.C. Brink, J.W. Dobrucki, J.A. Aten, M.I. Fousteri, G. Jansen, N.P. Dantuma, W. Vermeulen, L.H. Mullenders, A.B. Houtsmuller, P.J. Verschure, and R. van Driel. 2009. Heterochromatin protein 1 is recruited to various types of DNA damage. J Cell Biol. 185:577-86.

Mateos-Langerak, J., M. Bohn, W. de Leeuw, O. Giromus, E.M. Manders, P.J. Verschure, M.H. Indemans, H.J. Gierman, D.W. Heermann, R. van Driel, and S. Goetze. 2009. Spatially confined folding of chromatin in the interphase nucleus. Proc Natl Acad Sci USA. 106:3812-3817.

Tessadori, F., M.v. Zanten, P. Pavlova, R. Clifton, F. Pontvianne, L.B. Snoek, F.F. Millenaar, R.K. Schulkes, R.v. Driel, L.A.C.J. Voesenek, C. Spillana, C.S. Pikaard, P. Fransz, and A.J.M. Peeters. 2009. PHYTOCHROME B and HISTONE DEACETYLASE 6 Control Light- Induced Chromatin Compaction in Arabidopsis thaliana. PLoS Genetcics. 5:e1000638.

PhD Thesis

Brink, M.C. (2009, April 02). Chromatin architecture and the orchestration of gene expression. UvA Universiteit van Amsterdam (100 pag.). Prom./coprom.: prof.dr. R. van Driel & dr. P.J. Verschure.

Academic publications

Dinant, C., Luijsterburg, S.M., Höfer, T., Bornstaedt, G. von, Vermeulen, W., Houtsmuller, A.B. & Driel, R. van (2009). Assembly of multiprotein complexes that control genome function. J.Cell Biol., 185(1), 21-26.

Louwers, M., Bader, R., Haring, M., Driel, R. van, Laat, W. de & Stam, M. (2009). Tissue- and expression level–specific chromatin looping at maize b1 epialleles. Plant Cell, 21(3), 832-842.

Louwers, M.L.D., Splinter, E., Driel, R. van, Laat, W. de & Stam, M. (2009). Studying physical chromatin interactions in plants using Chromosome Conformation Capture (3C). Nature protocols, 4, 1216-1229.

Luijsterburg, M.S., Dinant, C., Lans, H., Stap, J., Wiernasz, E.S., Lagerwerf, S., Warmerdam, D.O., Lindh, M., Brink, M.C., Dobrucki, J.W., Aten, J.A., Fousteri, M.I., Jansen, G., Dantuma, N.P., Vermeulen, W., Mullenders, L.H.F., Houtsmuller, A.B., Verschure, P.J. & Driel, R. van (2009). Heterochromatin protein 1 is recruited to various types of DNA damage. J.Cell Biol., 185(4), 577-586.

Mateos-Langerak, J., Bohn, M., Leeuw, W. de, Giromus, O., Manders, E.M.M., Verschure, P.J., Indemans, M.H.G., Gierman, H.J., Heermann, D.W., Driel, R. van & Goetze, S. (2009). Spatially confined folding of chromatin in the interphase nucleus. Proc. Natl. Acad. Sci. U.S.A., 106(10), 3812-3817.

Muller, A.W.J. (2009). Emergence of Animals from Heat Engines – Part 1. Before the Snowball Earths. Entropy, 11(3- Nonequilibrium Thermodynamics), 463-512.

Solimando, L., Luijsterburg, M.S., Vecchio, L., Vermeulen, W., Driel, R. van & Fakan, S. (2009). Spatial organization of nucleotide excision repair

proteins after UV-induced DNA damage in the human cell nucleus. J. cell sci., 122(1), 83-91.

Stam, M. (2009). Paramutation: a heritable change in gene expression by allelic interactions in trans. Molecular Plant, 2(4), 578-588.

Tessadori, F.G., Zanten, M. van, Pavlova, P., Clifton, R., Pontvianne, F., Basten Snoek, L., Millenaar, F.F., Schulkes, R.K., Driel, R. van, Voesenek, L.A.C.J., Spillane, C., Pikaard, C.S., Fransz, P.F. & Peeters, A.J.M. (2009). PHYTOCHROME B and HISTONE DEACETYLASE 6 Control Light-Induced Chromatin Compaction in Arabidopsis thaliana. PLoS Genet, 5(9), e1000638.

Book Chapters

Fransz, P. (2009). Chromatin domains and function. In I. Meier (Ed.), Functional organization of the plant nucleus (Plant cell monographs, 14) (pp. 131-155). Berlin: Springer.

Stam, M. & Louwers, M.L.D. (2009). Paramutation: Heritable in Trans Effects. In J.L. Bennetzen & S. Hake (Eds.), Handbook of Maize (Genetics and Genomics) (pp. 405-427-chapter 20). New York, USA: Springer Science + Business Media.

Membership Editorial Board

Driel, R. van (Ed.). (2009). J. cell. biochem..

Driel, R. van (Ed.). (2009). J. Struct. Biol..

Invited lectures

Driel, R. van (2009, September 11). Dynamic chromatin folding inside the interphase nucleus. Leiden, the Netherlands, Lorentz Center Workshop: Physics goes DNA.

Driel, R. van (2009, February 09). Folding of chromatin in the human interphase nucleus. Jouy en Josas, France, INRA.

Driel, R. van (2009, March 02). Folding of chromatin in the human interphase nucleus: from experiment to quantitative and predictive model and back. Stockholm, Sweden, Karolinska Institute.

Driel, R. van (2009, September 20). In vivo assembly and functioning of a chromatin-associated complex. Jena, Germany, International Symposium Analysis of Biomolecular Machines in the Nanometer Range.

Driel, R. van (2009, September 01). In vivo assembly and functioning of a chromatin-associated complex. Ustron, Polen, Wilhelm Bernhard Nuclear Workshop.

Driel, R. van (2009, May 06). In vivo assembly and functioning of a chromatin-associated complex. Enschede, the Netherlands, University of Twente.

Driel, R. van (2009, February 08). Systeembiologie, wordt biologisch onderzoek volwassen…? Paradiso, Amsterdam, the Netherlands, Paradisolezingen 2009.

Driel, R. van (2009, April 21). Systems biology in the Netherlands. Stockholm, Sweden, Workshop on Swedish Systems Biology.

Driel, R. van (2009, October 01). Understanding chromatin-associated processes in the living cell; the choreography of DNA repair proteins as a paradigm. University of Groningen, Groningen, the Netherlands, 1st Symposium of Systems Genetics: Systems Genetics: from man to microbe, from genotype to phenotype.

Fransz, P.F. (2009, December 11). DNA sequencing, evolutionary history and epigenetics of an inversion in Arabidopsis. Nijmegen, the Netherlands, EPS Theme 4 Symposium Genome Plasticity.

Fransz, P.F. (2009, March 25). Dynamics of chromatin compaction in the plant nucleus. John Innes Institute, Norwich, UK, Plant Chromatin Biology and Nuclear Organisation.

Fransz, P.F. (2009, June 24). Genetic and epigenetic consequences of a paracentric inversion in Arabidopsis thaliana. Boone, North Carolina, USA, 17th International Chromosome Conference.

Fransz, P.F. (2009, June 23). Organization and dynamics of repetitive DNA sequences in heterochromatin domains of Arabidopsis under normal and stress conditions. Boone, North Carolina, USA, 17th International Chromosome Conference.

Stam, M. (2009, May 13). b1 paramutation: the heritable transfer of epigenetic information in trans. EMBL Heidelberg, Germany, EMBO Conference series on Chromatin and Epigenetics.

Stam, M. (2009, April 14). Chromatin structure analyses: b1 epialleles as a testcase. Amsterdam, the Netherlands, Department of Genetics, VU University Amsterdam.

Stam, M. (2009, September 03). Tissue- and expression level-specific chromatin looping at maize b1 epialleles. ETH Zürich, Switzerland, European Workshop on Plant Chromatin.

Stam, M. (2009, December 02). Tissue- and expression level-specific chromatin looping at maize b1 epialleles. Cologne, Germany, Max Planck Institute for Plant Breeding Research, invited by Franziska Turck.

Stam, M. (2009, June 21). Tissue- and expression level-specific chromatin looping at maize b1 epialleles. Bergamo, Italy, Eucarpia Meeting: Maize and Sorghum in the Genomics Era.

Verschure, P.J. (2009, July 01). Chromosome organization and epigenetic gene regulation of the eukaryotic genome. DKFZ-Heidelberg, Germany, German Cancer Research Center, Division of Molecular Genome Analysis.

Verschure, P.J. (2009, October 12). Epigenetic gene regulation of the eukaryotic genome. University Medical Center Utrecht, Utrecht, the Netherlands, 7th Dutch Chromatin Meeting: Systems Biology approaches using synthetic systems.

Verschure, P.J. (2009, October 02). Epigenetic gene regulation of the eukaryotic genome: Systems Biology approaches using synthetic systems. University of Groningen, Groningen, the Netherlands, 1st Symposium on Systems Genetics: Systems Genetics: from man to microbe, from genotype to phenotype.

Anink, L.C.M. (2009, October 14). The gene-regulatory potential of epigenetics: detailed analysis using synthetic epigenetic cell systems. Noordwijkerhout, the Netherlands, 5th NISB Symposium.

Epigenetic Regulation of Gene Expression

Key Publication

Boukarabila, H., Saurin, A.J., Batsché, E., Mossadegh, N., Lohuizen, M. van, Otte, A.P., Pradel, J., Muchardt, C., Sieweke, M. & Duprez, E. (2009). The PRC1 Polycomb group complex interacts with PLZF/RARA to mediate leukemic transformation. *Genes dev.*, 23(10), 1195-1206.

Academic publications (refereed)

Boukarabila, H., Saurin, A.J., Batsché, E., Mossadegh, N., Lohuizen, M. van, Otte, A.P., Pradel, J., Muchardt, C., Sieweke, M. & Duprez, E. (2009). The PRC1 Polycomb group complex interacts with PLZF/RARA to mediate leukemic transformation. *Genes dev.*, 23(10), 1195-1206.

Fluge, Ø., Gravdal, K., Carlsen, E., Vonen, B., Kjellevold, K., Refsum, S., Lilleng, R., Eide, T.J., Halvorsen, T.B., Tveit, K.M., Otte, A.P., Akslen, L.A. & Dahl, O. (2009). Expression of EZH2 and Ki-67 in colorectal cancer and associations with treatment response and prognosis. *Brit. J. Cancer*, 101, 1282-1289.

Molecular Cytology

Key publications

Gadella, T.W.J. (Ed.). (2009). *FRET and FLIM Techniques (Laboratory techniques in biochemistry and molecular biology).* Amsterdam: Elsevier Science (534 pp).

Mohammadi,T., Ploeger, G., Comvalius, A. D., Verheul, J., Martos, A., Alfonso, C., van Marle, J., Rivas, G. and den Blaauwen, T. (2009) The GTPase activity of *Escherichia coli* FtsZ determines the magnitude of the FtsZ polymer bundling by ZapA *in vitro*. Biochemistry **48:** 11056-11066.

Vos, W.H. de, Hoebe, R.A., Joss, G.H., Haffmans, W., Baatout, S., Oostveldt, P. van & Manders, E.M.M. (2009). Controlled light exposure microscopy reveals dynamic telomere microterritories throughout the cell cycle. *CYTOM PART A, 75A*(5), 428-439.

PhD Thesis

Ploeger, G.E.J. (2009, October 13). Functional analysis of ZapA: keeping the one ring together. UvA Universiteit van Amsterdam (186 pag.). Prom./coprom.: prof.dr. T.W.J. Gadella & dr. T. den Blaauwen.

Patents

Mano, S., Satou, K., Hoebe, R.A., Manders, E.M.M. (2009) Laser Scanning Microscope. (WO2009JP52973 , JP20080041499)

Manders, EMM, RA Hoebe. NL (13 October, 2009) Werkwijze voor het vormen van een afbeelding van een object. (NL2001464)

Academic publications (refereed)

Bellou, S., M.A. Hink, E. Bagli, E. Panopoulou, P.I.H. Bastiaens, C. Murphy and T. Fotsis. VEGF auto-regulates its proliferative and migratory ERK1/2 and p38 MAPK cascades by enhancing the expression of DUSP1 and DUSP5 phosphatases in endothelial cells. Am. J. Physiol. Cell. Physiol. 297, 1477 (2009).

Gadella Jr. T.W.J. (2009) Total internal reflection fluorescence lifetime imaging microscopy. In "FRET and FLIM imaging techniques" (ed. Gadella). Laboratory Techniques in Biochemistry and Molecular Biology (ser. Ed. P.C. Van der Vliet) Burlington: Academic Press. pp. 395-412.

Goedhart, J., and Gadella Jr., T.W.J. (2009) Fluorescence resonance energy transfert imaging of PKC signaling in living cells using genetically encoded fluorescent probes. J.R. Soc. Interface 6: S27-S34.

Kedrov, A., den Blaauwen, T., and Driessen, A.J.M. (2009) Thermodynamics of the protein translocation. In Johnson, M.L., Hoit, J.M. and Ackers, G.K., editors. Methods in Enzymology. Volume 466 Biothermodynamics, PartB:273-291.

G.-J. Kremers and J. Goedhart (2009) Visible fluorescent proteins for FRET. In "FRET and FLIM imaging techniques" (ed. Gadella). Laboratory Techniques in Biochemistry and Molecular Biology (ser. Ed. P.C. Van der Vliet) Burlington: Academic Press. pp. 171-224.

Mateos-Langerak, J., Bohn, M., Leeuw, W. de, Giromus, O., Manders, E.M.M., Verschure, P.J., Indemans, M.H., Gierman, H.J., Heermann, D.W., Driel, R. van & Goetze, S. (2009). Spatially confined folding of chromatin in the interphase nucleus. Proceedings of the National Academy of Sciences of the United States of America, 106(10), 3812-3817.

Michielse Caroline B; van Wijk Ringo; Reijnen Linda; Manders Erik M M; Boas Sonja; Olivain Chantal; Alabouvette Claude; Rep Martijn (2009) The nuclear protein Sge1 of Fusarium oxysporum is required for parasitic growth. PLoS pathogens 5(10):e1000637

Mohammadi,T., Ploeger, G., Comvalius, A. D., Verheul, J., Martos, A., Alfonso, C., van Marle, J., Rivas, G. and den Blaauwen, T. (2009) The GTPase activity of Escherichia coli FtsZ determines the magnitude of the FtsZ polymer bundling by ZapA in vitro. Biochemistry 48: 11056-11066.

Schafer, D.N., Müller, M., Marr, D.W., Bonn, M., Maarseveen, J. van & Squier, J. (2009). Coherent anti-Stokes Raman scattering microscopy for quantitative characterization of mixing and flow in microfluidics. Optics Letters, 34(2), 211-213.

Shcherbo, D., Souslova, E.A., Goedhart, J., Chepurnykh, T.V., Gaintzeva, A., Shemiakina, I.I., Gadella, T.W.J., Lukyanov, S. & Chudakov, D.M. (2009). Practical and reliable FRET/FLIM pair of fluorescent proteins. BMC BIOTECHNOL, 9(24).

Verhoeven, G.S., Alexeeva, S., Dogterom, M. & Blaauwen, T. den (2009). Differential bacterial surface display of peptides by the transmembrane domain of OmpA. PLoS ONE, 4(8), e6739.

Vermeer, J.E.M., Thole, J.M., Goedhart, J., Nielsen, E., Munnik, T. & Gadella (jr.), T.W.J. (2009). Imaging phosphatidylinositol 4-phosphate dynamics in living plant cells. Plant Journal, 57(2), 356-372.

Vos, W.H. de, Hoebe, R.A., Joss, G.H., Haffmans, W., Baatout, S., Oostveldt, P. van & Manders, E.M.M. (2009). Controlled light exposure microscopy reveals dynamic telomere microterritories throughout the cell cycle. CYTOM PART A, 75A(5), 428-439.

Book chapters

Kedrov, A., Blaauwen, T. den & Driessen, A.J.M. (2009). Thermodynamics of the protein translocation. In M.L. Johnson, J.M. Hoit & G.K. Ackers (Eds.), BIOTHERMODYNAMICS, PART B (Methods in Enzymology, 466) (pp. 273-291-chapter 12). Academic Press.

Kremers, G.J. & Goedhart, J. (2009). Visible fluorescent proteins for FRET. In Th.W.J. Gadella (Ed.), FRET and FLIM Techniques (LABORATORY TECHNIQUES IN BIOCHEMISTRY AND MOLECULAR BIOLOGY, 33) (pp. 171-233-chapter 5). ELSEVIER.

Vos, W.H. de, Hoebe, R.A., Joss, G., Manders, E.M.M. & Oostveldt, P. van (2009). Controlled light exposure microscopy reveals telomeric microterritories throughout the cell cycle. In A. Aretz, B. Hermanns-Sachweh & J. Mayer (Eds.), EMC 2008 14th European Microscopy Congress 1–5 September 2008, Aachen, Germany (pp. 169). Berlin Heidelberg: Springer.

Willems, P.H.G.M., Swarts, H.G., Hink, M.A. & Koopman, W.J.H. (2009). The Use of Fluorescence Correlation Spectroscopy to Probe Mitochondrial Mobility and Intramatrix Protein Diffusion. In W.S. Allison & I.E. Scheffler (Eds.), Mitochondrial Function, Part A: Mitochondrial Electron Transport Complexes and Reactive Oxygen Species (Methods in Enzymology, 456) (pp. 287-302-chapter 16). Elsevier Inc..

Membership editorial board

Gadella, T.W.J. (Ed.). (2009). FRET and FLIM Techniques (Laboratory techniques in biochemistry and molecular biology). Amsterdam: Elsevier Science.

Invited lectures

Berg van Saparoea, H.B. van den & Blaauwen, T. den (2009, October 11). Cellular localization of PBP1A in *Escherichia coli* and the effect of deletion of mrcA (ponA) on the morphology of the cell. Utrecht, the Netherlands, 8th general Assembly EUR-INTAFAR.

Berg van Saparoea, H.B. van den & Blaauwen, T. den (2009, March 22). Where, when and with whom? Charting the interactions among *Escherichia coli* peptidoglycan synthesis proteins by FRET. Normandoux, France, 7th general Assembly EUR-INTAFAR.

Blaauwen, T. den & Ploeg, R. van der (2009, March 19). High throughput FRET assay for morphogenetic-protein interaction inhibitors. Madrid, Spain, Divinocell kick off meeting.

Blaauwen, T. den (2009, August 24). ZapA and the assembly of the one ring. Oxford, UK, EMBO workshop “Frontiers of Prokaryotic cell biology".

Gadella (jr.), T.W.J. (2009, July 15). A twice brighter cyan fluorescent protein with monoexponential decay by FLIM screening. Genua, Italy, European Biophysics Societies Association (EBSA) 2009 conference.

Gadella (jr.), T.W.J. (2009, April 05). Fluorescence resonance Energy Transfer Microscopy. Krakow, Poland, Focus on Microscopy international Conference: keynote tutorial.

Gadella (jr.), T.W.J. (2009, October 07). FRET microscopy. Rotterdam, the Netherlands, Erasmus MC: OIC advanced course.

Gadella (jr.), T.W.J. (2009, August 27). Imaging signalling across the membrane with genetic encoded fluorescent biosensors. Bielefeld, Germany, 4th CeBiTec Symposium on Bioimaging.

Gadella (jr.), T.W.J. (2009, October 01). Imaging signalling networks. Wageningen, the Netherlands, Department of Biochemistry, Wageningen University.

Gadella (jr.), T.W.J. (2009, April 01). Visualizing signalling across the membrane. University of Basel. Switzerland, Inst. Biochemistry and Genetics, Dept. for Biomedicine.

Gadella Jr/, T.W.J. (2009, May 12) Visualizing signalling across the membrane. EMBL invited seminar, Heidelberg, Germany.

Hink, M.A. (2009, May 10). (Cross-) Correlation Spectroscopy (FCS/FCCS) for Cell Biology Applications. Heidelberg, Germany, EMBO Practical Course on Fluorescene.

Hink, M.A. (2009, June 10). Fluorescence fluctuation spectroscopy. Lisbon, Portugal, EMBO course on light microscopy in living cells.

Hink, M.A. (2009, June 15). Fluorescence fluctuation spectroscopy. Wageningen, the Netherlands, Bravissimo network workshop- Microspectroscopy: Monitoring Cellular Biochemistry in vivo.

Hink, M.A. (2009, May 10). Photon counting histogram & Practical aspects of FCS/FCCS. Heidelberg, Germany, EMBO Practical Course on Fluorescene (Cross-) Correlation Spectroscopy (FCS/FCCS) for Cell Biology Applications.

Manders, E.M.M. (2009, May 12). Controlled Light Exposure Fluorescence Microscopy (CLEM); "Towards non-toxic, ultra-sensitive microscopy". Utrecht, the Netherlands, Department of Medical Oncology, University Medical Center Utrecht.

Manders, E.M.M. (2009, June 12). Controlled Light Exposure Microscopy (CLEM) for prolonged live-cell imaging; "Towards non-toxic, ultra-sensitive microscopy". Maastricht, the Netherlands, Dutch Society for Cell Biology and the Dutch Histochemistry Foundation: Symposium "Advanced Microscopy and Vital Imaging".

Manders, E.M.M. (2009, August 31). Controlled Light Exposure Microscopy (CLEM) for prolonged live-cell imaging; "Towards non-toxic, ultra-sensitive microscopy". Amsterdam, the Netherlands, EMBO-meeting 2009.

Manders, E.M.M. (2009, April 06). Light Exposure Microscopy (CLEM); "Towards non-toxic, ultra-sensitive microscopy". Krakow, Poland, Focus on Microscopy 2009.

Manders, E.M.M. (2009, October 13). Quantitative Microscopy for systems biology. Noordwijkerhout, the Netherlans, 5th symposium of the Netherlands Institute for Systems Biology (NISB),.

Manders, E.M.M. (2009, September 07). Towards non-toxic, ultra-sensitive microscopy. Krakow, Poland, Department of Biophysics, Jagiellonian University.

Manders, E.M.M. (2009, September 08). Wide-Field Controlled Light Exposure Fluorescence Microscopy (CLEM); "Towards non-toxic, ultra-sensitive microscopy". Edinburgh, U.K., International Society of Developmental Biologists Congress.

Appendix 2,

Research Cluster **Plant Signalling**

Plant Physiology

Key publications

Mishkind, M.L., Vermeer, J.E.M., Darwish, E.M.A.M. & Munnik, T. (2009). Heat stress activates phospholipase D and triggers PIP accumulation at the plasma membrane and nucleus. *Plant Journal, 60*(1), 10-21.

Moerkercke, A.N.A.I. van, Schauvinhold, I., Pichersky, E., Haring, M.A. & Schuurink, R.C. (2009). A plant thiolase involved in benzoic acid biosynthesis and volatile benzenoid production. *Plant Journal, 60*(2), 292-302.

Academic publications

Arisz, S.A., Testerink, C. & Munnik, T. (2009). Plant PA signaling via diacylglycerol kinase. *BBA-MOL CELL BIOL L, 1791*(9), 869-875.

Bargmann, B.O.R., Laxalt, A.M., Riet, B. ter, Schooten, B. van, Merquiol, E., Testerink, C., Haring, M.A., Bartels, D. & Munnik, T. (2009). Multiple PLDs required for high salinity and water deficit tolerance in plants. *Plant Cell Physiol., 50*(1), 78-89.

Bargmann, B.O.R., Laxalt, A.M., Riet, B. ter, Testerink, C., Merquiol, E., Mosblech, A., Leon-Reyes, A., Pieterse, C.M.J., Haring, M.A., Heilmann, I., Bartels, D. & Munnik, T. (2009). Reassessing the role of phospholipase D in the Arabidopsis wounding response. *PLANT CELL ENVIRON, 32*(7), 837-850.

Bleeker, P.M., Diergaarde, P.J., Ament, K., Guerra, J., Weidner, M., Schütz, S., Both, M.T.J. de, Haring, M.A. & Schuurink, R.C. (2009). The role of specific tomato volatiles in tomato-whitefly interaction. *Plant Physiol., 151*(2), 925-935.

Darwish, E., Testerink, C., Khalil, M., El-Shihy, O. & Munnik, T. (2009). Phospholipid signaling responses in salt-stressed rice leaves. *Plant Cell Physiol., 50*(5), 986-997.

Mishkind, M., Vermeer, J.E.M., Darwish, E. & Munnik, T. (2009). Heat stress activates phospholipase D and triggers PIP2 accumulation at the plasma membrane and nucleus. *Plant j., 60*(1), 10-21.

Munnik, T. & Testerink, C. (2009). Plant phospholipid signaling: "in a nutshell". *J. lipid res., 50*, S260-S265.

Van Moerkercke, A., Schauvinhold, I., Pichersky, E., Haring, M.A. & Schuurink, R.C. (2009). A plant thiolase involved in benzoic acid biosynthesis and volatile benzenoid production. *Plant j., 60*(2), 292-302.

Non-refereed publications

Vermeer, J.E.M., Thole, J.M., Goedhart, J., Nielsen, E., Munnik, T. & Gadella (jr.), T.W.J. (2009). Imaging phosphatidylinositol 4-phosphate dynamics in living plant cells. *Plant j., 57*(2), 356-372.

Zonia, L. & Munnik, T. (2009). Uncovering hidden treasures in pollen tube growth mechanics. *Trends Plant Sci., 14*(6), 318-327.

Haring, M.A. (01-06-2009). Da liegt was in der Luft: Pflanzen kommunizieren mit Duftstoffen. *Lebendige Erde*, pp. 18-20.

Book Chapters

Kant, M.R., Bleeker, P.M., Wijk, M. van, Schuurink, R.C. & Haring, M.A. (2009). Plant Volatiles in Defence. In L.C. van Loon (Ed.), *Plant innate immunity* (ADVANCES IN BOTANICAL RESEARCH, 51) (pp. 613-666). Amsterdam: Academic Press.

Clark, D., Pichersky, E., Verdonk, J.C., Dudareva, N., Haring, M.A., Klahre, U. & Schuurink, R.C. (2009). Benzenoids Dominate the Fragrance of Petunia Flowers. In T. Gerats & J. Strommer (Eds.), *PETUNIA: Evolutionary, Developmental and Physiological Genetics* (pp. 51-69-chapter 3). New York: Springer.

Membership editorial board

Munnik, T. (Ed.). (2009). *Plant signaling and behavior*.

Munnik, T. (Ed.). (2009). *Planta*.

Munnik, T. (Ed.). (2009). *The Open Plant Science Journal*.

Invited lectures

Galvan Ampudia, C.S., Zalejski, C., Bogre, L., Offringa, R. & Testerink, C. (2009, May 14). *Osmotic stress-induced signals control root growth.* Tartu, Estonia, Conference on Plant Abiotic Stress – from signaling to development.

Haring, M.A. (2009, April 15). *Biologische rassen: weet wat je eet!* Rheden, the Netherlands, Biocongres.

Haring, M.A. (2009, December 02). *Cisgenese bis SMART breeding.* Witzenhausen, Germany, Witzenhäuser Konferenz: „Saat á la Carte ? - Gentechnik und Alternativen in der Diskussion“.

Haring, M.A. (2009, February 15). *Hoe de plantenveredeling tot gentechnologie is verworden….* Appelscha, the Netherlands, themamiddag 'Genetische manipulatie, een zegen of fatale vergissing?'.

Haring, M.A. (2009, March 23). *Is gentechnologie de toekomst van de landbouw?* Witmarsum, the Netherlands., NLTO Jaarvergadering.

Haring, M.A. (2009, April 28). *Novel Breeding techniques: molecular biology combined with tissue culture.* Paris, France, ITAB Conference.

Haring, M.A. (2009, March 17). *The role of transcription factors in tomato flavour volatile regulation.* Wageningen, the Netherlands, CBSG Summit.

Haring, M.A. (2009, March 03). *The role of volatiles in plant insect interactions.* Jena, Germany, IMPRS Symposium.

McLoughlin, F. (2009, December 07). *Phosphatidic acid is a lipid second messenger involved in early abiotic stress signaling.* Veldhoven, the Netherlands, Annual Meeting of the NWO-CW study groups Protein Research, Nucleic Acids and Lipids & Biomembranes.

Munnik, T. (2009, March 11). *Green light for phospholipid signals.* Bonn, Germany, Universität Bonn.

Munnik, T. (2009, February 01). *Phosphatidic acid signaling in plants.* Galveston, Texas, USA., Gordon Research Conference (GRC) on Plant Lipids.

Munnik, T. (2009, May 14). *Phosphoinositide signalling in plant stress signalling and development.* Tartu, Estonia, 2nd FA605 COST INPAS Conference: Plant Abiotic Stress – from signaling to development.

Munnik, T. (2009, January 29). *Phospholipid Signaling in Plant Stress and Development.* Ann Arbor, MI, USA, Michigan State University.

Munnik, T. (2009, December 17). *Phospholipid Signalling in Plant Stress and Development.* Fribourg, Switzerland, University of Fribourg.

Munnik, T. (2009, April 01). *Phospholipid Signalling in Plant Stress and Development.* Jena, Germany, Max Planck Institute for Chemical Ecology.

Munnik, T. (2009, January 27). *Phospholipid-based Signal Transduction.* Münster, Germany, University of Münster.

Munnik, T. (2009, April 03). *Phospholipids in Plant Stress Signalling and Development.* Halle, Germany, Leibniz Institute of Plant Biochemistry (IPB), Halle University.

Schuurink, R.C. (2009, March 17). *Benzoic acid and Benzenoid biosynthesis by Petunia flowers.* Cologne, Germany, University of Cologne.

Schuurink, R.C. (2009, July 16). *Genetic approaches to E-2-hexenal responses in Arabidopsis.* Pommersfelden, Germany, University of Würzburg.

Schuurink, R.C. (2009, December 18). *Mutations in GABA transaminase genes in plants or Pseudomonas reduce bacterial virulence.* Amsterdam, the Netherlands, JDPS Core-to-Core program.

Schuurink, R.C. (2009, March 09). *Novel tomatoes that counteract suppression of plant defences.* The Hague, the Netherlands, NWO-TTI-GG Meeting.

Schuurink, R.C. (2009, November 11). *Tomato and insects, a volatile interaction.* Utrecht, the Netherlands, 4th workshop on Plant-Insect Interactions.

Zonia, L. (2009, December 07). *Spatial and temporal integration of signaling networks in pollen tube growth.* Veldhoven, the Netherlands, NWO Scientific meeting on "Chemistry related to Biological & Medical sciences".

Plant–pathogen Interaction

Key Publications

Michielse, C.B., van Wijk, R., Reijnen, L., Boas, S., Cornelissen, B.J.C., Rep, M. (2009) Sge1, a putative transcriptional regulator is required for pathogenicity in Fusarium oxysporum f. sp. lycopersici and regulates infection phase specific genes.
PloS Pathogens 5: 1000637

Houterman, P.M., Ma, L.S., van Ooijen, G., de Vroomen, M., Cornelissen, B.J.C., Takken, F.L.W. and Rep, M. (2009) The effector protein Avr2 of the xylem-colonizing fungus Fusarium oxysporum activates the tomato resistance protein I-2 intracellularly.
The Plant Journal 58: 970-978

PhD Thesis

Jonkers, W. (2009, oktober 06). *The role of the F-box protein Frp1 in pathogenicity of Fusarium oxysporum.* UvA Universiteit van Amsterdam (137 pag.). Prom./coprom.: prof.dr. B.J.C. Cornelissen & dr. M. Rep.

Academic publications (refereed)

Burg, H.A. van den & Takken, F.L.W. (2009). Does chromatin remodeling mark systemic acquired resistance? *Trends Plant Sci., 14*(5), 286-294.

Coleman, J.J., Rounsley, S.D., Rodriguez-Carres, M., Kuo, A., Wasmann, C.C., Grimwood, J., Schmutz, J., Taga, M., White, G.J., Zhou, S., Schwartz, D.C., Freitag, M., Ma, L-j., Danchin, E.G.J., Henrissat, B., Coutinho, P.M., Nelson, D.R., Straney, D., Napoli, C.A., Barker, B.M., Gribskov, M., Rep, M., Kroken, S., Molnár, I., Rensing, C., Kennell, J.C., Zamora, J., Farman, M.L., Selker, E.U., Salamov, A., Shapiro, H., Pangilinan, J., Lindquist, E., Lamers, C., Grigoriev, I.V., Geiser, D.M., Covert, S.F., Temporini, E. & VanEtten, H.D. (2009). The genome of Nectria haematococca: Contribution of supernumerary chromosomes to gene expansion. *PLoS Genet, 5*(8), e1000618.

Houterman, P.M., Ma, L., Ooijen, G. van, Vroomen, M.J. de, Cornelissen, B.J.C., Takken, F.L.W. & Rep, M. (2009). The effector protein Avr2 of the xylem-colonizing fungus Fusarium oxysporum activates the tomato resistance protein I-2 intracellularly. *Plant j., 58*(6), 970-978.

Jonkers, W., Andrade Rodrigues, C.D. & Rep, M. (2009). Impaired colonization and infection of tomato roots by the Δfrp1 mutant of Fusarium oxysporum correlates with reduced CWDE gene expression. *Mol. Plant-Microbe Interact., 22*(5), 507-518.

Jonkers, W. & Rep, M. (2009). Lessons from fungal F-box proteins. *Eukaryotic Cell, 8*(5), 677-695.

Jonkers, W. & Rep, M. (2009). Mutation of CRE1 in Fusarium oxysporum reverts the pathogenicity defects of the FRP1 deletion mutant. *Mol. Microbiol., 74*(5), 1100-1113.

Lievens, B., Houterman, P.M. & Rep, M. (2009). Effector gene screening allows unambiguous identification of Fusarium oxysporum f. sp. lycopersici races and discrimination from other formae speciales. *FEMS microbiol. lett., 300*(2), 201-215.

Lievens, B., Baarlen, P. van, Verreth, C., Van Kerckhove, S., Rep, M. & Thomma, B.P.H.J. (2009). Evolutionary relationships between Fusarium oxysporum f. sp. lycopersici and F. oxysporum f. sp. radicis-lycopersici isolates inferred from mating type, elongation factor-1α and exopolygalacturonase sequences. *Mycol. Res., 113*(10), 1181-1191.

Lukasik, E. & Takken, F.L.W. (2009). STANDing strong, resistance proteins instigators of plant defence. *Curr. Opin. Plant Biol., 12*(4), 427-436.

Michielse, C.B., Wijk, R. van, Reijnen, L., Cornelissen, B.J.C. & Rep, M. (2009). Insight into the molecular requirements for pathogenicity of Fusarium oxysporum f. sp. lycopersici through large-scale insertional mutagenesis. *Genome Biology, 10*(1), R4.

Michielse, C.B. & Rep, M. (2009). Pathogen profile update: Fusarium oxysporum. *Molecular Plant Pathology, 10*(3), 311-324.

Michielse, C.B., Wijk, R. van, Reijnen, L., Manders, E.M.M., Boas, S., Olivain, C., Alabouvette, C. & Rep, M. (2009). The nuclear protein Sge1 of Fusarium oxysporum is required for parasitic growth. *PLOS Pathogens, 5*(10), e1000637.

Slootweg, E., Tameling, W., Roosien, J., Lukasik, E., Joosten, M., Takken, F., Bakker, J. & Goverse, A. (2009). An outlook on the localisation and structure-function relationships of R proteins in Solanum. *Potato Res., 52*(3), 229-235.

Takken, F.L.W. & Tameling, W.I.L. (2009). To nibble at plant resistance proteins. *Sci., 324*(5928), 744-746.

Invited lectures

Rep, M. (2009, maart 17). *Effectors of a xylem colonizing fungus.* Pacific Grove, CA, USA, 25th Fungal Genetics Conference.

Rep, M. (2009, januari 15). *Effectors of Fusarium oxysporum.* Versailles, France, Réunion FungEffector.

Rep, M. (2009, juni 17). *Evolution of virulence in the plant-pathogenic fungus Fusarium oxysporum.* Salamanca, Spain, University of Salamanca.

Rep, M. (2009, april 06). *Evolution of virulence in the plant-pathogenic fungus Fusarium oxysporum.* Lunteren, the Netherlands, ALW-discussion platform EPW, Lunteren.

Rep, M. (2009, september 02). *Plant-microbe interactions – finding the rules of the molecular game.* Amsterdam, the Netherlands, SILS Research Day.

Takken, F.L.W. (2009, augustus 01). *How to resist a resistance protein?* Oxford, UK, British Society for Plant Pathology, Presidential Meeting 2009.

Takken, F.L.W. (2009, juli 19). *How to resist tomato resistance proteins?* Quebec, Canada, XIV International Congress on Molecular Plant-MicrobeInteractions.

Appendix 3

Research Cluster SILS Center for NeuroScience

Animal Physiology and Cognitive Neuroscience

Key Publications

Lansink C.S., Goltstein P.M., Lankelma J.V., McNaughton B.L. and Pennartz C.M. (2009) Hippocampus leads ventral striatum in replay of place-reward information. *PLoS Biol. 7*: e1000173. doi: 10.1371/journal.pbio.1000173.

Huijbers W, Pennartz CMA, Cabeza R and Daselaar SM (2009) When learning and remembering compete: a functional MRI study. *PLoS Biology 7*: e1000011.

Peyrache et al. Replay of rule-learning related neural patterns in the prefrontal cortex during sleep. (2009) *Nat Neurosci 12*:919-926.

PhD Thesis

Pu, Z. (2009, October 01). *A temporal perspective on stress hormones and memory.* Universiteit van Amsterdam (125 pag.). Prom./coprom.: prof.dr. M. Joels & prof.dr. G. Fernandez.

Academic publications (refereed)

Battaglia, F.P., Kalenscher, T., Cabral, H., Winkel, J., Bos, J., Manuputy, R., Lieshout, T., Pinkse, F., Beukers, H. & Pennartz, C. (2009). The Lantern: An ultra-light micro-drive for multi-tetrode recordings in mice and other small animals. *Journal of Neuroscience Methods,* 178(2), 291-300.

Cappaert, N.L.M., Lopes da Silva, F.H. & Wadman, W.J. (2009). Spatio-temporal dynamics of theta oscillations in hippocampal-entorhinal slices. *Hippocampus,* 19(11), 1065-1077.

Claus, S., Leijten, F., Kallansee, P., Klepper, J., Lopes da Silva, F.H., Ronner, H., Velis, D., Viergever, M.A. & Kalitzin, S. (2009). An electro-encephalogram beta gap after induction with diazepam: A localization method in epileptogenic lesions. *Clinical Neurophysiology*, 120(7), 1235-1244.

Daselaar, S.M., Prince, S.E., Dennis, N.A., Hayes, S.M., Kim, H. & Cabeza, R. (2009). Posterior Midline and Ventral Parietal Activity is Associated with Retrieval Success and Encoding Failure. *Frontiers in Human Neuroscience,* 3(13), 1-10.

Duuren, E. van, Plasse, G. van der, Lankelma, J., Joosten, R.N.J.M.A., Feenstra, M.G.P. & Pennartz, C.M.A. (2009). Single-cell and population coding of expected reward probability in the orbitofrontal cortex of the rat. *Journal of Neuroscience*, 29(28), 8965-8976.

Huijbers, W., Pennartz, C.M.A. & Daselaar, S.M. (2010). Dissociating the "retrieval success" regions of the brain: Effects of retrieval delay. *NEUROPSYCHOLOGIA*, 48(2), 491-497.

Huijbers, W., Pennartz, C.M., Cabeza, R. & Daselaar, S.M. (2009). When learning and remembering compete: A functional MRI study. *PLoS Biology,* 7(1), e1000011.

Lansink, C.S., Goltstein, P.M., Lankelma, J.V., McNaughton, B.L. & Pennartz, C.M.A. (2009). Hippocampus leads ventral striatum in replay of place-reward information. *PLoS Biology*, 7(8), e1000173.

Lee, E., Oliveira-Ferreira, A.I., Water, E. de, Gerritsen, H., Bakker, M.C., Kalwij, J.A.W., Goudoever, T. van, Buster, W.H. & Pennartz, C.M.A. (2009). Ensemble recordings in awake rats: Achieving behavioral regularity during multimodal stimulus processing and discriminative learning. *Journal of the Experimental Analysis of Behavior*, 92(1), 113-129.

Loos, M., Sluis, S. van der, Bochdanovits, Z., Zutphen, I.J. van, Pattij, T., Stiedl, O., Brussaard, A.B., Borst, J.G., Elgersma, Y., Galjart, N., Horst, G.T. van der, Levelt, C.N., Pennartz, C.M., Smit, A.B., Spruijt, B.M., Verhage, M., Zeeuw, C.I. de & Spijker, S. (2009). Activity and impulsive action are controlled by different genetic and environmental factors. *Genes Brain and Behavior,* 8(8), 817-828.

Munck, J.C. de, Goncalves, S.I., Mammoliti, R., Heethaar, R.M. & Lopes da Silva, F.H. (2009). Interactions between different EEG frequency bands and their effect on alpha-fMRI correlations. *NEUROIMAGE*, 47(1), 69-76.

Pennartz, C.M.A., Berke, J.D., Graybiel, A.M., Ito, R., Lansink, C.S., Meer, M. van der, Redish, A.D., Smith, K.S. & Voorn, P. (2009). Corticostriatal interactions during learning, memory processing, and decision making. *Journal of Neuroscience*, 29(41), 12831-12838.

Pennartz, C.M.A. (2009). Identification and integration of sensory modalities: Neural basis and relation to consciousness. *Consciousness and Cognition*, 18(3), 718-739.

Peyrache, A., Benchenane, K., Khamassi, M., Wiener, S.I. & Battaglia, F.P. (2009). Principal component analysis of ensemble recordings reveals cell assemblies at high temporal resolution. *Journal of computational neuroscience*.

Peyrache, A., Benchenane, K., Khamassi, M., Wiener, S.I. & Battaglia, F.P. (2009). Replay of rule-learning related neural patterns in the prefrontal cortex during sleep. *Nature Neuroscience*, 12, 919-926.

Proceedings

Kalenscher, T. (2009). Decision-making and Neuroeconomics. In *Encyclopedia of Life Sciences*. Chichester John Wiley & Sons, Ltd..

Book chapters

Gorter, J.A., Lopes da Silva, F.H. & Aronica, E. (2009). Patterns of gene expression in epileptogenesis: Micro-Array studies in rats. In P.A. Schwartzkroin (Ed.), *Encyclopedia of Basic Epilepsy Research* (pp. 240-250). Oxford: Elsevier.

Lopes da Silva, F.H. (2009). Epilepsy as a disease of the Dynamics of Neuronal Networks – models and predictions. In B. Schelter, J. Timmer & A. Schulze-Bonhage (Eds.), *Seizure Prediction in Epilepsy: From Basic Mechanisms to Clinical Applications* (pp. 97-108-chapter 7). Weinheim, Germany: Wiley VCH Verlag.

Lopes da Silva, F.H. & Gorter, J.A. (2009). Epileptogenesis and Plasticity. In P.A. Schwartzkroin (Ed.), *Encyclopedia of Basic Epilepsy Research* (pp. 221-227). Oxford: Elsevier.

Taverna, S. & Pennartz, C.M.A. (2009). Intrinsic synaptic connectivity of the nucleus accumbens: Lateral inhibition, functions of fast-spiking interneurons and neuromodulation. In H.N. David (Ed.), *The nucleus accumbens: Neurotransmitters & related behaviours* (pp. 63-79). Trivandrum: Research Signpost.

Membership editorial board

Pennartz, C.M.A. (Ed.). (2009). *Eur. j. neurosci.*.

Pennartz, C.M.A. (Ed.). (2009). *J. Neurosci.*.

Invited lectures

Battaglia, F.P. (2009, May 05). *Hippocampal-prefrontal coherence affects storage and sleep replay of information in the cerebral cortex.* Göttingen, Germany, Conference at the Bernstein Center for Computational Neuroscience.

Battaglia, F.P. (2009, June 17). *Models of spontaneous activity and connectivity development for an attractor neural network with grid cell behavior.* Verona, Italy, Spring Hippocampal Research Conference.

Battaglia, F.P. (2009, January 16). *Sleep, Memory and the transfer of information in the brain.* Wageningen, the Netherlands, Noldus Information System symposium.

Battaglia, F.P. (2009, January 20). *Sleep, Memory and the transfer of information in the brain.* Veldhoven, the Netherlands, Physics@FOM.

Battaglia, F.P. (2009, July 22). *Theta rhythm, sharp waves, slow waves: oscillations shape hippocampal/ neocortical interactions.* Berlijn, Germany, Workshop on Cortical Oscillations, Computational Neuroscience Conference.

Daselaar, S.M. (2009, September 23). *The default mode network is associated with retrieval success but encoding failure.* Chapel Hill, USA, Memory Disorders Research Society (MDRS).

Lopes da Silva, F.H. (2009, July 10). *Alpha rhythm images seen from inside and outside of the brain.* Aveiro, Portugal, University of Aveiro: BrainImaging -workshop.

Lopes da Silva, F.H. (2009, January 26). *Brain dynamics: re-entry signal pathways, mechanisms of phasing and de-phasing neuronal activities.* Paris, France, Réunion d'Hiver de la Société de Neurophysiologie Clinique de Langue Française.

Lopes da Silva, F.H. (2009, June 23). *Computational neurophysiology of transitions between normal and epileptic brain states.* Leiden, the Netherlands, Lorentz Center workshop: "Brain Waves".

Lopes da Silva, F.H. (2009, June 05). *Ictogenesis: Focus or Network?* Kansas City, Missouri, USA, 4th International Workshop on Seizure Prediction.

Lopes da Silva, F.H. (2009, November 17). *Models of oscillatory phenomena: Brain rhythms.* Paris-Rocquencourt, France, INRIA Advanced School: "Cardiac and brain electrophysiology: modeling and simulation" - Institut national de recherche en informatique et en automatique / centre de recherche INRIA.

Lopes da Silva, F.H. (2009, November 16). *Origin of bioelectric signals in the brain.* Paris-Rocquencourt, France, Advanced School: "Cardiac and brain electrophysiology: modeling and simulation" - Institut national de recherche en informatique et en automatique / centre de recherche INRIA.

Lopes da Silva, F.H. (2009, March 25). *Rhythms of the Brain: physiological sources; EEG/MEG/fMRI patterns.* Münster, Germany, Neuroscience Colloquium at the Münster University.

Lopes da Silva, F.H. (2009, May 02). *The oscillating brain: Physiology and modeling of brain rhythms: the role of re-entry circuits.* Maastricht, the Netherlands, Brain Connectivity Workshop 2009.

Pennartz, C.M.A. (2009, October 19). *Corticostriatal interactions during learning and memory processing.* Chicago, USA, Society for Neuroscience: symposium.

Pennartz, C.M.A. (2009, October 20). *Foraging in a contextually differentiated and dynamically cued environment – hippocampal and ventral striatal representations.* Chicago. U.S.A, Satellite meeting on Neuroscience of Foraging at the Society for Neuroscience.

Pennartz, C.M.A. (2009, June 22). *Identification and integration of sensory modalities: neural basis and relation to consciousness.* Amsterdam, the Netherlands, International Summer School, Cognitive Science Center Amsterdam.

Pennartz, C.M.A. (2009, January 27). *Neural ensembles in ventral striatum and hippocampus: coding and replay of reward and contextual information.* Copper Mountain, Co., U.S.A, Winter Conference on Brain Research.

Pennartz, C.M.A. (2009, June 15). *Opportunities and challenges in ensemble recordings from freely behaving rodents.* Ashburn, Va., U.S.A, Janelia Farm Research Campus, Howard Hughes Medical Institute.

Pennartz, C.M.A. (2009, September 15). *Surfing the waves of expectancy: oscillatory activity in orbitofrontal cortex codes reward prediction.* Barcelona, Spain, International Brain and Cognitive Systems Summer School.

Pennartz, C.M.A. (2009, October 23). *Unraveling the fabric of goal-directed learning: Neural coding and cross-structural interactions in corticostriatal systems.* Boston, Mass. U.S.A, Invited lecture at the Massachusetts Inst. Technology.

Cellular and Systems Neurobiology

Key publications

Academic publications

Aronica, E., Boer, K., Doorn, K.J., Zurolo, E., Spliet, W.G.M., Rijen, P.C. van, Baayen, J.C., Gorter, J.A. & Jeromin, A. (2009). Expression and localization of voltage dependent potassium channel Kv4.2 in epilepsy associated focal lesions. *Neurobiology of Disease, 36*(1), 81-95.

Boer, Y.W., Crino, P.B., Gorter, J.A., Nellist, M., Jansen, F.E., Spliet, W.G., Rijen, P.C. van, Wittink, F.R.A., Breit, T.M., Troost, D, Wadman, W.J. & Aronica, E. (2009). Gene Expression Analysis of Tuberous Sclerosis Complex Cortical Tubers Reveals Increased Expression of Adhesion and Inflammatory Factors. *BRAIN PATHOL*, 1-20.

Cagnan, H., Meijer, H.G.E., Gils, S.A. van, Krupa, M., Heida, T., Rudolph, M., Wadman, W.J. & Martens, H.C.F. (2009). Frequency-selectivity of a thalamocortical relay neuron during Parkinson's disease and deep brain stimulation: a computational study. *Eur. j. neurosci., 30*(7), 1306-1317.

Cappaert, N.L.M., Lopes da Silva, F.H. & Wadman, W.J. (2009). Spatio-temporal dynamics of theta oscillations in hippocampal-entorhinal slices. *Hippocampus, 19*(11), 1065-1077.

Chameau, P., Inta, D., Vitalis, T., Monyer, H., Wadman, W.J. & Hooft, J.A. van (2009). The N-terminal region of reelin regulates postnatal dendritic maturation of cortical pyramidal neurons. *Proc. Natl. Acad. Sci. U.S.A., 106*(17), 7227-7232.

De Herdt, V., Puimege, L., De Waele, J., Raedt, R., Wyckhuys, T., El Tahry, R., Libert, C., Wadman, W., Boon, P. & Vonck, K. (2009). Increased rat serum corticosterone suggests immunomodulation by stimulation of the vagal nerve. *Journal of Neuroimmunology, 212*(1-2), 102-105.

Gorter, J.A. (2009). Leukocyten veroorzaken lekkage van de bloedhersenbarrière met epilepsie tot gevolg. *Epilepsie, 7*, 17-18.

Holtman, L., Vliet, E.A. van, Schaik, R. van, Queiroz, C.M., Aronica, E. & Gorter, J.A. (2009). Effects of SC58236, a selective COX-2 inhibitor, on epileptogenesis and spontaneous seizures in a rat model for temporal lobe epilepsy. *Epilepsy res., 84*(1), 56-66.

Lewis, A.S., Schwartz, E., Chan, C.S., Noam, Y., Shin, M., Wadman, W.J., Surmeier, D.J., Baram, T.Z., Macdonald, R.L. & Chetkovich, D.M. (2009). Alternatively spliced isoforms of TRIP8b differentially control h channel trafficking and function. *J. Neurosci., 29*(19), 6250-6265.

Pekcec, A., Unkrüer, B., Schlichtiger, J., Soerensen, J., Hartz, A.M.S., Bauer, B., Vliet, E.A. van, Gorter, J.A. & Potschka, H. (2009). Targeting prostaglandin E2 EP1 receptors prevents seizure-associated P-glycoprotein up-regulation. *J. pharmacol. exp. ther., 330*(3), 939-947.

Queiroz, C.M., Gorter, J.A., Lopes da Silva, F.H. & Wadman, W.J. (2009). Dynamics of evoked local field potentials in the hippocampus of epileptic rats with spontaneous seizures. *J. neurophysiol., 101*(3), 1588-1597.

Raedt, R., Van Dycke, A., Van Melkebeke, D., De Smedt, T., Claeys, P., Wyckhuys, T., Vonck, K., Wadman, W. & Boon, P. (2009). Seizures in the intrahippocampal kainic acid epilepsy model: Characterization using long-term video-EEG monitoring in the rat. *ACTA NEUROL SCAND, 119*(5), 293-303.

Smit-Rigter, L.A., Champagne, D.L. & Hooft, J.A. van (2009). Lifelong impact of variations in maternal care on dendritic structure and function of cortical layer 2/3 pyramidal neurons in rat offspring. *PLoS ONE, 4*(4), e5167.

Somjen, G.G., Kager, H. & Wadman, W.J. (2009). Calcium sensitive non-selective cation current promotes seizure-like discharges and spreading depression in a model neuron. *J. comput. neurosci., 26*(1), 139-147.

Strien, N.M. van, Cappaert, N.L.M. & Witter, M.P. (2009). The anatomy of memory: An interactive overview of the parahippocampal–hippocampal network. *Nat. rev., Neurosci, 10*(4), 272-282.

Toering, S.T., Boer, K., Groot, M. de, Troost, D., Heimans, J.J., Spliet, W.G.M., Rijen, P.C. van, Jansen, F.E., Gorter, J.A., Reijneveld, J.C. & Aronica, E. (2009). Expression patterns of synaptic vesicle protein 2A in focal cortical dysplasia and TSC-cortical tubers. *Epilepsia, 50*(6), 1409-1418.

Vliet, E.A. van, Aronica, E., Redeker, S., Boer, K. & Gorter, J.A. (2009). Decreased expression of synaptic vesicle protein 2A, the binding site for levetiracetam, during epileptogenesis and chronic epilepsy. *Epilepsia, 50*(3), 422-433.

Vliet, E.A. van (2009). Farmacoresistente epilepsie: mogelijke oorzaken. *Epilepsie, 3*(7), 27-29.

Vliet, E.A. van, Edelbroek, P.M. & Gorter, J.A. (2009). Improved seizure control by alternating therapy of levetiracetam and valproate in epileptic rats. *Epilepsia*, 1-9.

Wyckhuys, T., Geerts, P.J., Raedt, R., Vonck, K., Wadman, W.J. & Boon, P. (2009). Deep brain stimulation for epilepsy: Knowledge gained from experimental animal models. *ACTA NEUROL BELG, 109*(2), 63-80.

Zeldenrust, F. & Wadman, W.J. (2009). Two forms of feedback inhibition determine the dynamical state of a small hippocampal network. *Neural Networks, 22*, 1139-1158.

Gorter, J.A., Lopes da Silva, F.H. & Aronica, E. (2009). Patterns of gene expression in epileptogenesis: Micro-Array studies in rats. In P.A. Schwartzkroin (Ed.), *Encyclopedia of Basic Epilepsy Research* (pp. 240-250). Oxford: Elsevier.

Lopes da Silva, F.H. & Gorter, J.A. (2009). Epileptogenesis and Plasticity. In P.A. Schwartzkroin (Ed.), *Encyclopedia of Basic Epilepsy Research* (pp. 221-227). Oxford: Elsevier.

Gorter, J.A. (2009, juli 02). *Strategies to prevent epileptogenesis.* Budapest, Hungary, 28th International Epilepsy Congress.

Vliet, E.A. van (2009, oktober 12). *Blood-brain barrier damage and inflammation in epilepsy: consequences for seizure progression?* Amsterdam, the Netherlands, University of Amsterdam: Masterclass.

Vliet, E.A. van (2009, januari 20). *Epilepsie: voorkomen of genezen?* Amsterdam, the Netherlands, University of Amsterdam: Voorlichtingsdag Psychobiologie.

Vliet, E.A. van (2009, januari 23). *Pharmacoresistance to phenytoin, levetiracetam and valproate in an animal model for temporal lobe epilepsy.* Utrecht, the Netherlands, Wetenschapsdag Sectie Wetenschappelijk Onderzoek van de Nederlandse Liga tegen Epilepsie.

Vliet, E.A. van (2009, november 16). *Pharmacoresistant epilepsy: is there a cure?* Amsterdam, the Netherlands, Graduate School Neuroscience Amsterdam: PhD course.

Membership editorial board

Gorter, J.A. (Ed.). (2009). *Epilepsia*.

Teixeira de Queiroz, C.M. (Ed.). (2009). *Front. integr. neurosci.*.

Invited lectures

Gorter, J.A. (2009, July 02). *Strategies to prevent epileptogenesis.* Budapest, Hungary, 28th International Epilepsy congress.

Vliet, E.A. van (2009, October 12). *Blood-brain barrier damage and inflammation in epilepsy: consequences for seizure progression?* Amsterdam, the Netherlands, University of Amsterdam: masterclass.

Vliet, E.A. van (2009, January 20). *Epilepsie: voorkomen of genezen?* Amsterdam, the Netherlands, University of Amsterdam: Voorlichtingsdag Psychobiologie.

Vliet, E.A. van (2009, January 23). *Pharmacoresistance to phenytoin, levetiracetam and valproate in an animal model for temporal lobe epilepsy.* Utrecht, the Netherlands, Wetenschapsdag Sectie Wetenschappelijk Onderzoek van de Nederlandse Liga tegen Epilepsie.

Vliet, E.A. van (2009, November 16). *Pharmacoresistant epilepsy: is there a cure?* Amsterdam, the Netherlands, PhD course Graduate School Neuroscience Amsterdam.

Hormonal Regulation of Signal Transduction in the Brain

Key publications

Oomen, C.A., Girardi, C.E.N., Cahyadi, R., Verbeek, E.C., Krugers, H., Joëls, M. & Lucassen, P.J. (2009). Opposite effects of early maternal deprivation on neurogenesis in male versus female rats. *PLoS One, 4*(1), e3675-3688

PhD Theses

Pu, Z. (2009, October 01). *A temporal perspective on stress hormones and memory.* UvA Universiteit van Amsterdam (125 pag.). Prom./coprom.: prof.dr. M. Joels & prof.dr. G. Fernandez.

Verbrugge, I. (2009, June 19). *Combining radiotherapy with death ligands in cancer treatment: feasibilty and molecular mechanisms.* UvA Universiteit van Amsterdam (108 pag.). Prom./coprom.: prof.dr. J. Borst & dr M. Verheij.

Academic publications

Alfarez, D.N., De Simoni, A., Velzing, E.H., Bracey, E., Joëls, M., Edwards, F.A. & Krugers, H.J. (2009). Corticosterone reduces dendritic complexity in developing hippocampal CA1 neurons. *Hippocampus, 19*(9), 828-836.

Bagot, R.C., Hasselt, F.N. van, Champagne, D.L., Meaney, M., Krugers, H. & Joels, M. (2009). Maternal care determines rapid effects of stress mediators on synaptic plasticity in adult rat hippocampal dentate gyrus. *Neurobiology of Learning and Memory, 92*, 292-300.

Boekhoorn, K. & Lucassen, P.J. (June 2009). Nieuwe neuronen in volwassen hersenen. *Tijdschrift voor Neuropsychiatrie & Gedragsneurologie*, 119-123.

Boer, K., Lucassen, P.J., Spliet, W.G.M., Vreugdenhil, E., Rijen, P.C. van, Troost, D., Jansen, F.E. & Aronica, E. (2009). Doublecortin-like (DCL) expression in focal cortical dysplasia and cortical tubers. *Epilepsia, 50*(12), 2629-2637.

Champagne, D.L., Kloet, E.R. de & Joëls, M. (2009). Fundamental aspects of the impact of glucocorticoids on the (immature) brain. *Seminars in Fetal & Neonatal Medicine, 14*(3), 136-142.

Gemert, N.G. van, Carvalho, D.M.M., Karst, H., Laan, S. van der, Zhang, M., Meijer, O.C., Hell, J.W. & Joels, M. (2009). Dissociation between rat hippocampal CA1 and dentate gyrus cells in their response to corticosterone: effects on calcium channel protein and current. *Endocrynology, 150*(10), 4615-4624.

Henckens, M.J.A.G., Hermans, E.J., Pu, Z., Joëls, M. & Fernández, G. (2009). Stressed memories: How acute stress affects memory formation in humans. *Journal of Neuroscience, 29*(32), 10111-10119.

Heuts, B.A. (2009). Lasius Niger houdt rechts, vooral als het druk wordt op zijn verticale straten op bomen. *Forum Formicidarum*, 5-9.

Jaworski, J., Kapitein, L.C., Montenegro Gouveia, S., Dortland, B.R., Wulf, P.S., Grigoriev, I., Camera, P., Spangler, S.A., Di Stefano, P., Demmers, J., Krugers, H., Defilippi, P., Akhmanova, A. & Hoogenraad, C.C. (2009). Dynamic microtubules regulate dendritic spine morphology and synaptic plasticity. *Neuron, 61*(1), 85-100.

Joosen, M.J.A., Jousma, E., Boom, T.M. van den, Kuijpers, W.C., Smit, A.B., Lucassen, P.J. & Helden, H.P.M. van (2009). Long-term cognitive deficits accompanied by reduced neurogenesis after soman poisoning. *NeuroToxicology, 30*(1), 72-80.

Joëls, M., Krugers, H.J., Lucassen, P.J. & Karst, H. (2009). Corticosteroid effects on cellular physiology of limbic cells. *Brain Research, 1293*, 91-100.

Joëls, M. (2009). Stress, the hippocampus, and epilepsy. *Epilepsia, 50*(4), 586-597.

Joëls, M. & Baram, T.Z. (2009). The neuro-symphony of stress. *Nature Reviews. Neuroscience, 10*(6), 459-466.

Krugers, H. & Hoogenraad, C.C. (2009). Hormonal Regulation of AMPA receptor trafficking and memory formation. *Frontiers in Synaptic Neuroscience, 1*, 1-8.

Liebmann, L., Karst, H. & Joëls, M. (2009). Effects of corticosterone and the beta-agonist isoproterenol on glutamate receptor-mediated synaptic currents in the rat basolateral amygdala. *European Journal of Neuroscience, 30*(5), 800-807.

Lucassen, P.J., Scheper, W. & Someren, E.J.W. van (2009). Adult neurogenesis and the unfolded protein response; new cellular and molecular avenues in sleep research. *Sleep Medicine Reviews, 13*(3), 183-186.

Lucassen, P.J., Bosch, O.J., Jousma, E., Krömer, S.A., Andrew, R., Seckl, J.R. & Neumann, I.D. (2009). Prenatal stress reduces postnatal neurogenesis in rats selectively bred for high, but not low, anxiety: Possible key role of placental 11ß-hydroxysteroid dehydrogenase type 2. *European Journal of Neuroscience, 29*(1), 97-103.

Marlatt, M.W., Hoozemans, J.J.M., Veerhuis, R. & Lucassen, P.J. (2009). Alzheimer's disease and adult neurogenesis: Are endogenous stem cells part of the solution? *US Neurology, 5*(1), 12-14.

Martin, S., Henley, J.M., Holman, D., Zhou, M., Wiegert, O., Spronsen, M. van, Joëls, M., Hoogenraad, C.C. & Krugers, H.J. (2009). Corticosterone alters AMPAR mobility and facilitates bidirectional synaptic plasticity. *PLoS One, 4*(3), e4714.

Oomen, C.A., Girardi, C.E.N., Cahyadi, R., Verbeek, E.C., Krugers, H., Joëls, M. & Lucassen, P.J. (2009). Opposite effects of early maternal deprivation on neurogenesis in male versus female rats. *PLoS One, 4*(1), e3675.

Pu, Z., Krugers, H.J. & Joëls, M. (2009). Beta-adrenergic facilitation of synaptic plasticity in the rat basolateral amygdala in vitro is gradually reversed by corticosterone. *Learn Memory, 16*(2), 155-160.

Smeets, T., Wolf, O.T., Giesbrecht, T., Sijstermans, K., Telgen, S. & Joëls, M. (2009). Stress selectively and lastingly promotes learning of context-related high arousing information. *Psychoneuroendocrinology, 34*(8), 1152-1161.

Zhou, M., Conboy, L., Sandi, C., Joëls, M. & Krugers, H.J. (2009). Fear conditioning enhances spontaneous AMPA receptor-mediated synaptic transmission in mouse hippocampal CA1 area. *European Journal of Neuroscience, 30*(8), 1559-1564.

Book Chapters

Bao, A.M, Lucassen, P.J. & Swaab, D.F. (2009). Neuroendocrinology of Psychiatric Disorders. In Binder, Hirokawa & Windhorst (Eds.), *Encyclopedia of Neuroscience* (pp. 2641-2645). Heidelberg: Springer.

Joels, M. & Karst, H. (2009). Adrenal Steroids: Biphasic Effects on Neurons. In L.R. Squire (Ed.), *Encyclopedia of Neuroscience* (pp. 131-134). Elsevier.

Joels, M., Karst, H., Krugers, H. & Kloet, E.R. de (2009). Corticosteroid actions on electrical activity in the brain. In A.M. Etgen & D.W. Pfaff (Eds.), *Molecular mechanisms of hormone actions on behavior* (pp. 305-328-chapter 11). Elsevier.

Joels, M., Karst, H., Krugers, H. & Kloet, E.R. de (2009). Corticosteroid Actions on Electrical Activity in the Limbic Brain. In D.W. Pfaff, A.P. Arnold, A.M. Etgen, S.E. Fahrbach & R.T. Rubin (Eds.), *Hormones, Brain and Behavior, 2e* (CELLULAR AND MOLECULAR MECHANISMS OF HORMONE ACTIONS ON BEHAVIOR, volume 3) (pp. -chapter 42). Elsevier.

Joels, M. & Karst, H. (2009). Effects of stress on the function of hippocampal cells. In H. Soreq, D. Kaufer & A. Friedman (Eds.), *The sights and sounds of stress and anxiety: Molecular, cellular and physiological aspects of stress research* (pp. 55-70). John Wiley & Sons, Inc.

Lucassen, P.J., Boekhoorn, K. & Francis, F. (2009). Cortical development - disorders. In M.D. Binder, N. Hirokawa & U. Windhorst (Eds.), *Encyclopedia of Neuroscience* (pp. 894-896). Heidelberg: Springer.

Lucassen, P.J., Meerlo, P., Naylor, A.S., Dam, A.M. van, Dayer, A.G., Czeh, B. & Oomen, C.A. (2009). Do depression, stress, sleep disruption, and inflammation alter hippocampal apoptosis and neurogenesis? In C.M. Pariante (Ed.), *Understanding depression: A translational approach* (pp. 139-156). Oxford: Oxford University Press.

Lucassen, P.J. & Swaab, D.F. (2009). Endocrine disorders of development and growth. In M.D. Binder, N. Hirokawa & U. Windhorst (Eds.), *Encyclopedia of Neuroscience* (pp. 1103-1106). Heidelberg: Springer.

Lucassen, P.J. & Swaab, D.F. (2009). Hypothalamo-pituitary-adrenal axis, stress and depression. In M.D. Binder, N. Hirokawa & U. Windhorst (Eds.), *Encyclopedia of Neuroscience* (pp. 1892-1895). Heidelberg: Springer.

Lucassen, P.J. & Swaab, D.F. (2009). Neuroendocrinology of eating disorders. In Binder, Hirokawa & Windhorst (Eds.), *Encyclopedia of Neuroscience* (pp. 2635-2637). Heidelberg: Springer.

Lucassen, P.J. & Swaab, D.F. (2009). Neuroendocrinology of tumours. In Binder, Hirokawa & Windhorst (Eds.), *Encyclopedia of Neuroscience* (pp. 2645-2648). Heidelberg: Springer.

Swaab, D.F. & Lucassen, P.J. (2009). Drinking disorders and osmoregulation. In M.D. Binder, N. Hirokawa & U. Windhorst (Eds.), *Encyclopedia of Neuroscience* (pp. 1010-1014). Heidelberg: Springer.

Swaab, D.F. & Lucassen, P.J. (2009). Hypothalamo-neurohypophysial system. In M.D. Binder, N. Hirokawa & U. Windhorst (Eds.), *Encyclopedia of Neuroscience* (pp. 1888-1892). Heidelberg: Springer.

Swaab, D.F. & Lucassen, P.J. (2009). Neuroendocrinology. In Binder, Hirokawa & Windhorst (Eds.), *Encyclopedia of Neuroscience* (pp. 2631-2635). Heidelberg: Springer.

Book

Joels, M. (2009). *Een zeepaardje in je hoofd.* Amsterdam: Bert Bakker.

Membership editorial board

Lucassen, P.J. (Ed.). (2009). *Frontiers in Neurogenesis*.

Invited lectures

Joels, M. (2009, September 14). *A dual role for mineralocorticoid receptors in the limbic brain.* Istanbul, Turkey, 22nd ECNP Congress.

Joels, M. (2009, September 09). *Action mechanism of stress hormones on neural structure and synaptic plasticity.* Rhodes, Greece, PENS / IBRO Summerschool.

Joels, M. (2009, March 09). *Corticosteroid effects on limbic neurons.* Bordeaux, France, INSERM U862.

Joels, M. (2009, April 26). *Genomic versus nongenomic corticosteroid effects in brain.* Istanbul, Turkey, 11th European Congress of Endocrinology.

Joels, M. (2009, October 04). *Glutamate transmission as target for rapid and delayed corticosteroid actions.* Milano, Italy, Biennial Meeting of the Italian Neuroscience Society.

Joels, M. (2009, April 20). *Rapid corticosteroid actions in brain: Mechanism and functional relevance.* New Orleans, USA, Annual Meeting of the American Physiological Society.

Joels, M. (2009, March 20). *Stress and cognitive function.* Dresden, Germany, Spring School on Stress.

Joels, M. (2009, December 11). *Stress and memory, from adaptation to disease.* Amsterdam, the Netherlands, 1st Meeting of the European Society for Cognitive and Affective Neuroscience.

Joels, M. (2009, March 06). *The influence of single and repetitive stress on limbic function: focus on corticosteroids.* Cape Ferrat, France, Servier Conference on Mood Disorders.

Joels, M. (2009, November 25). *The stressed brain, in health and disease.* Utrecht, the Netherlands, Annual Rudolf Magnus Lecture.

Krugers, H. (2009, October 31). *Emotionele herinneringen in een reageerbuis?* Amsterdam, the Netherlands, University of Amsterdam, BachelorDay.

Krugers, H. (2009, June 05). *Hormonal regulation of AMPAR trafficking and learning and memory.* Doorwerth, the Netherlands, 8th Endo-Neuropsycho Meeting.

Krugers, H. (2009, May 19). *Remembering fearful experiences: Molecular mechanisms and role of early life events.* Rijswijk, the Netherlands, BPRC Meeting.

Krugers, H. (2009, September 09). *Remembering fearful experiences: Molecular mechanisms and role of early life events.* Nijmegen, the Netherlands, Donders Centre for Neuroscience.

Krugers, H. (2009, March 26). *Stress hormones modulate AMPAR mobility and facilitate synaptic plasticity.* Göttingen, Germany, 8th Göttingen Meeting of the German Neuroscience Society.

Krugers, H. (2009, March 07). *Waarom onthouden we stressvolle en emotionele gebeurtenissen zo goed?* Amsterdam, the Netherlands, University of Amsterdam: Bachelordag.

Lucassen, P.J. (2009, June 04). *Changes in neurogenesis in Alzheimer (models).* Doorwerth, the Netherlands, EndoNeuroPsycho ENP Meeting.

Lucassen, P.J. (2009, June 05). *Doublecortin-like proteins during development and in developmental pathologies.* Doorwerth, the Netherlands, ENP Meeting.

Lucassen, P.J. (2009, January 26). *Neurogenesis in relation to Alzheimer's disease and mouse models for dementia.* Colorado, USA, Winterschool on Neuroscience.

Lucassen, P.J. (2009, January 22). *Neurogenesis, stress and depression.* Virgin Islands, USA, Winter Conference on Neuroscience.

Lucassen, P.J. (2009, January 12). *Stem cells in the adult brain.* Groningen, the Netherlands, Graduate School BCN.

Lucassen, P.J. (2009, July 29). *Structural plasticity and neurogenesis in relation to stress and depression.* Oxford, UK, The British Association for Psychopharmacology Meeting.

Lucassen, P.J. (2009, December 02). *Structural plasticity in dementia (models).* Leuven, Belgium, NEURAD Meeting.

Appendix 4

Research cluster Life Science Technologies

Mass Spectrometry of Biomacromolecules

Key Publications

Kramer, G., Sprenger, R.R., Back, J.W., Dekker, H.L., Nessen, M.A., Maarseveen, J.H. van, Koning, L.J. de, Hellingwerf, K.J., Jong, L. de & Koster, C.G. de (2009). Identification and quantitation of newly synthesized proteins in Escherichia coli by enrichment of azidohomoalanine-labeled peptides with diagonal chromatography. *Mol Cell Proteomics, 8*(7), 1599-1611.

Nessen, M.A., Kramer, G., Back, J.W., Baskin, J.M., Smeenk, L.E.J., Koning, L.J. de, Maarseveen, J.H. van, Jong, L. de, Bertozzi, C.R., Hiemstra, H. & Koster, C.G. de (2009). Selective enrichment of azide-containing peptides from complex mixtures. *J. proteome res., 8*(7), 3702-3711.

Academic publications (refereed)

Boot, R.G., Breemen, M.J. van, Wegdam, W., Sprenger, R.R., Jong, S. de, Speijer, D., Hollak, C.E.M., Dussen, L. van, Hoefsloot, H.C.J., Smilde, A.K., Koster, C.G. de, Vissers, J.P.C. & Aerts, J.F.M.G. (2009). Gaucher disease: A model disorder for biomarker discovery. *Expert Review of Proteomics, 6*(4), 411-419.

Butler, G., Rasmussen, M.D., Lin, M.F., Groot, P.W.J. de, Klis, F.M. & Cuomo, C.A. (2009). Evolution of pathogenicity and sexual reproduction in eight Candida genomes. *Nature, 459*(7247), 657-662.

Cate, J.M. ten, Klis, F.M., Pereira-Cenci, T., Crielaard, W. & Groot, P.W.J. de (2009). Molecular and cellular mechanisms that lead to Candida biofilm formation. *J. dent. res., 88*(2), 105-115.

Groot, P.W.J. de, Brandt, B.W., Horiuchi, H., Ram, A.F.J., Koster, C.G. de & Klis, F.M. (2009). Comprehensive genomic analysis of cell wall genes in Aspergillus nidulans. *Fungal Genet. Biol., 46*(1), S72-S81.

Henderickx, H.J.W., Raemakers-Franken, P.C., Wal, S. van der, Koster, C.G. de, Duchateau, A.L.L. & Sonke, T. (2009). Flow injection analysis electrospray ionization mass spectrometry for high-throughput screening of a gene library for amidase activity. *Anal. biochem., 394*(2), 159-163.

Jackson, A.P., Gamble, J.A., Yeomans, T., Moran, G.P., Saunders, D., Harris, D., Aslett, M., Barrell, J.F., Butler, G., Citiulo, F., Coleman, D.C., Groot, P.W.J. de, Goodwin, T.J., Quail, M.A., McQuillan, J., Munro, C.A., Pain, A., Poulter, R.T., Rajandream, M-A., Renauld, H., Spiering, M.J., Tivey, A., Gow,

N.A.R., Barrell, B., Sullivan, D.J. & Berriman, M. (2009). Comparative genomics of the fungal pathogens Candida dubliniensis and Candida albicans. *Genome res., 19*(12), 2231-2244.

Klis, F.M., Sosinska, G.J., Groot, P.W.J. de & Brul, S. (2009). Covalently linked cell wall proteins of Candida albicans and their role in fitness and virulence. *FEMS Yeast Res., 9*(7), 1013-1028.

Kramer, G., Sprenger, R.R., Back, J.W., Dekker, H.L., Nessen, M.A., Maarseveen, J.H. van, Koning, L.J. de, Hellingwerf, K.J., Jong, L. de & Koster, C.G. de (2009). Identification and quantitation of newly synthesized proteins in Escherichia coli by enrichment of azidohomoalanine-labeled peptides with diagonal chromatography. *Mol Cell Proteomics, 8*(7), 1599-1611.

Moreno-Ruiz, E., Ortu, G., Groot, P.W.J. de, Cottier, F., Loussert, C., Prévost, M.C., Koster, C. de, Klis, F.M., Goyard, S. & d'Enfert, C. (2009). The GPI-modified proteins Pga59 and Pga62 of Candida albicans are required for cell wall integrity. *Microbiology, 155*(6), 2004-2020.

Müller, M.Q., Koning, L.J. de, Schmidt, A., Ihling, A., Syha, Y., Rau, O., Mechtler, K., Schubert-Zsilavecz, M. & Sinz, A. (2009). An innovative method to study target protein-drug interactions by mass spectrometry. *J. of med. chem., 52*(9), 2875-2879.

Nessen, M.A., Kramer, G., Back, J.W., Baskin, J.M., Smeenk, L.E.J., Koning, L.J. de, Maarseveen, J.H. van, Jong, L. de, Bertozzi, C.R., Hiemstra, H. & Koster, C.G. de (2009). Selective enrichment of azide-containing peptides from complex mixtures. *J. proteome res., 8*(7), 3702-3711.

Wegdam, W., Moerland, P.D., Buist, M.R., Ver Loren van Themaat, E., Bleijlevens, B., Hoefsloot, H.C.J., Koster, C.G. de & Aerts, J.F.M.G. (2009). Classification-based comparison of pre-processing methods for interpretation of mass spectrometry generated clinical datasets. *PROTEOME SCI, 7*, 19.

Wortman, J.R., Gilsenan, J.M., Joardar, V., Deegan, J., Clutterbuck, J., Andersen, M.R., Archer, D., Bencina, M., Braus, G., Coutinho, P., Döhren, H. von, Doonan, J., Driessen, A.J., Durek, P., Espeso, E., Fekete, E., Flipphi, M., Estrada, C.G., Geysens, S., Goldman, G., Groot, P.W.J. de, Hansen, K., Harris, S.D., Heinekamp, T., Helmstaedt, K., Henrissat, B., Hofmann, G., Homan, T., Horio, T., Horiuchi, H., James, S., Jones, M., Karaffa, L., Karányi, Z., Kato, M., Keller, N., Kelly, D.E., Kiel, J.A., Kim, J.M., Klei, I.J. van der, Klis, F.M., Kovalchuk, A., Kraševec, N., Kubicek, C.P., Liu, B., MacCabe, A., Meyer, V., Mirabito, P., Miskei, M., Mos, M., Mullins, J., Nelson, D.R., Nielsen, J., Oakley, B.R., Osmani, S.A., Pakula, T., Paszewski, A., Paulsen, I., Pilsyk, S., Pócsi, I., Punt, P.J., Ram, A.F.J., Ren, Q., Robellet, X., Robson, G., Seiboth, B., Solingen, P. van, Specht, T., Sun, J., Taheri-Talesh, N., Takeshita, N., Ussery, D., Kuyk, P.A. van, Visser, H., Vondervoort, P.J. van, Vries, R.P. de, Walton, J., Xiang, X., Xiong, Y., Zeng, A.P., Brandt, B.W., Cornell, M.J., Hondel, C.A. van den, Visser, J., Oliver, S.G. &

Turner, G. (2009). The 2008 update of the *Aspergillus nidulans* genome annotation: A community effort. *Fungal Genet. Biol., 46*(1), S2-S13.

PhD Theses

Smit, S. (2009, September 22). *Statistical data processing in clinical proteomics.* UvA Universiteit van Amsterdam (116 pag.). Prom./coprom.: prof.dr. A.K. Smilde, prof.dr. C.G. de Koster & dr.ir. H.C.J. Hoefsloot.

Peters, R.A.H. (2009, January 22). *Characterisation of polymeric network structures.* UvA Universiteit van Amsterdam (214 pag.) (Maastricht: Universitaire Pers Maastricht). Prom./coprom.: prof.dr. S. van der Wal, prof.dr.ir. P.J. Schoenmakers & prof.dr. C.G. de Koster.

Invited lectures

Koster, C. de (2009, March 26). *High throughput LC-FT-ICR-MS quantification of yeast glycolytic proteins.* Kerkrade, the Netherlands, Ned. Ver. voor Massaspectrometrie.

Koster, C. de (2009, January 28). *Jump into high resolution mass spectrometry or keep your TOF's and quadrupoles up and running?* Amsterdam, the Netherlands, Fourth Int. Symp. on Separation and Characterization of natural and synthetic macromolecules.

Koster, C.G. de (2009, August 31). *High throughput LC-FT-ICR-MS quantification of yeast protein degradation.* Bremen, Germany, International Mass Spectrometry Conference.

Koster, C.G. de (2009, June 26). *Identification and quantitation of newly synthesized protein in Escherichia coli.* Utrecht, the Netherlands, Symposium Nederlands Proteomics Platform.

Nessen, M., Hiemstra, H., Koster, C.G. de, Jong, L. de & Maarseveen, J.H. van (2009, October 19). *Selective capturing and analysis of azide-labelled biomolecules.* Lunteren, the Netherlands, Annual Meeting NWO/CW Studiegroup OS/SR/BMC.

Nessen, M., Kramer, G., Back, J.W., Maarseveen, J.H. van, Koning, L.J. de, Jong, L. de, Hiemstra, H. & Koster, C.G. de (2009, November 02). *Selective enrichment of azide-labelled peptides for mass spectrometric analysis of cellular proteome dynamics.* Lunteren, the Netherlands, Annual Meeting NWO/CW and NVMS.

Nessen, M., Kramer, G., Back, J.W., Maarseveen, J.H. van, Koning, L.J. de, Jong, L. de, Hiemstra, H. & Koster, C. de (2009, March 26). *Selective purification of azide-containing peptides from complex mixtures.* Kerkrade, the Netherlands, Ned. Ver. voor Massaspectrometrie.

Membership Editorial Board

Groot, P.W.J. de (Ed.). (2009). *FEMS Yeast Res.*.

BioSystems Data Analysis

Key Publications

Velzen, E.J.J. van, Westerhuis, J.A., Duynhoven, J.P.M. van, Dorsten, F.A. van, Grün, C.H., Jacobs, D.M., Duchateau, G.S.M.J., Vis, D.J. & Smilde, A.K. (2009). Phenotyping tea consumers by nutrikinetic analysis of polyphenol end metabolites. *J. Proteome Res., 8*(7), 3317-3330.

Cakir, T., Hendriks, M.M.W.B., Westerhuis, J.A. & Smilde, A.K. (2009). Metabolic network discovery through reverse engineering of metabolome data. *Metabolomics, 5*(3), 318-329.

PhD Thesis

Smit, S. (2009, September 22). *Statistical data processing in clinical proteomics.* UvA Universiteit van Amsterdam (116 pag.). Prom./coprom.: prof.dr. A.K. Smilde, prof.dr. C.G. de Koster & dr.ir. H.C.J. Hoefsloot.

Academic publications (refereed)

Berg, R.A. van den, Van Mechelen, I., Wilderjans, T.F., Van Deun, K., Kiers, H.A.L. & Smilde, A.K. (2009). Integrating functional genomics data using maximum likelihood based simultaneous component analysis. *BMC Bioinformatics, 10*(340).

Berg, R.A. van den, Rubingh, C.M., Westerhuis, J.A., Werf, M.J. van der & Smilde, A.K. (2009). Metabolomics data exploration guided by prior knowledge. *Anal. Chim. Acta, 651*(2), 173-181.

Boot, R.G., Breemen, M.J. van, Wegdam, W., Sprenger, R.R., Jong, S. de, Speijer, D., Hollak, C.E.M., Dussen, L. van, Hoefsloot, H.C.J., Smilde, A.K., Koster, C.G. de, Vissers, J.P.C. & Aerts, J.F.M.G. (2009). Gaucher disease: A model disorder for biomarker discovery. *Expert Review of Proteomics, 6*(4), 411-419.

Braaksma, M., Smilde, A.K., Werf, M.J. van der & Punt, P.J. (2009). The effect of environmental conditions on extracellular protease activity in controlled fermentations of Aspergillus niger. *Microbiology, 155*(10), 3430-3439.

Cakir, T., Hendriks, M.M.W.B., Westerhuis, J.A. & Smilde, A.K. (2009). Metabolic network discovery through reverse engineering of metabolome data. *Metabolomics, 5*(3), 318-329.

Hooff, S.R. van, Koster, J., Hulsen, T., Schaik, B.D.C. van, Roos, M., Batenburg, M.F. van, Versteeg, R. & Kampen, A.H.C. van (2009). The

construction of genome-based transcriptional units. *OMICS: A Journal of Integrative Biology, 13*(2), 105-114.

Peters, S., Velzen, E.J.J. van & Janssen, H.G. (2009). Parameter selection for peak alignment in chromatographic sample profiling: objective quality indicators and use of control samples. *Analytical and Bioanalytical Chemistry, 394*(5), 1273-1281.

Schalkwijk, D.B. van, Graaf, A.A. de, Ommen, B. van, Bochove, K. van, Rensen, P.C.N., Havekes, L.M., Pas, N.C.A. van de, Hoefsloot, H.C.J., Greef, J. van der & Freidig, A.P. (2009). Improved cholesterol phenotype analysis by a model relating lipoprotein life cycle processes to particle size. *J. lipid res., 50*(12), 2398-2411.

Smilde, A.K., Werf, M.J. van der, Schaller, J.P. & Kistemaker, C. (2009). Characterizing the precision of mass-spectrometry-based metabolic profiling platforms. *Analyst, 134*(11), 2281-2285.

Smilde, A.K., Kiers, H.A.L., Bijlsma, S., Rubingh, C.M. & Erk, M.J. van (2009). Matrix correlations for high-dimensional data: the modified RV-coefficient. *Bioinformatics, 25*(3), 401-405.

Thissen, U., Wopereis, S., Berg, S.A.A. van, Bobeldijk, I., Kleemann, R., Kooistra, T., Dijk, K.W. van, Ommen, B. van & Smilde, A.K. (2009). Improving the analysis of designed studies by combining statistical modelling with study design information. *BMC Bioinformatics, 10*, 52.

Timmerman, M.E., Kiers, H.A.L., Smilde, A.K., Ceulemans, E. & Stouten, J. (2009). Bootstrap confidence intervals in multi-level simultaneous component analysis. *Br. J. Math. Stat. Psychol., 62*, 299-318.

Van Deun, K., Smilde, A.K., Werf, M.J. van der, Kiers, H.A.L. & Van Mechelen, I. (2009). A structured overview of simultaneous component based data integration. *BMC Bioinformatics, 10*, 246.

Velzen, E.J.J. van, Westerhuis, J.A., Duynhoven, J.P.M. van, Dorsten, F.A. van, Grün, C.H., Jacobs, D.M., Duchateau, G.S.M.J., Vis, D.J. & Smilde, A.K. (2009). Phenotyping tea consumers by nutrikinetic analysis of polyphenol end metabolites. *J. Proteome Res., 8*(7), 3317-3330.

Verouden, M.P.H., Westerhuis, J.A., Werf, M.J. van der & Smilde, A.K. (2009). Exploring the analysis of structured metabolomics data. *Chemometrics Intell. Lab. Syst., 98*(1), 88-96.

Verouden, M.P.H., Nootebaart, R.A., Westerhuis, J.A., Werf, M.J. van der, Teusink, B. & Smilde, A.K. (2009). Multi-way analysis of flux distributions across multiple conditions. *J. Chemometr., 23*(7-8), 406-420.

Wegdam, W., Moerland, P.D., Buist, M.R., Ver Loren van Themaat, E., Bleijlevens, B., Hoefsloot, H.C.J., Koster, C.G. de & Aerts, J.F.M.G. (2009).

Classification-based comparison of pre-processing methods for interpretation of mass spectrometry generated clinical datasets. *PROTEOME SCI, 7*, 19.

Westerhuis, J.A., Velzen, E.J.J. van, Hoefsloot, H.C.J. & Smilde, A.K. (2009). Data analysis strategies in nutritional metabolomics. *G.I.T. Laboratory Journal Europe, 13*(1-2), 17-19.

Wopereis, S., Rubingh, C.M., Erk, M.J. van, Verheij, E.R., Vliet, T. van, Cnubben, N.H.P., Smilde, A.K., Greef, J. van der, Ommen, B. van & Hendriks, H.F.J. (2009). Metabolic profiling of the response to an oral glucose tolerance test detects subtle metabolic changes. *PLoS ONE, 4*(2), e4525.

J.J. Jansen, N.M. van Dam, H.C.J. Hoefsloot and A.K. Smilde. (2009) Crossfit analysis: a novel method to characterize the dynamics of induced plant responses, *BMC Bioinformatics,* 10:425.

Book Chapter

Duynhoven, J.P.M. van, Velzen, E.J.J. van, Gross, G., Dorsten, F.A. van, Westerhuis, J.A. & Smilde, A.K. (2009). NMR-based metabonomics approaches for the assessment of the metabolic impact of dietary polyphenols on humans. In M. Guðjónsdóttir, P.S. Belton & G.A. Webb (Eds.), *Magnetic Resonance in Food Science: Challenges in a Changing World* (pp. 20-28). London: RSC Books.

Hoefsloot, H.C.J., Vis, D.J., Westerhuis, J.A., Smilde, A.K. & Jansen, J.J. (2009). Multiset data analysis: ANOVA simultaneous component analysis and related methods. In S.D. Brown, R. Tauler & B. Walczak (Eds.), *Comprehensive Chemometrics* (pp. 453-472). Oxford: Elsevier.

Membership editorial board

Smilde, A.K. (Ed.). (2009). *J. Chemometr.*.
Westerhuis, J.A. (Ed.). (2009). *J. Chemometr.*.

Invited lectures

Hoefsloot, H.C.J. (2009, June 02). *Data analysis in systems biology.* Leiden, the Netherlands, Lorentz Center workshop: Experimental design in systems biology.

Hoefsloot, H.C.J. (2009, April 22). *Hormone regulation for understanding endocrine dysfunction.* Amsterdam, the Netherlands, 6th International Symp.on Networks in Bioinformatics.

Hoefsloot, H.C.J. (2009, October 09). *Networks.* Noordwijkerhout, the Netherlands, NMC Meeting.

Hoefsloot, H.C.J. (2009, February 06). *Protein network analysis.* Amsterdam, the Netherlands, NISB Workshop: Systems biology of of the synapse.

Hoefsloot, H.C.J. (2009, June 14). *The analysis of X-omics data.* Amsterdam, the Netherlands, Free University: Statistics for life science seminars.

Hoefsloot, H.C.J. (2009, March 12). *The analysis of X-omics data.* Amsterdam, the Netherlands, CWI-Life science seminars.

Kampen, A.H.C. van (2009, October 16). *Novel information management approaches for the development of knowledge bases to support systems biology.* Noordwijkerhout, the Netherlands, NCSB Kickoff meeting.

Smilde, A.K. (2009, November 20). *From metabolomics data to biological networks and back.* Newark, USA, Eastern Analytical Symposion.

Smilde, A.K. (2009, November 12). *From metabolomics data to biological networks and back.* Wageningen, the Netherlands, VOC Jubilee Meeting.

Smilde, A.K. (2009, November 20). *Metabolomics: a crucial part of systems biology.* Halifax, Canada, Dalhouse University.

Smilde, A.K. (2009, June 15). *Multiway methods with a priori knowledge.* Nuria, Spain, TRICAP Congress.

Westerhuis, J.A. (2009, July 01). *Conquering biological variation by cross-over design and paired data analysis.* Norwich, UK, Metabomeeting.

Westerhuis, J.A. (2009, November 01). *Conquering biological variation by cross-over design and paired data analysis: applications from the food industry.* Barcelona, Spain, Biomarker Summit.

Westerhuis, J.A. (2009, June 02). *Metabolomics data: Structure and noise.* Leiden, the Netherlands, Lorentz Center workshop.

Micro Array Department and Integrated Bioinformatics Unit

Key Publications

Jonker M.J., Bruning O., van Iterson M., Schaap M.M., van der Hoeven T.V., Vrieling H., Beems R.B., de Vries A., van Steeg H., Breit T.M., Luijten M. Finding transcriptomics biomarkers for in vivo identification 1 of (non-)genotoxic carcinogens using wild-type and Xpa/p53 mutant mouse models. *Carcinogenesis* 2009 Oct;30(10):1805-12.

de Leeuw W.C., Rauwerda H., Inda M.A., Bruning O., Breit T.M. SigWinR.; the SigWin-detector updated and ported to R. *BMC Res Notes* 2009 Oct 6;2(1):205.

Garinis G.A., Uittenboogaard L.M., Stachelscheid H., Fousteri M., van IJcken W., Breit T.M., van Steeg H., Mullenders L.H., van der Horst G.T., Brüning J.C., Niessen C.M., Hoeijmakers J.H., Schumacher B. Persistent transcription-blocking DNA lesions trigger somatic growth attenuation associated with longevity. *Nat Cell Biol. 2009 May;11(5):604-15.*

Academic publications (refereed)

Boer, Y.W., Crino, P.B., Gorter, J.A., Nellist, M., Jansen, F.E., Spliet, W.G., Rijen, P.C. van, Wittink, F.R.A., Breit, T.M., Troost, D, Wadman, W.J. & Aronica, E. (2009). Gene Expression Analysis of Tuberous Sclerosis Complex Cortical Tubers Reveals Increased Expression of Adhesion and Inflammatory Factors. *BRAIN PATHOL*, 1-20.

Garinis, G.A., Uittenboogaard, L.M., Stachelscheid, H., Fousteri, M.I., IJcken, W. van, Breit, T.M., Steeg, H. van, Mullenders, L.H.F., Horst, G.T.J. van der, Brüning, J.C., Niessen, C.M., Hoeijmakers, J.H.J. & Schumacher, B. (2009). Persistent transcription-blocking DNA lesions trigger somatic growth attenuation associated with longevity. *Nature cell biology, 11*(5), 604-615.

Hackenberg, C., Engelhardt, A., Matthijs, H.C.P., Wittink, F., Bauwe, H., Kaplan, A. & Hagemann, M. (2009). Photorespiratory 2-phosphoglycolate metabolism and photoreduction of O2 cooperate in high-light acclimation of Synechocystis sp. strain PCC 6803. *Planta, 230*(4), 625-637.

Jonker, M.J., Bruning, O., Iterson, M. van, Schaap, M.M., Hoeven, T.V. van der, Vrieling, H., Beems, R.B., Vries, A. de, Steeg, H. van, Breit, T.M. & Luijten, M. (2009). Finding transcriptomics biomarkers for in vivo identification of (non-)genotoxic carcinogens using wild-type and Xpa/p53 mutant mouse models. *CARCINOGENESIS, 30*(10), 1805-1812.

Oomes, S.J.C.M., Jonker, M.J., Wittink, F.R.A., Hehenkamp, J.O., Breit, T.M. & Brul, S. (2009). The effect of calcium on the transcriptome of sporulating B.subtilis cells. *Int. J. Food Microbiol., 133*, 234-242.

Wassink, I., Rauwerda, H., Neerincx, P.B.T., Vet, P.E. van der, Breit, T.M., Leunissen, J.A.M. & Nijholt, A. (2009). Using R in Taverna: RShell v1.2. *BMC Research Notes, 2*(138).

van Hooff S.R., Koster J., Hulsen T., van Schaik B.D.C., Roos M., van Batenburg M.F., Versteeg R., van Kampen A.H.C. (2009) The construction of genome-based transcriptional units. *OMICS,* 2009 Apr;13(2):105-14.

Bosnacki D., Pronk T.E., de Vink E.P. (2009) *In Silico* Modelling and Analysis of Ribosome Kinetics and aa-tRNA Competition. *Lecture Notes in Bioinformatics: Transactions on Computational System Biology XI. Priami C, Back R-J, Petre I (eds.) Springer Verlag*. pp 69-89.

de Leeuw W.C., Rauwerda H., Inda M.A., Bruning O., Breit T.M.(2009) SigWinR; the SigWin-detector updated and ported to R. *BMC Res Notes* 6;2(1):205.

H.Rauwerda, I. Wassink, P.B.T. Neerincx, P.E. van der Vet, T.M. Breit, J.A.M. Leunissen and A. Nijholt (2009) Using R in Taverna: RShell v1.2 *BMC Res Notes* 2009 Jul 16;2:138.

Wassink I., Rauwerda H., van der Vet P., Breit T.M., Nijholt A. E-BioFlow: Different Perspectives on Scientific Workows. *Communications in Computer and Information Science 2009*

Fikkert, W., Vet, P. van der, Rauwerda, H., Breit, T. & Nijholt, A. (2009). Gestures to intuitively control large displays. In M.S. Dias, S. Gibet, M.M. Wanderley & R. Bastos (Eds.), *Gesture-based human-computer interaction and simulation: 7th International Gesture Workshop, GW 2007, Lisbon, Portugal, May 23-25, 2007: Revised selected papers Vol. 5085. Lect. Notes Comput. Sci.* (pp. 199-204). Berlin: Springer.

Neerincx, P.B.T., Rauwerda, H., Nie, H., Groenen, M.A.M., Breit, T.M. & Leunissen, J.A.M. (2009). OligoRAP – an Oligo Re-Annotation Pipeline to improve annotation and estimate target specificity. In *BMC Proceedings 2009* (pp. S4-S4).

Wassink, I., Vet, P.E. van der, Wolstencroft, K., Neerincx, P.B.T., Roos, M., Rauwerda, H. & Breit, T.M. (2009). Analysing scientific workflows: why workflows not only connect web services. In L.J. Zhang (Ed.), *2009 IEEE Congress on Services -1-* (pp. 314-321). Los Alamitos: IEEE Computer Society Press.

Book Chapter

Fikkert, W., Vet, P. van der, Rauwerda, H., Breit, T.M. & Nijholt, A. (2009). Gestures to Intuitively Control Large Displays. In M. Sales Dias, S. Gibet, M.M. Wanderley & R. Bastos (Eds.), *Gesture-Based Human-Computer Interaction and Simulation* (Lecture Notes in Computer Science, 5085) (pp. 199-204-chapter 22). Berlin/Heidelberg/New York: Springer.

Pronk, T.E., During, H.J., Schieving, F. & Werger, M.J.A. (2009). Diversity by Temporal Oscillations in Plant Communities with a Differential Timing of Reproduction. In I.N. Haugen & A.S. Nilsen (Eds.), *Game Theory: Strategies, Equilibria, and Theorems* (pp. 313-333-chapter 13). Hauppauge, NY: Nova Science Publishers.

SILS -- Verschillenanalyse begroting - realisatie 2009

Begroting	**GS1**	**GS2**	**GS3**
1. Baten	10,877	1,942	3,245
2. Personele lasten	-4,843	-1,209	-2,392
3. Overige lasten	-5,006	-1,420	-2,243
Resultaat	1,028	-687	-1,390

Realisatie	**GS1**	**GS2**	**GS3**
1. Baten	7,772	4,015	4,382
2. Personele lasten	-5,399	-1,662	-1,654
3. Overige lasten	-2,637	-2,245	-2,913
Resultaat	-265	108	-185

Verschil (Realisatie minus begroting)	**GS1**	**GS2**	**GS3**
1. Baten	-3,105	2,073	1,137
2. Personele lasten	-556	-453	738
3. Overige lasten	2,369	-825	-670
Resultaat	-1,293	795	1,205

Analyse van de verschillen per categorie en per geldstroom

1. Baten	**GS1**	**GS2**	**GS3**
Begroot	**10,877.0**	**1,942.0**	**3,245.0**
Interne baten			
Budget			
5%-budgetkorting 2009	-318.0	0.0	0.0
BSIK bijdrage (restanttoekenning)	-50.0	0.0	0.0
Verrekening onderwijs	123.0	0.0	0.0
Verrekening vergoeding ow-management	813.0	0.0	0.0
	568.0	*0.0*	*0.0*
Matching			
Matching: nieuwe systematiek (inhaalcorrectie)	-77.1	372.6	-295.5
Matching: accommoderen CvB-overhead	931.3	-429.7	-501.6
Matching: overig	-4,186.8	2,251.4	1,935.4
	-3,332.6	*2,194.3*	*1,138.3*
Attentie: de 3348,2 moet zijn:			
Interne bijdrage (via interne order)	*125.5*	*44.1*	*-169.6*

Interne bijdragen			
Afdelingsresultaat WP	-37.2	0.0	0.0
Afdelingsresultaat OBP	148.5	0.0	0.0
Verrekening vergoeding ow-management	-684.9	0.0	0.0
Terugboeking uit GS2 naar GS1 VN	70.4	-70.4	0.0
Overige interne bijdragen	-63.6	16.0	26.8
	-566.8	*-54.4*	*26.8*
	-3,205.9	*2,184.0*	*995.5*
Externe baten			
Contractonderzoek			
Contractonderzoek: OHW-effect inhaalmatching		-372.6	295.5
Contractonderzoek: hogere omzet	83.1	249.1	-385.9
	83.1	-123.5	-90.4
Meer/minder overige baten	33.4	12.6	232.0
	116.5	-110.9	141.6
Verschil	-16.0	-0.1	-0.1
Werkelijk	**7,771.6**	**4,015.0**	**4,382.0**

2. Personele lasten

Begroot	**-4,843.0**	**-1,209.0**	**-2,392.0**
PID			
Hoeveelheidsverschil	572.9	-293.9	850.1
Prijsverschil	-243.6	-65.0	-125.0
Afronding/onverklaard	65.3	-6.1	-1.4
	394.6	-365.0	723.7
Inzet niet via tijdsverantwoording	-352.0	40.1	172.2
	42.6	-324.9	895.9
Opslagen PID			
Opslag ziekte, wachtgeld, overige PL	-357.7	-113.8	-126.0
PNID			
Verschil	-240.9	-14.0	-32.2
Verschil	-0.1	0.0	0.1
Werkelijk	**-5,399.1**	**-1,661.7**	**-1,654.2**

3. Overige lasten

Begroot	**-5,006.0**	**-1,420.0**	**-2,243.0**
Primaire overige lasten			
Subsidies en overdrachten	-13.8	-1.3	-9.0
Afschrijvingen	-351.5	0.0	0.0
Huisvestingskosten	-6.1	-0.2	-0.3

Overige kosten	236.4	128.4	-196.3
	-135.0	126.9	-205.6
Financiële lasten	-1.6	0.1	3.4
Toerekening diensten en verrekening intrafacultair			
Diensten GDS (variabel)	-2.0	0.0	-127.4
Toerekening binnen eenheid: bovennormoverhead	123.3	0.0	0.0
Toerekening binnen eenheid: projectadm.	0.0	0.0	-166.3
	121.3	0.0	-293.7
Overhead / werkplekoverhad			
Overhead: opslagen PL	357.7	113.8	126.0
Hoeveelheidsverschil	66.7	-198.2	556.0
Prijsverschil	5.4	59.4	69.2
Overig/afronding	67.2	-21.9	46.6
Afdelingsoverhead/werkplekoverhead: opslagen PL	*497.0*	*-46.9*	*797.8*
Instituutsoverhead	956.5	-475.3	-470.4
Centrale universitaire overhead	930.4	-429.7	-501.6
	2,383.9	-952.0	-174.1
Verschil	0.1	-0.2	0.0
Werkelijk	**-2,637.3**	**-2,245.1**	**-2,913.0**

Aanvullende toelichting formatie en GPL	**GS1**	**GS2**	**GS3**
Aantal fte begroot (WP+OBP)	73.0	24.7	52.9
GPL begroot (naar geldstroom)	65.1	49.0	45.2
Aantal fte werkelijkheid	64.2	30.7	34.1
GPL werkelijk	68.9	51.1	48.9
Verschil fte	8.8	-6.0	18.8
Verschil GPL werkelijkheid - GPL begroting	-3.8	-2.1	-3.7

Contact details

****Director**: Dr. H.D. Veldhuis

Manager Business and Finance: Dr. Ir. J. C. Huijser

Website: www.science.uva.nl/sils/home.cfm

***Management Contact Address**:

Mrs E.C.M. Lutz, Secretary to the Director
Sciencepark 904, 1098 XH Amsterdam
Tel: 0031 (20) 525 5187
Fax: 0031 (20) 525 7934
E-mail: E.C.M.Lutz-Langezaal@uva.nl

Postal address:
Swammerdam Institute for Life Sciences
Universiteit van Amsterdam
Postbus 94215, Postkast 2A, 1090 GE Amsterdam

***Secretariats**:

Mrs B.E. Fabius, Mrs A.M. Hendriks
Nieuwe Achtergracht 166, 1018 WV Amsterdam
Building C, room 3.13
Tel: 0031 (20) 525 6970 / 5055
Fax: 0031 (20) 525 6971
E-mail: B.E.Fabius@uva.nl, A.M.Hendriks@uva.nl

Mrs L.M.Wind
Sciencepark 904, 1098 XH Amsterdam
Tel: 0031 (20) 525 7931
Fax: 0031 (20) 525 7934
E-mail: L.M.Wind@uva.nl

Mrs A. F. Eekhof
Sciencepark 904, 1098 XH Amsterdam
Tel: 0031 (20) 525 7638
Fax: 0031 (20) 525 7709
E-mail: A.F.Eekhof@uva.nl

*) As from August 2010 all groups of the SILS have been housed on Science Park, secretariats: room C2-202 and room C3-272, management contact address: b.e.fabius@uva.nl.
**) As from in the middle of 2010 director of the SILS is: Prof.dr.W.J.Stiekema.