The Graduate School EXPERIMENTAL PLANT SCIENCES

EXPERIMENTAL PLANT SCIENCES

self-evaluation report 2015-2020

Summary and case studies
Genome Biology Unit

October 2021

Summary Genome Biology Unit

The Genome Biology Unit (GBU) aims to explore, understand, and exploit biological diversity, in genomes and traits of individuals, populations, and across species. Key to these aims is the study of how evolutionary processes have shaped the diversity we see within and between populations. To investigate the basis of biological diversity, the unit develops methodology and tools to study variation within genes and genomes, with a strong focus on the analysis of genomic data and its integration with other -omics and genetic data. The unit furthermore probes the connections between organisms' genotypes and their phenotypes, with large efforts towards accurate phenotyping and the development of statistical methods to link the genotype to the phenotype. The unit is made up of the chair groups Bioinformatics, Biosystematics, Genetics, and Plant Breeding and was formed in 2018. Besides their joint focus on genomes, these groups host research on a variety of other topics which benefit from, or contribute to, the research of GBU.

GBU thus increases fundamental knowledge on biological diversity and the processes that generate it. As such, the genomic and genetic knowledge generated by the GBU is key for biotechnology companies addressing societal challenges related to food and energy security, health, and sustainability, in particular breeding companies that use it in their breeding programmes. In our activities, we connect fundamental research and applications thereof, both to find inspiration and to achieve impact on society either directly or via the many different private and public organizations we cooperate with.

GBU researchers collaborate scientifically with a wide range of partners within Wageningen University & Research, including the other EPS research units. GBU is involved in many national and international projects, many funded by grants for fundamental science, including ERC and NWO grants. Our main societal stakeholders are found in industry, particularly in plant breeding, biotechnology, and chemistry. We collaborate with a wide range of companies in public-private initiatives; the close relation with Wageningen Research further facilitates knowledge transfer. GBU staff are involved in setting the national science agenda, hold board positions in public-private collaboration organizations or act as advisors for companies. We contribute to outreach in the form of interviews or commentaries in the media, the organization of activities for the public, or projects for primary and secondary education. Finally, we are involved in major MSc-programmes and train PhD students who readily find employment in industry and academia.

Over the review period, the GBU has shown a consistently high output of scientific publications in peer review journals that have a significant impact in its research domain and has attracted funding for both founding research and for research with public and private partners to contribute to solving more immediate societal problems. Moreover, a substantial number of personal grants were obtained and GBU has appointed young academic talent across all areas of expertise to strengthen and sustain the unit. Lastly, we have continued to be engaged with society including via press releases, interviews in media, through the development of teaching material, and through training and education for professionals.

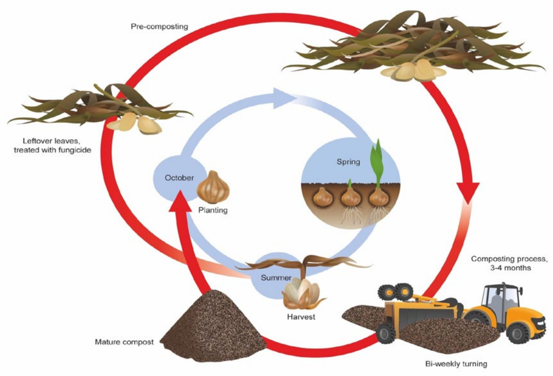
Our strategy for the period to come is to strengthen the organization and coordination of GBU to identify emerging research questions, explore possibilities of how results can be applied to societal challenges, and generally enhance the coherence and sustainability of the unit. Moreover, through intensifying the communication and collaboration with other partners within EPS, WUR, and nationally and internationally we aim making the "brand" GBU visible to apply our conceptual expertise, knowledge, and critical mass to tackle key challenges that require a multidisciplinary approach.

Case studies

Case 1 - Understanding and using the genetic and genomic information of polyploids

Many of the crops we use for food, feed, fibre, fuel and flowers are polyploids. Genetic improvement of such crops has for a long time been hampered by their complex genetic inheritance. With the advent of novel -omics techniques, efficient and faster crop improvement has come within reach for the first time in history. However, knowing which alleles to combine to achieve the best phenotypic result remains a major challenge. We embarked on this journey about 10 years ago and began developing different software tools to enable more informed, faster and more precise breeding (software examples include PedigreeSim, fitPoly, polymapR, polyqtlR, Pedihaplotyper etc). The research was taken up despite scepsis about the possible success, but has since then proven to be very successful as exemplified by a number of large projects involving many different companies (the current program has 10 different vegetable, ornamental, fruit and field crops companies) and collaboration with the US funded NSF project Tools for Genomics-Assisted Breeding in Polyploids. This has led to a wide range of well-cited scientific papers in peer-reviewed journals and to workshops for scientists and researchers from companies around the world, many of whom are now implementing genomics-assisted breeding in their polyploid crops. One of the members of the research theme, dr. Peter Bourke, graduated *cum laude* from Wageningen University, received the Hugo de Vries Award from the Royal Botanical Society of the Netherlands (KNBV) for his thesis (2018) and became tenure tracker within Plant Breeding (2020). This research has enabled us to zoom in on haplotypes determining phenotypic trait values and led to integrated tetraploid and hexaploid genetic maps that we generated in potato and chrysanthemum.

Case 2 - One-health risks of a circular economy

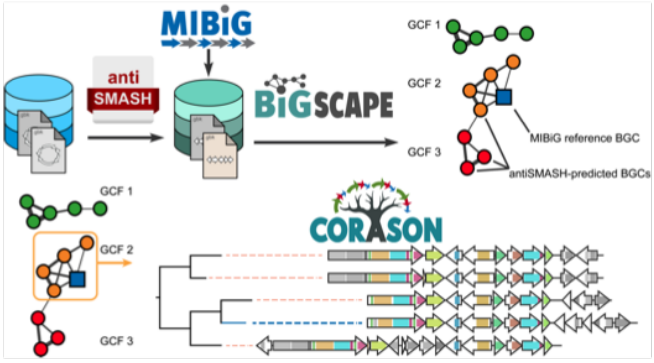


A. fumigatus is a common saprophytic fungus whose main habitat is decaying plant material. It also is the most prevalent airborne fungal pathogen causing fatal invasive infections in immunocompromised patients. A wide range of clinical diseases may be caused by *A. fumigatus* affecting millions of patients worldwide with high mortality rates. Few drugs for treatment are available, and alarmingly, resistance to medical azoles is a rapidly spreading problem, with environmental resistance selection being the dominant route indicated by identical genetic resistance mechanisms in (agro)environmental isolates and in azole-naive patients. Although *A. fumigatus* is not a phytopathogen, many (agro) environmental azoles were found to exhibit activity against *A. fumigatus*, causing cross-resistance.

GBU works on understanding the evolutionary and ecological mechanisms driving the development and spread of azole resistance, and on ways to prevent this. It does so in close collaboration with Radboud University Medical Center (prof. dr. Paul Verweij) and with an international alliance of scientists and stakeholders such as ministries, the chemical industry, and governmental organizations. Commissioned by the Ministry of Health, Sports and Welfare (VWS), we conducted a first screen for potential hotspots in the Dutch environment and found that ways of stockpiling/composting and the concentration and type of (agricultural /industrial) azoles present are important parameters in defining a hotspot for *A. fumigatus* resistant to medical azoles. Commissioned by the Ministry of Agriculture, we carried out an in-depth study focussing on the Dutch bulb-sector which included year-round sampling and resistance phenotyping and genotyping on three farms, as well as sampling of the local agricultural circular system. We found that·of the isolated *A. fumigatus*, roughly 50% is resistant to the two indicator azoles tebuconazole (agricultural azole) and itraconazole (medical azole). Genetic characterization showed that resistance mechanisms found in hotspot locations are the same as those in isolates from patients in clinical environments. Based on these results and accompanying research of the Dutch *A. fumigatus* surveillance led by prof. Verweij, the medical protocol of treating aspergillosis has been adjusted so that it does not rely solely on administration of medical azoles, and the Dutch Minister of Agriculture has ordered the Authorisation of Plant Protection Products and Biocides (Ctgb) to develop a protocol for the Dutch bulb-sector for organic waste management containing environmental azoles. Adherence to this protocol is mandatory for use of azoles in this sector and the protocol has gone into effect as of March 2021. GBU runs the project to monitor its success and effectiveness.

Case 3 - Unraveling the mystery of specialized metabolites for science and society

Specialized metabolites (SMs) are chemical compounds produced by organisms that are not essential for development and growth, but help them to thrive in their ecological niches. Most plants and microbes have evolved to produce a specific set of SMs, for interaction and communication with the environment and hosts, defend against attacking species or recruit beneficial ones. Particularly complex networks of such interactions are found in microbiomes, both in human and in soil. SMs are also used in many biotechnological applications, e.g. as antibiotics or drugs and as taste and fragrance compounds.



In 2015, dr. Marnix Medema joined GBU as a tenure track researcher. He rapidly started and expanded a research group, building on his expertise in mining biosynthetic gene clusters (BGCs) producing SMs and extending this to plants and microbiomes, pathway elucidation and computational metabolomics. Following on his highly successful antiSMASH software (webserver used over 1 million times) and accompanying databases, his group defined community standards for reporting BGCs (MIBIG) and delivered computational methods to further organize, explore and interpret large BGC collections (PlantiSMASH, GutSMASH, CORASON, BIG-SCAPE, BIG-FAM, BIG-SLICE etc.). These tools led to a large number of publications on method development and biological applications (including in *Science*, *Nature*, *Cell*, *Nature Chemical Biology*), and have been widely adopted by both the scientific community and biotechnology industry.

Marnix's work is supported by grants from a range of funders, many involving (inter)national collaborations, including an ERC Starting Grant, NWO XL, NWO Gravitation (MiCRop) and two NWO Venis. The success of research on SMs also helped GBU attract a tenure track researcher on computational metabolomics, dr. Justin van der Hooft. Overall, this provides a clear example of GBU's goal to advance science while providing society with knowledge and methods needed for progress on challenges related to health, food security and the environment.

The Graduate School EXPERIMENTAL PLANT SCIENCES

EXPERIMENTAL PLANT SCIENCES

self-evaluation report 2015-2020

Summary and case studies Plant Development and Adaptation

October 2021

Summary Plant Development and Adaptation

The Plant Development and Adaptation Research Unit (PDA) unites chair groups in the fields of Biochemistry, Plant Developmental Biology and Plant Physiology. Collectively, research teams in the unit focus on investigating the intrinsic (core) mechanisms that underlie multicellular plant development, as well as the control of these core mechanisms by external factors. While there is a strong emphasis on and strength in curiosity-driven, basic research, the unit also excels in translating their research to societal challenges or interests from private and public partners. In the past years, the unit has performed very well in terms of research output, and is clearly developing synergy between the individual teams. The past years were marked by transition in leadership in all constituent groups, as well as the rejuvenation and increase in diversity of scientific staff. A number of new tenure-track faculty have been appointed, and these have successfully started new research directions in the unit. With its current team of principal investigators, the unit is well postioned to consolidate its international position in the field of plant development and adaptation. To maximize its efficiency and impact, the unit will benefit from increasing the synergy from intensifying collaboration between the unit's groups, which will be achieved through a well-defined action plan. Furthering synergy and diversity will also allow the unit to consolidate excellence in both fundamental and translational research and increase its ability to respond to opportunities to participate in larger research consortia.

Case 1 Cell shape and polarity

Plant morphogenesis critically relies on the control of shape and division orientation of individual cells and the coordination among cells. A key question therefore is how these processes are regulated. Groups in the research unit have collaborated to address this question, chiefly using the Arabidopsis embryo as a simple model. Funded by an ERC Starting Grant (Weijers; 2011-2016), the BIC group developed an approach to microscopically and computationally analyze cell shape and division in the embryo (Yoshida et al., *Dev. Cell* 2014), and developed a set of tools for imaging subcellular structures (Liao and Weijers, *Plant J.*, 2018). In close collaboration, the PDB and BIC groups used a modeling and imaging strategy to explore how the interaction between cell shape and microtubule properties steers division orientation (Chakrabortty et al., *Curr. Biol.* 2018). The BIC group next identified a new family of polarly localized SOSEKI proteins that influence division orientation in embryos (Yoshida et al., *Nature Plants* 2019). Much of this work formed the basis for an ERC Advanced Grant (Weijers, 2019-2024) on plant cell polarity. In collaboration, the BIC and PDB groups biochemically characterized SOSEKI proteins and demonstrated their conservation across land plants (van Dop et al., *Cell* 2020). The PDB group further developed the imaging/computation approach to study cell shape and fate in the moss Physcomitrium (Tang et al. *New. Phytol*. 2020). This work, and the collaborations developed, are an excellent starting point for deepened and continued collaborations towards dissecting the fundaments of cell polarity, shape and division in plants.

Case 2 Seed Science

Seeds represent a critical stage in the survival of plants and can survive harsh environmental conditions such as extreme drought, high- and low temperatures. For their survival, seeds depend on their interaction with the environment. Germination is extensively translationally regulated (Bai et al, *New Phytologist* 2017, 2018) and very much determined by mRNA's that are expressed during seed germination and stored in the dry mature seed (Bai et al, *Plant Physiology* 2020).

In 2012, Leónie Bentsink received a NWO-open ALW grant, in which the role of seed-stored mRNAs and translation in the control of seed dormancy was studied. The outcomes of this project were the foundation for the current research line investigating mRNAs and their translation, funded by NWO (Open Technology Programme and NWO-VICI domain AES). The current projects aim at identifying the mechanism underlying this translational regulation, but also have an applied angle.

The interest of the seed industry in this type of research is indicated by their contribution to the above-mentioned projects and as such expands the funding possibilities.

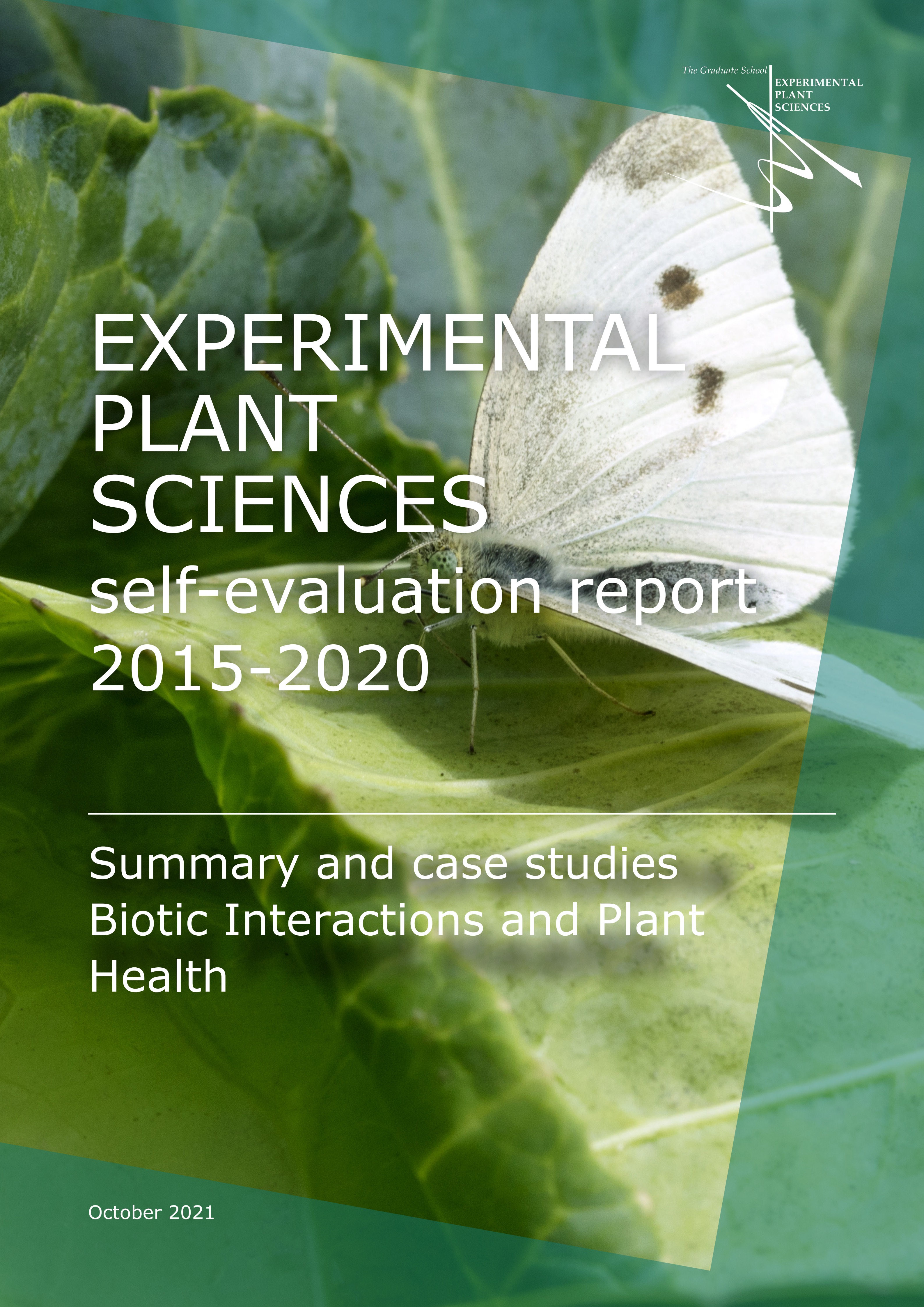
Recently, a structural collaboration in the field of seed physiology and technology has been started between the Wageningen Seed Science Centre (WSSC, Bentsink and Wageningen Research partners) and industrial partners. This collaboration will strengthen the links between the globally oriented and highly innovative seed industry and our research group. WSCC also aims to draw the attention of students to the field of seed science and technology, increase the number of young people with interest for a profession in the seed sector and maintain and improve the infrastructure for research and education in seed science and technology. The recent appointment of Bentsink as Professor of Seed Science will clearly contribute to all these aims by strengthening our research and teaching profile in this topic.

Case 3 Connections beyond Plant Development and Adaptation

Besides the projects and collaborations within our research unit highlighted, we have a strong portfolio of recently acquired formal collaborative projects beyond the research unit, both nationally and internationally. Our participation and leading roles in the NWO-AES programs LettuceKnow, Holland Innovative Potato, and the large infrastructural facility NPEC, show our excellent network and our crucial role in the Dutch research landscape. We are coordinator of the EU project "ROOT" to improve resilience of tomato.

The Dutch LettuceKnow consortium aims to improve resilience and architecture of lettuce, through both molecular and physiological approaches as well as developing state-of-the art genomic and genetic tools for this crop (Testerink, Heidstra). This work will be synergistic with our future focus on understanding and steering lettuce seed priming and germination (Bentsink, AES-VICI). For the LettuceKnow project, the expertise of PDB in CRISPR-Cas9 technology is a key contribution to the consortium. Further, the development of innovations in genome editing have recently been strengthened (TT Swarts).

The Dutch consortium MiCRop aims to increase stress resilience of crops through microbiome recruitment (Co-PI Testerink, in consortium with WU-BIPH, UvA, Utrecht, NIOO, VU). Besides contributing to the major joint research effort to investigate the mechanisms of how microbes help plant resilience to nutrient starvation, pathogens and drought in 100 species across 5 plant families including crops and wild relatives, PDA will focus on tomato and rice as key crops and build on our previous and ongoing work in gene regulatory networks that affect root branching in salinity and water deficit conditions.



The Graduate School EXPERIMENTAL PLANT SCIENCES

EXPERIMENTAL PLANT SCIENCES

self-evaluation report 2015-2020

Summary and case studies Biotic Interactions and Plant Health

October 2021

Summary Biotic Interactions and Plant Health

The Biotic Interactions and Plant Health (BIPH) unit aims to unravel the interactions between plants and members of their associated communities, both above- and belowground, and including both beneficial and harmful species. Climate change, biodiversity declines, and the increasing global demand for safe food challenge us to develop novel concepts of how biotic interactions affect the resilience of plant production systems. BIPH performs fundamental research to increase our knowledge on plant/biotic interactions and applies this knowledge to develop novel sustainable strategies to promote plant health in temperate and tropical climatic zones.

For the current review period, the BIPH unit set four strategic aims: (1) to develop novel concepts of the genetic and molecular mechanisms underlying host and non-host responses of plants to beneficial organisms and harmful attackers both in isolation and as members of a multitrophic complex; (2) to connect such mechanistic studies on individual interspecific interactions, usually in the laboratory, to community dynamics under field conditions; (3) to translate this knowledge to develop a more circular agriculture based on crop health management within a biodiverse environment that promotes beneficial organisms, mitigates the effects of detrimental organisms while preserving high yield; (4) to train the next generation of scientists in the field of biotic interactions and plant health for academia, industry, and public office.

Because of the recent inception of BIPH, our strategy first focused on stimulating novel collaborations between BIPH unit members by providing funds for two collective research programs on multitrophic interactions and by encouraging joint grant applications by unit researchers. We also developed a shared vision for recruiting new scientific staff with areas of expertise positioned between chair groups and research units. As most of our funding for research demand private sector contributions focusing on valorization, we also paid special attention to improving our competitiveness for personal grants to fund more basic research. To this end, our talented PhD students, postdocs, and junior staff members received personal mentoring and special coaching by our VENI/VIDI/VICI- and ERC-laureates. We also stimulated our young researchers to aim for high scientific and societal impact. Furthermore, we hired several full-time academic lecturers to take over a significant amount of teaching from our staff members to create a more sustainable balance between time for teaching, research, and acquisition.

Our strategy has been successful, as becomes clear from the more than 1200 publications by BIPH researchers, most of which is generated within the framework of national and international collaborations (i.e., ±85%). A large number of our publications were published in prestigious interdisciplinary journals such as Cell, Science, Nature and PNAS, which has been instrumental in the acquisition of nine prestigious personal grants (from NWO and ERC) by our junior staff members. Furthermore, BIPH researchers have taken the lead in several large research consortia focusing on biotic interaction and plant health (e.g., Gravitation program MiCrop). In addition, BIPH stably acquired one third of her funding through contract research (i.e., ±25 FTE/year), mostly in private public partnerships. These partnerships with industry and (non-)governmental organizations offered an effective means for the translational components in our research, providing a channel to reach out to specific target groups and the public. In parallel, we engaged with society through large numbers of press releases, interviews in media and television broadcasting, and through training and education for professionals.

Our strategy for the coming years will be more focused on extending our collaborations to other research units in- and outside EPS. Establishing stronger connections with the research units Genome Biology and Plant Development and Adaptations, for instance, we enable us to share expertise and use novel technological advances to further our knowledge on mechanisms and evolution of biotic interactions, and to apply this knowledge in integrated plant health management

systems. Therefore, we will recruit staff members in tenure track positions specifically connecting the BIPH chair groups with the chair groups in other research units (both in- and outside EPS).

Case study Learning from Nature to Protect Crops:

In nature, devastating pests and diseases are rare despite the abundant presence of herbivorous insects and plant pathogens and common occurrence of abiotic stress. Plants have evolved to defend themselves in numerous ways. In agriculture, our crops have lost many of these defence characteristics. To develop sustainable alternatives, we have executed a multidisciplinary and innovative NWO-funded programme, Learning from Nature to Protect Crops (budget 6.5 M€), to mine the natural reservoir of plant defence mechanisms (**strategic aims 1 and 2**). This has been done by using state-of-the-art high-throughput technologies to explore the natural potential and exploit genetic variation, genes, and markers to unravel novel resistance mechanisms against biotic and abiotic stresses for plant breeding. We coordinated this research programme with Utrecht University. The team consisted of research groups from Wageningen University, Utrecht University, and the University of Amsterdam plus thirteen companies and in total ten early career scientists have been trained, of which five by BIPH members. It yielded a range of high-impact papers, including the full-consortium paper on 'Genetic architecture of plant stress resistance: multi-trait genome-wide association mapping' (Thoen et al. 2017, New Phytologist 213: 1346–1362). One of the early career scientists from the BIPH research unit involved in the project has been awarded with a prestigious personal VENI grant. The project has resulted in 9 PhD theses and ca 40 papers in high-ranking journals, many of which were collaborative papers among partners in the programme.

Case study Microbial imprinting for crop resilience (MiCRop):

A new imperative in the life sciences is the realization that microbes are important drivers, rather than passengers, of the wellbeing of humans, animals, and plants. Host-associated microbiomes, also referred to as "the second genome of eukaryotes", have a largely unexplored potential to expand the genomic capabilities of their hosts - providing tolerance to environmental stress. Plant roots house one of the most diverse, yet vastly neglected, microbial communities on Earth. With a national team consisting of the University of Amsterdam. Wageningen University, Utrecht University, VU University Amsterdam and the Netherlands Institute for Ecology we execute a national NWO-funded Gravitation program (20.4 M€) that integrates next-generation microbiomics approaches to identify functional traits involved in plant microbiome assembly to maximize their activities for enhanced plant growth and resilience to environmental stress. We aim to (1) unlock how wild and cultivated plant species, across the plant kingdom, recruit their microbial partners to cope with environmental stress, maximize nutrient uptake, optimize growth, and prime their immune system and (2) harness microbiome functions to optimize future crop resilience and performance in a changing climate. Two of the four stress factors that we will focus on are herbivorous insects and plant pathogenic microbes, in the context of abiotic stresses such as drought and phosphate stress (Fig. 2). We will study the evolution of plant-microbiome interactions and identify opportunities for future plant breeding at an unprecedented scale. MiCRop perfectly aligns with the National Science Agenda route 'Sustainable production of safe and healthy food' and addresses the key aspect of the 'Green biodiversity game changer' by making future farming systems more sustainable, climate resilient, while preserving soil health (i.e., **strategic aims 2, 3 and 4)**.