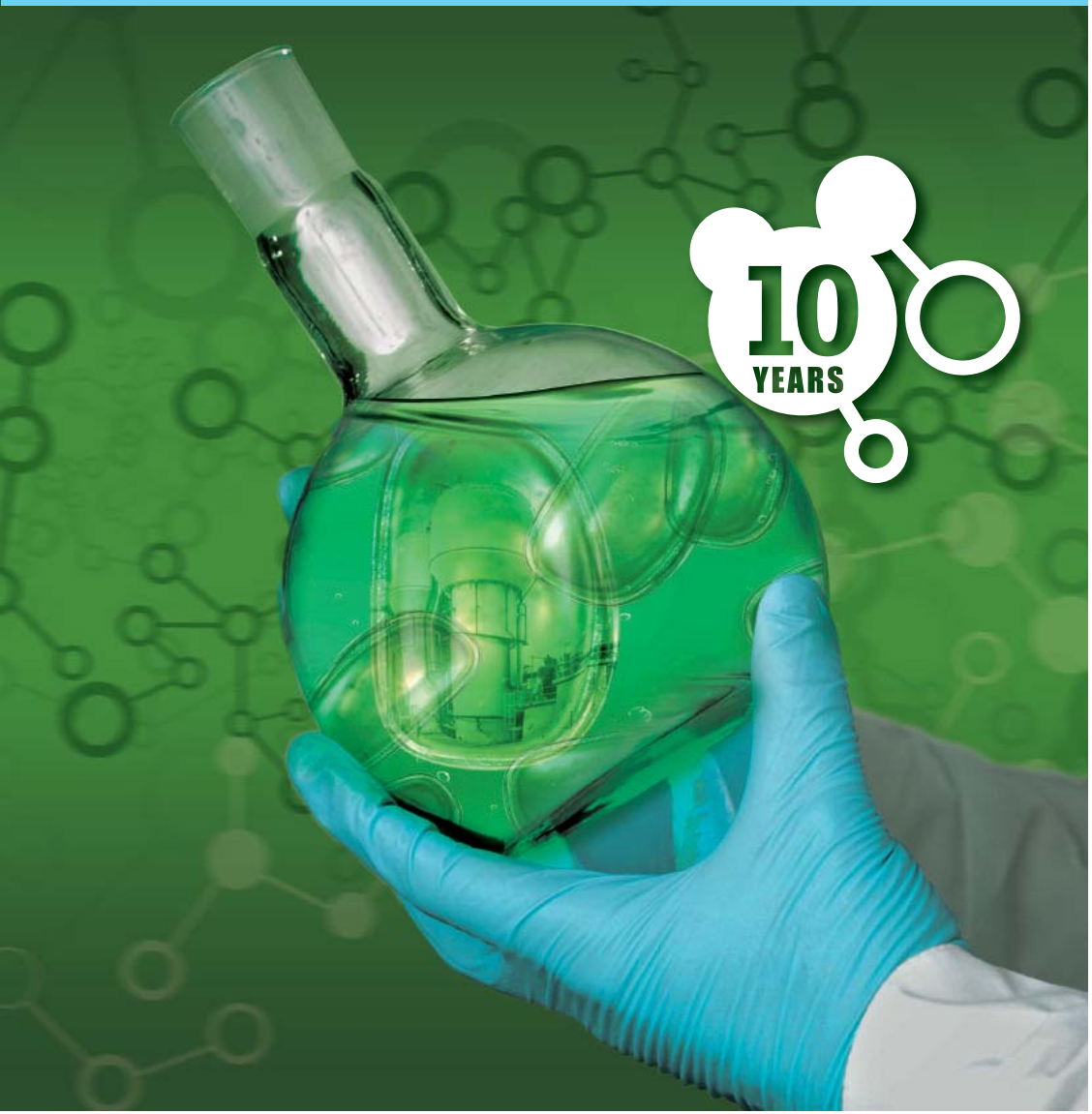
BE-Basic Foundation Annual Report **2014**



Building our Biobased Economy together

BE-Basic
Foundation

Colophon

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We thank all scientists and parties involved for their cooperation

10 YEARS

Shared determination to build the biobased economy

We are very pleased to present our 10-year anniversary version of the Annual Report 2014. Ten years ago we started our activities in two separate consortia - B-Basic and Ecogenomics, which merged in 2010 into one consortium and in 2012 became the BE-Basic Foundation. This special report reflects the advances we have made since then. In these 10 years, we have worked hard to investigate, develop and test industrial biobased solutions to build a sustainable society. Since 2004 we have been bringing together the best scientists, experts and commercial companies in the Netherlands to develop those innovations. Our spectrum of activities has expanded considerably due to our international alliances with industry and governments, particularly in South and North America and South-East Asia.

BE-Basic owes its success to the high level of integration of its research and innovation activities within the partnership. Its integrated approaches in developments along cascaded biobased value chains cover not only scientific and industrial technological solutions, but ensure optimal environmental and sustainability impacts. This is also due in part to its wide network of active cooperating international partnerships. And the determination of everyone involved in the BE-Basic Foundation to reach a sustainable, biobased world, ensures we are breaking new ground.

Since 2004 we have been bringing together the best scientists, experts and commercial companies in the Netherlands

This special edition of the Annual Report includes interviews with scientists, directors and CEOs of the start-ups created under the auspices of BE-Basic. In addition, our industrial partners provide an overview of the highlights and progress they have achieved over the past 10 years within their specific areas of interest. We are taking you behind the scenes of 10 years of BE-Basic and have asked researchers to tell their stories. And we look into the future. We are ready to take that next step, to upscale our innovations and turn them into real, practical solutions. It is time to show society the added value of biobased solutions from an economic, environmental and sustainability point of view. The biobased economy is no longer just a dot on the horizon. It has moved closer to becoming a reality and will be visibly implemented in society soon. The BE-Basic Foundation will continue to go full out in stimulating and supporting activities which focus on the actual implementation of the biobased economy for all of us.

Bram Brouwer and Luuk van der Wielen
Board of Directors BE-Basic Foundation

BE-Basic milestones

Ten years ago B-Basic and Ecogenomics set out separately to discover and deliver essential building blocks for the creation of a biobased economy. The nature of the consortium has always been to initiate and stimulate collaborations between academia and industry. The impact of that strategy on BE-Basic's growth and reach is illustrated here.

2004

Start Ecogenomics - BSIK
Start B-Basic - BSIK

2005

2006

2007

Valorisation grant Ecogenomics - NGI
Venture Challenge MLS

2008

Venture Challenge W2C

2009

Start FES business plan
Venture Challenge ClearDetections

2010

Grant for Ecolinc – NGI
Start BE-Basic Consortium - FES
Incorporation W2C BV
BIRD Engineering discovers FDCA technology

2011

OPBC-Malaysia
EFRO-subsidy BPF
MoU with BIOEN/FAPESP for joint annual calls
Incorporation MLS BV
Incorporation ClearDetections BV

2012

Establishment BE-Basic Foundation
Merger Kluyver centre
Incorporation BDS Chile BV
Incorporation BioProcess Pilot Facility BV
Incorporation BLGG Research (Soil Cares Research) BV

2013

Grant AMBIC - TKI
Grant ISIM - TKI
Grant EBD - TKI
Establishment BE-Basic Brazil Office
Start Vietnam-BE-Basic program
Incorporation Delft Advanced Biorenewables BV
Incorporation Marlin Purification
BIRD Engineering acquired by Purac (now Corbion) to scale-up FDCA technology

2014

Incorporation IBPR
Start operations POET-DSM
Start operation GranBio (Brazil) with DSM (BE-Basic –based) technology
First run MOOC 'Technology of Biobased Products'

10 YEARS

BE-Basic Foundation

Milestone programme
Milestone innovation

focus

The dynamics of high risk/high gain projects

Biobased solutions: small steps to big results

We know where we want to be in terms of the biobased economy but we still need to make scientific advances and technological improvements in various biobased value chains. Cascading the processes to fully grasp the added value from biomass is also an important aspect. The BE-Basic Flagships include a number of different high risk/high gain projects – research which if it achieves its goal, may bring about radical improvements and spur on the biobased economy. These are usually long-term projects going from laboratory to piloting scale before industrial implementation can occur and the results are not always immediately made public. How do researchers deal with such a situation?

One example of a high risk/high gain project is the research into the biobased production of caprolactam, a major component in the production of nylon. If you can produce caprolactam in a biosynthetic way as opposed to a chemical one, you are making important industrial processes much more sustainable. For a few years now, researchers in Flagship 2 are working on developing biobased caprolactam, and it will be at least five to 10 years before large-scale production will become an option. Research leader professor Dick Janssen: "It might seem to require a long time to the outside world but the research itself is extremely dynamic. What we can do now was unimaginable 10 years ago. We've made enormous advances, especially thanks to bioinformatics and DNA synthesis."

Almost is not enough

Professor Arnold Driessen is also working towards a long-term goal: producing antibiotics currently made semi-synthetically entirely by biosynthesis. "This would shorten the production process and have an impact on the price and ecological footprint. We need to remove several bottlenecks. The great thing about BE-Basic is that academic researchers work closely with partners in industry. It is very satisfying to have a company benefit from your knowledge." In order to achieve sustainable antibiotic production, Driessen's team has to design enzymes.

Sometimes you want to shout it from the rooftops and you don't want to be scooped by another research team

"We are beginning to better understand how to do it, but we are not there yet. And the irritating thing about this profession is that getting it almost right is still completely wrong." Janssen has the same experience. "We had to stop considering one entire pathway for producing caprolactam. This was not a pleasant thing to do, because it had involved a lot of work. But it is sensible to build clear go/no go moments into high risk research."

Cooperation and cross-fertilisation

These sort of partial results can, nevertheless, take the research further. "You can get ideas from things that did not quite work out," says Driessen. Bram Brouwer, the managing director of BE-Basic, puts this down to the structure of the consortium itself. "What helps is having people look at a single result from different perspectives," he says. "A partner from industry might say 'but if this can be done, maybe that can be done as well'. And that might trigger the researcher to take the next step. Within BE-Basic, it is definitely 'a good thing to do' for researchers to deviate from the main research. High risk/high gain research has a high level of serendipity but you can always give it a helping hand." In addition, technology developed in one research project can be used in another. As the management team, Luuk van der Wielen, myself and the Flagship managers are able to view all the results as they come in and we search for horizontal connections between different projects and flagships. For example, the screening techniques developed in Flagship 7 have contributed to the caprolactam and antibiotics projects. The added value which BE-Basic has as a science and

innovation platform is in the way we promote transboundary interactions within the consortium itself, and promote collaborations with other consortia nationally and internationally."

Shout it from the rooftops

The Flagships have also achieved a number of good results. Wageningen University has identified a building block for caprolactam production in plants and is studying how to use it as an alternative. The outside world rarely hears this sort of news as it happens. "A result like that gives you a rush," laughs Brouwer. "A sort of 'I know something others don't know yet' feeling. But it can be tricky as well, because you don't want to go public too soon, in order to avoid problems with intellectual property filing. However, we keep a keen eye ensuring the 'potential for IP evaluation' as short as possible within BE-Basic. All the partners have to decide within three weeks prior to submission for publication if there is a patentable option and if they wish to be part of the patent filing process. And if they do, it has to be completed within a couple of months. Otherwise the scientists, who are eager to publish, are waiting on tenterhooks for too long." Driessen knows the feeling. "Sometimes you want to shout it from the rooftops and you don't want to be scooped by another research team. And you have to justify what is being done with public money. But the outstanding alliances within BE-Basic mean this is rarely a problem. The bottom line is that we all want to achieve significant things."

More exciting, more spectacular

State of the art technology and methods are essential in high risk/high gain projects. "You have to keep on your toes to maintain your added value," says Janssen. "And that requires a lot of inventiveness and effort. Our links to EU research projects are also important. Scientists are willing to exchange information." Janssen anticipates the necessary technological developments. "Bioinformatics and computational sciences are on the up and DNA synthesis will speed up over the next five years. We are moving from experiments to modelling and simulation. That makes it more exciting and more spectacular." "We are working with one of the largest enzymes and high throughput is not yet an option," adds Driessen. "It is good to know that within five years it will be possible." The new techniques mean that today's research questions are being answered more quickly, says Janssen. "But then we will have even wilder ideas. The things we don't yet dare put down on paper will be the new high risk/high gain projects."

The start-up: an essential link to the market

One of BE-Basic's ultimate aims is to ensure that knowledge gleaned in the lab can be used commercially. Start-ups are essential in this process. They take the technology forward by upscaling and solving any problems that emerge. Setting up and supporting start-ups is one of the BE-Basic Foundation's key performance indicators. The original target was five but in the meantime six start-ups have been actively funded by grants from BE-Basic.

ClearDetections: preventing plant damage through DNA diagnostics

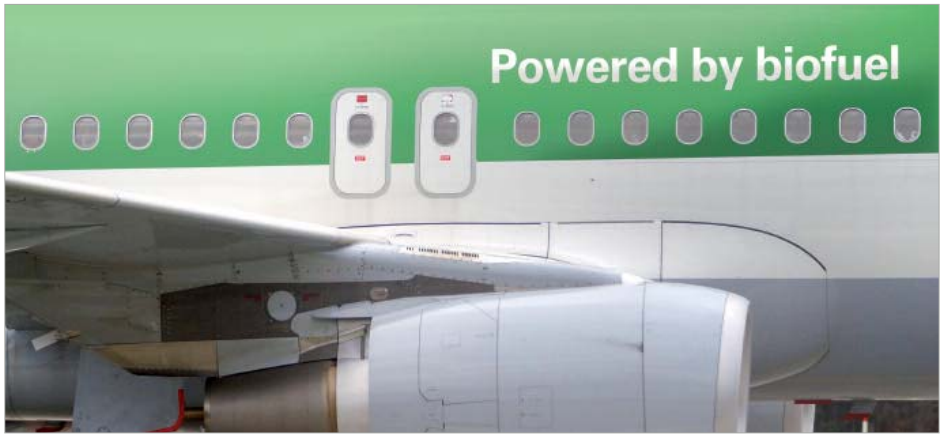
ClearDetections produces diagnostic tests to track down and identify nematodes, microscopic round worms which live in soil. "These tiny creatures are responsible for over 15% of the annual crop failures," says Renske Landeweert, director of the three-year-old company. "By identifying them early, we can make a considerable contribution to the worldwide demand for food." In addition, knowledge of nematodes is crucial for the sustainable production of biomass. Optimal biomass production requires agricultural systems that find the balance between maximum biomass production and maintenance of soil fertility. "Within the BE-Basic project SURE/SUPPORT programme we are helping to develop a decision support tool to assess the quality of biomass refinery residues as fertiliser. The alliance allows us to further develop our expertise and our techniques."

ClearDetections' tests are based on DNA detection. The company uses a unique database with over 3,000 nematode DNA sequences in it and it is growing by the day. The database allows the company to develop tailor-made tests. "The tests are currently available to laboratories and we'd like them to be used by all main agricultural inspection labs around the world," says Landeweert. "That requires a change in thinking. Nematology is currently based on visual inspection through a microscope. It takes some time getting used to the idea of an analysis based on DNA, where you no longer see the pathogens. Financing can also be challenging because labs are used to investing in people rather than methods, such as our diagnostic tests."

Market perspectives
Landeweert's mindset has changed since becoming an entrepreneur. "I pay much more attention to the perspective of the customer when it comes to translating science into something which makes a practical difference," she says. "We've just invested in our own lab and more staff. As a start-up, you try to keep costs as low as possible so we were using the lab facilities and technicians from our partners. But there comes a point when you have other priorities. I wanted to seize the opportunities offered by the market. The university, understandably, has other obligations, such as education. So before you know it, the momentum has ebbed away. Our alliance is still solid in essence, but it is good that we, as ClearDetections, have taken this step and have our own facilities. It inspires us to do new things."

We can make a considerable contribution to the worldwide demand for food

Necessity
Future developments include a handy test which farmers too can use on their land. "A successful biobased economy entails producing more from the available land. We are now able to analyse the biological state of the soil from the nematode population, something which is currently interesting mainly to university groups and research institutions. A localised test would enable you to prevent plant damage easily and give farmers tailor-made advice about how to keep their soil in optimum condition. We still need to make some technical advances to get there, but that is my ultimate aim."



Delft Advanced Biorenewables: commercialises promising process technology

In purely scientific terms, biotechnology currently offers lots of prospects for a profitable transition to a biobased economy. But it is still quite a jump to go from the lab to the market. Delft Advanced Biorenewables (DAB), founded in 2012, selects promising bio(process) technologies to commercialise. "The process really begins with an idea and a patent," says managing director Kirsten Steinbusch. "We work closely together with Delft University of Technology. DAB translates the idea into a working concept that can be upscaled with our other partners, the Bioprocess Pilot Facility (BPF) and BE-Basic, to get technology ready for the market."

"Things which work well in the lab often lead to unexpected challenges when you scale them up," says Steinbusch. "DAB is a platform that can help industry to overcome some of these challenges. We look for commercial partners who would like to bring the technology onward in practice or to help them with bioprocess technological solutions." For example, DAB developed a reactor concept that allows the production of jet fuel and diesel from oil-like molecules without forming an emulsion. The prototype is now being tested in the BPF. "At the moment you have to add expensive chemicals and energy-intensive downstream processing equipment to avoid this emulsification. The benefit of the reactor is that it cut the costs of the energy and equipment you need and also reduces the impact on the environment. Every cent counts in the market for biofuels and this technology could make all the difference," Steinbusch says, with enthusiasm.

Seize the day
The idea to set up DAB came out of some Delft University-ideas, shaped later as a BE-Basic research project themselves. "It would be such a pity if an interesting and elegant technology like this would simply remain on a desk because a university is not in the position to continue the development," says Steinbusch. "I got involved in biotechnology because I personally have a drive to solve societal issues related to energy or to the environment. DAB allows me to put my efforts into bringing together the technology, expertise, people and companies that can make a difference. We have a dedicated team that can speed up developments." The alliance with the BPF is essential in this. "Whatever happens, scaling up cannot be done using university facilities but we can also guarantee the client confidentiality by scaling up in a closed environment."

Multiple technologies
DAB's main development is the advanced biofuels and biorenewables technique with BE-Basic, Delft University of Technology and the BPF. "The technique is planned to be demonstrated at pilot scale in 2018 within the BE-Basic project," says Steinbusch. "In addition, with this strong consortium, we offer our expertise, research capacity and upscaling service to commercial partners to develop other bio(process) technologies."

ChainCraft: from food waste to industrial building block

The basis for ChainCraft (formerly called Waste2Chemical) stems from a breakthrough in fermentation technology. "Normally, in mono culture fermentation, one organism delivers the desired building blocks. We, however, can make high-value fatty acids from heterogeneous raw materials in reactors with multiple bacteria," says Niels van Stralen, ChainCraft's director. "Take organic waste, for example. This is much more sustainable than a first generation feedstock like sugar or starch and organic waste is cheaper than a raw material. Furthermore, we can use equipment which does not have to be sterile."

Kirsten Steinbusch, now a shareholder in ChainCraft, discovered the new fermentation method seven years ago while researching biofuels at Wageningen University, one of BE-Basic's partners. Van Stralen was involved in the R&D work at that time. "At a certain point, the fermentation rates and yields were at a level where they became industrially relevant," he says. "That was the perfect moment to start a company." This revolutionary discovery won prizes, obtained subsidies from the BE-Basic Foundation to speed up the transfer from research to innovation, and went on to attract outside investment. Within BE-Basic it now performs pilot research and application tests on the chemicals produced. "The lab phase took some time, since the complexity is enormous when you consider we have multiple bacteria in a reactor rather than just one active organism," says Van Stralen. "The pilot phase is, however, proceeding more quickly than expected."

Easily applied

ChainCraft's innovative methods dovetail neatly with the anaerobic digestion technology currently used in the production of biogas. "Ideally this means you can retrofit existing biogas production facilities to use our technology, which is an advantage in terms of the required capital investments," Van Stralen points out. "ChainCraft is located at the Simadan site in the Port of Amsterdam, where we are currently successfully testing our pilot facility and a new demonstration plant is at the conceptual design stage. We are working on this with Rotie, one of the Netherlands' biggest food waste and fat collectors," says Van Stralen. "They are supplying the raw materials."

Further expansion

"Industry is surprised we can produce these fatty acids using biobased technology," he says. "We are now focusing on the niche market for C6 fatty acids. These are relatively scarce, due to their low presence in several oil palm streams, but the demand is high and thus they are more valuable." ChainCraft is ambitious. "We hope the first full sized plant will be operational in 3-5 years' time, and we will be preparing for more. In addition, we have started developing new technologies. ChainCraft is no one trick pony. Taking our vision on fermentation processes as a starting point, we want to use our knowledge and expertise to innovate multiple processes and products. The continued support from the BE-Basic Foundation spurs these innovations on significantly."

BioDetection Systems Chile: looking for new application opportunities for biobased safety assessment

Around the turn of the century, Bram Brouwer, director of BioDetection Systems, discovered an innovative way to detect dioxin in food. This was an important step in the improvement of food safety. The methodology was developed further and expanded to cover other contaminant compounds. Then, in 2011, the subsidiary company BDS Chile was launched. "The trigger was a crisis in Chile around dioxin in pork but we took a wider perspective in setting up an entire company there," says Brouwer. "We wanted to use our methodology to measure the safety of food, feed, and biomass and Chile's agricultural sector offers excellent opportunities to do this."

Brouwer's methodology, named CALUX, has caused a paradigm shift in food, feed and environmental safety and quality assessment. "Traditionally we measure substances by their chemical structure and properties," says Brouwer. "But if cells are exposed to a dangerous substance you get a biochemical reaction as a proxy for toxic effects. What we do is measure the cumulative effect of many chemical substances in one analysis. This means you can use one assay to check the presence of a toxic response as a proxy of safety in a complex mixture within a sample matrix." This breakthrough also offers great opportunities for even more complex mixtures of natural compounds and contaminants that may be present in biomass. "Biomass is becoming increasingly diverse and we want to process even more waste materials," Brouwer says. "Then you have to be able to measure whether it contains dangerous compounds. BE-Basic and BDS, both in Amsterdam and Chile, have joined forces to carry out this research."

Confidence

BDS Chile got off to a flying start. "It is a joint venture with a Chilean laboratory," Brouwer says. "They contributed the facilities and the people. We brought in the technology. This enabled us to be up and running within only three months. In addition, our dioxin measuring system opened doors. Governments are often nervous about

new techniques and there can be a lack of regulation. But if there is a food crisis, you don´t want to waste any time and want to use an innovative technology that can be applied at high throughput scale. From the second year on we were out of the red. At present we are exploring avenues to test both the residues from mining and from biomass in Chile, Brazil and other countries in South America."

Speeded-up process
The alliance with BE-Basic has accelerated the process. "We have produced several CALUX reporter cells which cover a wide array of biochemical outcome pathways, and thus can be used to map the profiles of beneficial and adverse compounds present in various matrices of food, feed, plant-based beneficials and crude biomass," says Brouwer. "In addition we are mapping the presence of beneficial bioactive compounds (i.e. with antibiotic, antitumor and antiobesogenic activity) in soil and marine environments. And we are searching for enzymes which are suitable for the bioremediation of toxic compounds that are produced during, for example, fermentation processes."

SoilCares Research: offers low threshold sensor technology to improve soil quality

Four Landrovers belonging to SoilCares Research are driving around Kenya with a mobile lab, testing soil samples. Local farmers can find out about the quality of their soil within two hours. The test has been made possible thanks to the unique sensor the company has developed. "Our added value comes from combining sensor technology with extended expertise in soil processes so that we can make a reliable, affordable analysis quickly," says director Peter van Erp. "This means we can help farmers improve their yields in a very concrete way."

The mobile lab is just one of the ways SoilCares Research technology can be applied in a practical sense. Blgg started on developing the sensors 10 years ago. The approach was so successful that a separate division, Blgg Research, was set up. In 2013, that unit continued independently as SoilCares Research. "We've been working intensively with BE-Basic all that time," says Van Erp. "Our strength comes from knowing how to extract credible information about soil quality from the sensors' measurements. That expertise in soil processes and how you can improve soil health is being developed together with BE-Basic."

A proper use of biomass
SoilCares Research and BE-Basic are working together on improving the sustainability of agriculture. "This means improving crop yields and ensuring biomass is produced and processed in a more sustainable way," says Van Erp. "We are doing more research into growing crops. How can you best do this without impoverishing the land? What is the minimal soil organic matter content that is sustainable for agriculture? At the same time, you can use the waste left after the biomass has been processed to enrich the soil. But you need to know if the waste is safe. In Flagship 3 we are working with partners to develop a support tool to help assess this."

Large numbers
SoilCares Research also offers high quality analysis tools for labs. "This is high-end technology which allows you to make very precise calculations. Nevertheless, we are also looking at the big numbers – a practical tool for farmers that may be less precise but which gives extremely useful information about the nurture status of their land, the yield they are after and the quality. If we do this on a big scale, we can increase the yield per hectare and contribute to solving the global food and energy problems. We've had enthusiastic reactions from the market to our pilots."

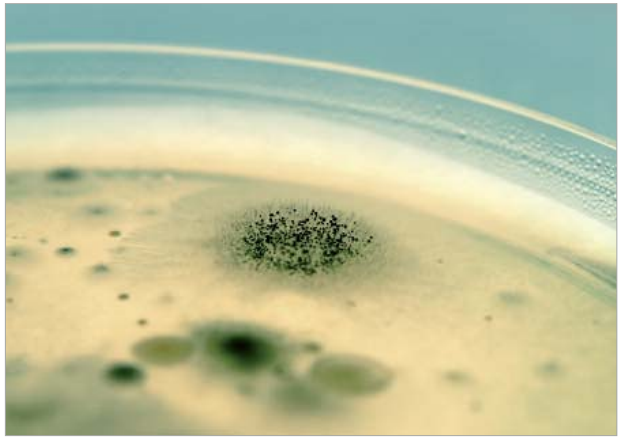
MicroLife Solutions: a nursery for new enzymes and antibiotics from nature

Every day in a laboratory in Amsterdam's Science Park, three MicroLife Solutions researchers are producing a never-ending stream of sequencing data. The company is investigating which enzymes are suitable for, say, processing and detoxifying biomass waste materials or which novel bioactive compounds may result in new antibiotics. The basis of these potential bioactivities is ecogenomics. Known antibiotics suffer a major problem in terms of resistance. In nature, however, it may be possible to identify bioactivities with new scaffolds that avoid potential resistance. MicroLife Solutions is the bridge between science and the market in terms of these potentially beneficial compounds.

"Researchers from several participating universities and institutes provide us with the potential bioactivities," says Thierry Janssens, unit director of MicroLife Solutions. "We perform the valorization part of the work. We look at whether or not it is possible to actually produce these compounds. Then we investigate their bioactivity spectrum and test their toxicity to find out if they can be safely used on people, animals and plants. We also try to discover the mode of action of the bioactive compounds and their biosynthesis. We will produce a portfolio of information for every substance to underscore their value as lead compounds. Many big companies prefer to leave this valorization process to specialised SMEs. Our results provide a value proposition, and allow them to evaluate how to use an agent in products and processes, if indeed it is suitable to come on the market."

Valorization process
MicroLife Solutions was founded in 2011 by Bram Brouwer, Hans van Veen and Jos Raaijmakers. "Over the past decade, we have become interested in translating scientific discoveries into usable applications," says Raaijmakers. "The Venture Challenge set up by the Netherlands Genomics Initiative helped us take this step." In 2013, the company set up its own laboratory at the Science Park in Amsterdam. "Now we have the infrastructure and the apparatus to allow us to carry out valorization processes for everyone working in this area of expertise," says Janssens.

Diversity
Currently MicroLife Solutions is carrying out many valorization activities within the framework of scientific work supported by the BE-Basic Foundation. "We have a wide field of expertise," says Janssens. "The biobased economy needs new enzymes, and microorganisms with improved properties (such as thermostability or improved degradation potential for substances such as lignin). New technology is making it possible to identify them, if you look in the right places. We aim to launch several new enzymes in the coming years and are looking for partners to develop new antibiotics using antimicrobial agents which show interesting bioactivity spectra and are safe to use."
Raaijmakers is pleased MicroLife Solutions' valorization pipeline is starting to become a reality. "In the years ahead, the company can focus on the most promising compounds."



Piloting in a **plug-and-play factory**

"Our pilot facility is based in a former industrial pilot building and that is what makes us unique," says BPF director Hans van Leeuwen. "Piloting is often done in larger labs but we work in an industrial environment, and that offers more successful scale up possibilities." The Bioprocess Pilot Facility (BPF) is situated in the Biotech Campus at Delft University, a state-of-the-art, 5000 m² facility for industrial biotechnology. It is an open access facility, allowing companies and academic institutions to develop new sustainable production processes based on biological materials. The facility has been specifically designed to enable the transition from laboratory to industrial scale.

The BPF started in 2012 on the BioTech Campus Delft. "We employ operators who have years of experience in large-scale fermentation and downstream processing. And in terms of testing options, we are a one-stop shop," says Van Leeuwen. "We offer the entire cycle, covering the full supply chain, from a large variety of biomasses to the end product. The BFP is a plug-and-play facility with all its unit operations. After an industrial pilot phase in our pilot facility you can scale up to the commercial scale much faster and with less risk. And different researchers from the BE-Basic programme come to the BPF to work with us and carry out the pilots."

The innovation valley of death

Many fledgling businesses meet it at some point: the innovation valley of death. Lab results may be promising but how do you take the step to commercial production? A lack of capital, a lack of knowledge about process technology and a lack of facilities can lead to a brick wall when it comes to upscaling. BE-Basic had been thinking about the innovation valley of death from the beginning and that is why it was involved in the development of the BPF from the initiation stage. "In general, piloting is key in bioprocessing. Even if it is expensive, it is a form of risk mitigation and ensures a bridge between the lab and the factory phases," says Van Leeuwen. "Piloting in the BPF offers proof of concept on a semi-industrial scale and makes it possible to collect reliable data for engineering and safety studies. It is also possible to produce volumes of the product for pre-marketing or application tests or pre-clinical and toxicology trials."

Boardroom celebrations

A pilot run is important because processes work differently on an industrial scale. "You should not do experiments in a pilot study, which you can also do at a laboratory scale. The whole process is too expensive for that," says Van Leeuwen. "If potential clients come to us, we often advise them to make some changes before we start the pilot, which we mimic on a lab scale before starting. This is our added value. And once the process is established and up and running in our facility, you sometimes see them celebrating in the boardroom. It is, of course, terrific if you can show during a pilot that a process works on a semi-industrial scale or that the product has the targeted quality."

Center: Hans van Leeuwen

History

B(E)-Basic came up with the idea for the BPF because piloting is considered a crucial step towards upscaling the various activities and the development of a biobased economy. The BPF was launched in 2012 as a joint venture between DSM, Corbion and Delft University of Technology, and is a partner of BE-Basic. New pre-treatment and food-grade facilities were opened in March 2015.

Modular set-up

The BPF allows users to construct complex operations by linking separate process modules such as pre-treatment and hydrolysis or fermentation and/or downstream processing. The facility also has a special food grade module.

Feedstock delivery point and size reduction area

Module 1
Pre-treatment and hydrolysis

In this module, dry and wet residues can be pre-treated, hydrolysed and prepared for the fermentation phase.

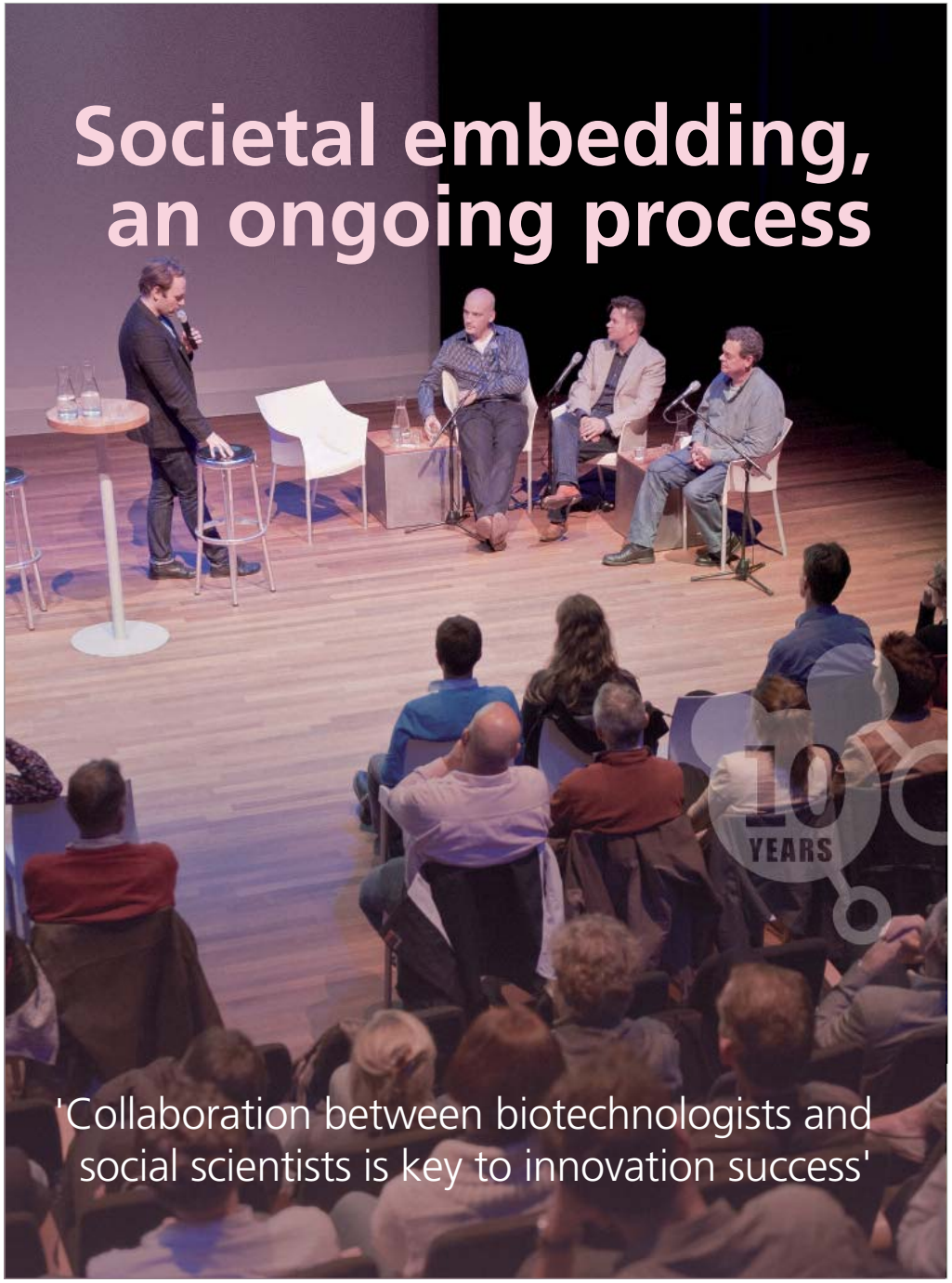
Bioprocess Pilot Facility

Module 2 Fermentation
In the Fermentation module, bioconversions are processed by means of microorganisms (bacteria, yeasts or fungi) or enzymes to obtain the desired product.

Module 3 Downstream processing
In this module, products are extracted, purified and isolated from the (fermentation) process stream. The unit operations can be combined on request to obtain the desired product.

Module 4 Food
Processes and products requiring a food-grade quality can be prepared in a dedicated area.

Societal embedding, an ongoing process



'Collaboration between biotechnologists and social scientists is key to innovation success'

"The transition to a sustainable biobased economy depends both on new technological solutions and the social adoption of innovations," says Patricia Osseweijer, chairwoman of the Economy, Policy and Sustainability (EBD) programme. "Recent research from Erasmus University shows that 75% of innovation success depends on investments in social innovation. This supports our observations." The EBD programme (Flagship 11) started in 2012 and advises the partners of BE-Basic and the government about the pathways to a biobased economy through its projects such as the Macro-Economic Study and the Innovation & Societal Roadmap.

Many steps have been taken so far. A BE-Basic inventory of public perceptions showed that people are not familiar with the concept of a biobased economy and while they are positive about such a development, they are more negative about biofuels. Together with NGOs a new tool has been developed to facilitate the sourcing of sustainable wood for energy. In addition the macro-economic study updates previous research from 2009, providing important data for business decision making and political incentives. The Flagship also supports the Dutch representation on the International Energy Agency and the Committee Corbey, which advises on the sustainable introduction of biobased technology. For the latter a study on biomass needs and availability in 2030 was recently carried out. "But now we have to integrate this knowledge into R&D innovation," says Osseweijer. "Therefore, we are focussing on horizontal projects - projects which run across several Flagships – so that expertise on the societal aspects and sustainability is included in the designs for process and product development," she says.

Horizontal projects from Asia to Rotterdam

One of the horizontal projects focuses on the complete biojet fuel and bioplastics chain in ASEAN (Vietnam and Malaysia) and Brazil. "We are looking at the socio-economic and environmental aspects of the different process steps in analysing different feedstocks and options for recycling and maintaining soil quality in specific regions. This brings together different disciplines in an integral impact analysis, with the aim to provide a decision support tool for business development," she says.

Another project in preparation aims to map the changes required for a green economy. The Port of Rotterdam features the second biggest petrochemical complex in the world. A transition to renewable energy and materials production to meet climate change targets requires substantial changes. But we do have the knowledge base required for this transition and a large chemical industry, so the Netherlands can be a frontrunner in establishing a strong biobased economy. Recent availability studies show that enough sustainable biomass can be produced to meet such demands, and that the ports will be playing a role. The project takes a 20% replacement of fossil feedstocks by biomass feedstocks in 2030 as a starting point. It analyses the required changes in infrastructure, like transport, training and employment which are linked to the most promising business cases. "BE-Basic is going to work in interdisciplinary teams to determine the technological and socio-economic aspects of the entire chain," Osseweijer explains.

Winning recognition

BE-Basic's integrated scientific approach is winning recognition. "The way we couple technological innovation to sustainability and societal embedding is unique," Osseweijer points out. "We were asked to join the scientific advisory committee delivering a report on bioenergy to the Scientific Committee on Problems of the Environment (SCOPE) hosted by the UN." Patricia Osseweijer has also just been awarded the Distinguished Lorentz Fellowship (DLF) for her cutting-edge research at the interface between social and technological sciences. The Lorentz fellow believes the transition to the biobased economy can be sharpened up across the board. "It needs a different mindset, more integrated action and fewer reports" she says. "In the meantime, BE-Basic is preparing for the future with the educational programme launched in 2014. Education is the basis. And, of course, we will continue working on bridging paradigms in science, and in that way we are helping to facilitate the transition from a fossil fuel to a biobased economy."

Public discussion will bear fruit

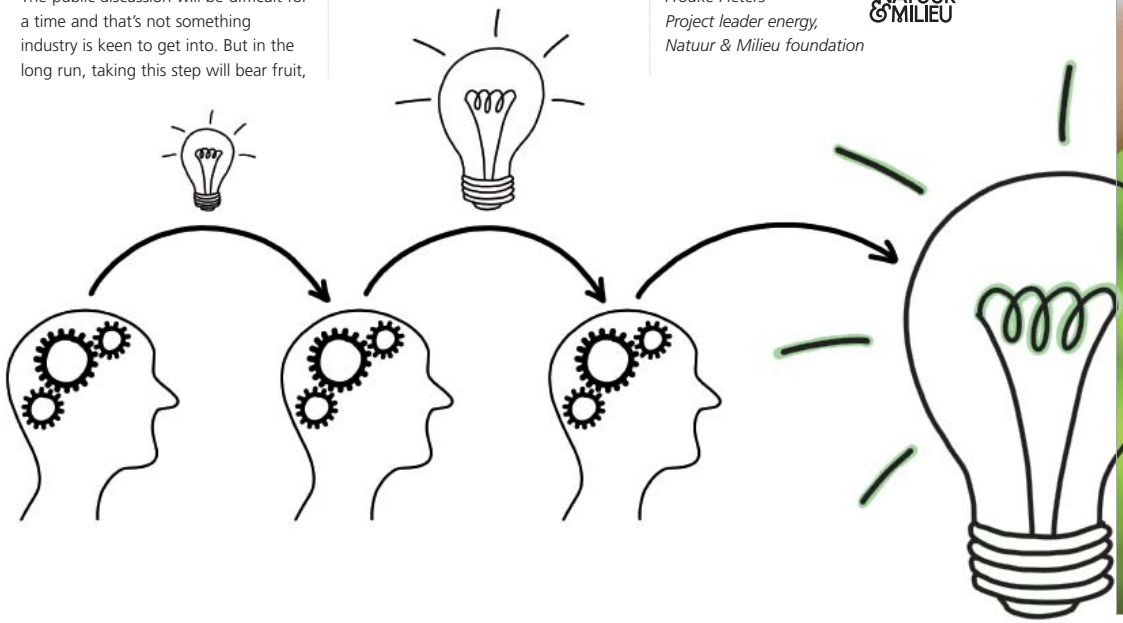
"The biobased economy is a reality right now and it is time to get society actively involved," says Frouke Pieters, project leader energy at foundation Natuur & Milieu, a Dutch environmental organisation. "In the early days, the move towards a biobased economy was mainly top down and technology-driven. Now you have to engage citizens and non-governmental organisations in the debate, to ensure a sustainable system, otherwise society will turn a deaf ear." Pieters was project leader of the Societal & Innovation Roadmap produced within BE-Basic which will be presented to the government in 2015. "The roadmap is a start towards helping the biobased economy to take root," she says.

Pieters had experienced that new products can generate resistance if people are simply confronted by them. "You can buy bioplastic bags at high street chemists," she points out. "The first time people are exposed to a product like this, they are sceptical. They ask what it is made of and ask if it can be recycled. Sometimes their doubts are justified. For example, the product could be competing with food. The public discussion will be difficult for a time and that's not something industry is keen to get into. But in the long run, taking this step will bear fruit, otherwise investments are made that have no business case because society does not accept the products."

Natuur en Milieu backs the use of waste materials to make biobased products. "But we also realise that science and industry face a learning curve which in some cases starts with the first generation of biomass. We ask critical questions about how they see the development of the second generation. And consumers have the right to know the answers as well." Research is still being carried out into the best ways of communicating with consumers. "It could be an out of the box idea such as introducing a biobased product like nappies – which are pretty polluting after all. Such a bottom-up approach could well do the trick."

Frouke Pieters
Project leader energy,
Natuur & Milieu foundation

NATUUR & MILIEU



WWF: 100% renewable energy in 2050

"The Energy Report of the World Wildlife Fund for Nature shows that by 2050 it will be possible to get all the energy we need worldwide from renewable sources. To reach that target, we first have to save energy, then focus on wind and sun generation and ensure as much road transport as possible is powered by electricity. We see the biobased economy as one means to contribute to this. The effect on nature and biodiversity itself is crucial, and should be taken into account when sourcing for biomass. We therefore believe that only materials which have been certified by the RSB (Roundtable on Sustainable Biomaterials) should be used as a demonstration of their sustainable production. Biofuel should only be an option where there is no alternative in the foreseeable future, such as in air travel. In terms of biobased research, we would be very happy if cascading really took off and integrated chains come together in which there is synergy between materials, food and energy production. However, it is essential that scientists do more and better research into the social acceptance of these technological advances. Only then can you judge if a bio-energy innovation will be accepted and is therefore really feasible. For example, we are working together with partners like ENECO and SkyNRG towards the development of certified bio-energy."

Arjette Stevens
Senior advisor biomass to the WWF in the Netherlands

Biobased solutions at home, on your plate and in your car

Nine notable results from the BE-Basic programme

10 YEARS

BE-Basic started in 2004 with a number of basic ideas for biobased solutions. It was clear from the beginning that a lot of research and inventiveness would be needed to turn these ideas into practical applications, or solutions. Ten years on, we have a number of tangible products. Nine are being used in construction, in packaging, in science and in agriculture. And more are on the way!

Self-healing concrete

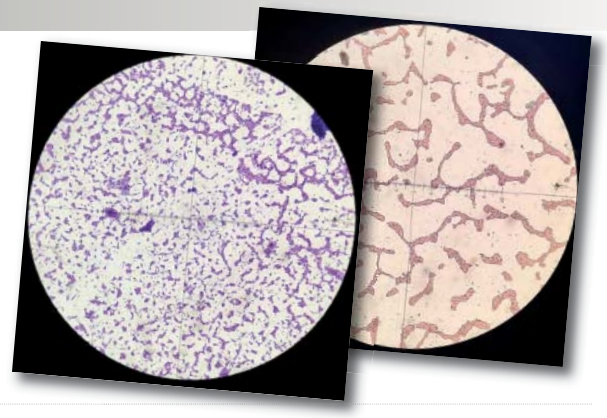
Concrete which repairs itself when cracks appear was first developed in 2009 by Delft University of Technology's Henk Jonkers and a team of partners. The self-healing concrete is based on bacteria which produce calcite when fed and activated. Calcite, a natural cement, then repairs the cracks, prolonging the life of the concrete structure. With BE-Basic's help, this process is now being developed into a fully-fledged product. The bacteria and its foodstuff are added to the concrete in tiny capsules which only open when the concrete has hardened and cracked. The team has developed a capsule made of clay which is suitable for structures that don't need heavy load-bearing capacities. It has already been used in an irrigation channel in Ecuador. In addition, a capsule based on bioplastic which can take more pressure has been developed together with Corbion.

Lifecycle costing

The next challenge is to make the product profitable enough for commercial use. "This needs to be discussed with building owners," says Jonkers. "This concrete adds roughly 0.5 percentage points to the construction costs which can often be the builder's entire margin, even though it is advantageous to the building owner. Self-healing concrete lasts longer and needs fewer repairs. You easily cover your costs over the lifecycle of a building. We are now working with partners, such as the Limburg Water Board, to demonstrate this." The construction sector has already shown interest in the product. "The development of a product for use in new buildings needs time," says Jonkers. "That is why the building sector itself asked us if we could adapt the principle to cement used in repairs. That product will be commercially available within two years." *See also Flagship 4, page 46*

Speeding up the engineering of genetically modified microorganisms

Biobased processes are more profitable if the production is based on organisms that convert the raw materials into relevant products with a maximum yield. Modifying DNA by adapting cells is very time-consuming. A new technique for strain engineering in yeast has been developed within BE-Basic that dramatically increases the capacity to engineer and test genetically modified microorganisms. The technique is based on a combination of gene synthesis, in vivo homologous recombination and CRISPR/Cas9-based approaches. It ensures the DNA strands can be recombined with multiple genetic modifications more quickly and within the yeast cell itself, rather than in a test tube. Based on the initial results, the researchers expect to be able to make the process three to four times faster. An open-source tool, http://yeastriction.tnw.tudelft.nl, allows for the identification of suitable Cas9 target sites in specific yeast strains.



notable results

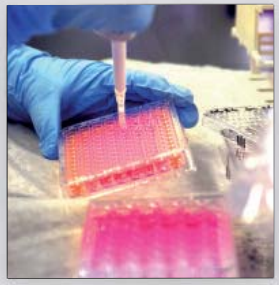
A new way of looking for novel antibiotics

The traditional way of identifying new antibiotics generally involves testing single microbial strains in an axenic culture. NIOO researcher Jos Raaijmakers and his department have discovered that some antimicrobial compounds are only produced when microorganisms are growing in close association with other microorganisms or with eukaryotes (plants, fungi). This ecology-based method of 'nature mining' opens up a rich pallet of new opportunities to discover potential antibiotics/antifungals for pharma and agriculture. The research team at NIOO has identified several bioactive compounds, in particular volatile organic compounds (VOCs), that inhibit the growth of multidrug resistant hospital bacteria and plant pathogenic fungi. "These initial screenings have been successful and, together with the BE-Basic startup Microlife Solutions. and with BioDetection Systems, we feel there is a real potential for the discovery and production of new lead compounds, with optimal activity profile and low toxicity that ultimately should be tested in clinical trials," says Raaijmakers.

Stimulating plants for improved food quality

This project began as a sideline of the search for bacteria that can stimulate plant growth and enhance plant biomass (Flagship 7). Researchers discovered that specific microorganisms applied to plant seeds or roots, changed the plants' secondary metabolism leading to an increase of specific plant metabolites and triggering the biosynthesis of yet unknown plant metabolites. In terms of food production, there are real benefits in stimulating plants to produce substances which are advantageous to the health of humans and animals. Researchers have started to expand this principle to other plant species (e.g. broccoli) to induce the production of health-promoting plant substances, which are activity profiled and selected for minimal toxicity by BioDetection Systems.

A new way of bioanalysis for biobased safety



The raw materials used in biobased processes have to be safe for man, animal and nature. The company BioDetection Systems together with Amsterdam's VU University developed CALUX screening systems, initially to check for dioxin in food. This unique method uses cells which produce light when exposed to dangerous substances. This allows the safety of complex mixtures to be assessed in a single test. Thanks to research carried out by BE-Basic, the CALUX method is now being used to assess biomass, waste products, and biobased materials. The development process for this new approach to bioanalysis was carried out without using animals and the tests themselves meet all government regulations.

See also the article about BDS Chile on page 15

A standardised tool for assessing soil quality

Helping farmers who are aiming to produce biomass with a minimal addition of nutrients while maximising production and reducing the environmental impact is key to developing a sustainable biobased economy.

Eiko Kuramae, from BE-Basic partner the Dutch Institute of Ecology (NIOO-KNAW), is working on a project to develop functional microbial biodiversity indicators for soil quality. The aim is to develop tools that predict soil quality, plant growth promotion and greenhouse gas emissions in different land use regimes.

"We are looking at microbial functions related to nitrogen and carbon cycles, at soil organic matter and at the recycling of residues for the maintaining of soil quality and soil organic matter," she says. "Research is still ongoing in both the Netherlands and Brazil. The diagnostic tool will eventually be used to monitor the impact of biomass production and to drive improvements of soil quality to produce biomass in a sustainable manner." Although the tool is not yet ready, the team has identified some interesting candidate microorganisms and functions with good predictability for in the three key areas. These will ultimately be incorporated in a decision support device which can be used by individual farmers.

Kuramae stresses the importance of working in an international team in the development process. "In part, the research has so far achieved what I had hoped when we started out," she says. "However, to develop the tools is much more complex than I thought. During the research so far, which has been in close collaboration with our partners in Brazil, I have learned which parameters are essential to further improve the suitability of the tools to be developed." It will probably take 2-3 more years of development, validation and testing before a marketable tool will be available.

notable results

Cellulosic ethanol

Dutch king Willem-Alexander made the trip to Iowa for the grand opening of Project LIBERTY in September 2014. The project is a joint venture between DSM and POET to produce cellulosic ethanol using ground-breaking technology. BE-Basic made a significant contribution to the development of the highly specialized ethanol fermentation step in this process. The factory processes agricultural residues - the cobs and some stalks and leaves of corn plants - into ethanol.

"Using baker's yeast to turn sugars into alcohol is a proven way of producing ethanol," says professor Jack Pronk, of Delft University of Technology. "But you can't use ordinary baker's yeast when dealing with plant residues because it lacks some essential genetic information. For my group, research on this topic started 12 years ago. Together with researchers based in Nijmegen, we showed that a gene from a fungus, which was originally isolated from elephant dung, carries a special gene that was a key 'missing link' in conversion of sugars from plant residues by yeast."

Proof of principle

Funded to a large extent via BE-Basic, a research programme was set up to build on this first invention. Further in-depth analysis and genetic modification of the yeast has since yielded additional breakthrough innovations. A few years ago DSM, the industrial partner of this programme, went public with their 'all you can eat yeast' platform: engineered yeast strains that can efficiently convert all sugars in agricultural residues into ethanol. "Five years ago we provided an academic proof of principle. DSM and POET have since taken on the immense challenge of translating this into large-scale industrial implementation - which requires a lot more than just yeast research. In my opinion, this collaboration represents an ideal division of roles: academic scientists develop new concepts and commercial companies use their strengths to make them a reality."

Ethanol and human capital

At full capacity, the plant can convert over 700 tonnes of biomass per day to produce ethanol at a rate of 76-90 million litres per year. DSM and POET license the technology to other industrial partners and continue to work with academia to improve its efficiency. Pronk's work is far from finished. "It is tremendously inspiring to see our ideas being used in large factories. But we should not measure the value of academic research in factories alone," he says. "The BE-Basic consortium trains a unique new generation of researchers. As we speak, they are discovering new ways to further improve ethanol production and to sustainably produce a whole variety of other products. Within BE-Basic, they see big scientific challenges as well as the urgent needs of industry and society. We will depend on these young researchers to drive innovation towards a more sustainable world. They are, in my opinion, BE-Basic's most important asset."

Optimising the purification in complex fermentation processes

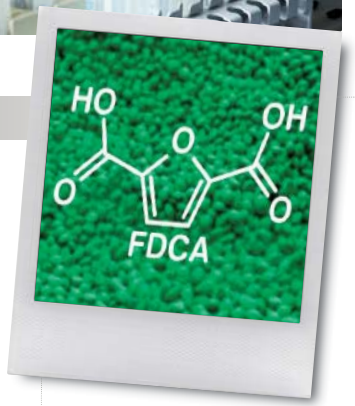
How do you isolate potentially useful components for biopharmaceuticals from a complex fermentation process? Researchers from Delft University of Technology, DSM and Synthon are developing a unique method to improve purification processes within the BE-Basic programme. "Rational design allows us to analyse which compounds are in a complex mixture and what their properties are," says Emile van de Sandt, Principal Scientist Downstream Processing at DSM. "We can use this to design the optimal purification process in silico. The design shows immediately if the process works on a larger scale. Until now, upscaling has been a question of trial and error." The method is now being fine-tuned in case studies, including at DSM, and has produced a software tool that can be used by the various partners. Several years ago the Institute for Nanotechnology at the University of Twente and Karlsruhe Institute of Technology joined the initiative. "The Karlsruhe group helps us with the complex data analysis. Twente is ensuring that we can consistently reduce the amount of product we need for a proper analysis," says Van de Sandt. "In the end we will be able to test newly developed derivatives individually and estimate the purification process at a far earlier stage."

Returns

"When we began years ago, this was our ultimate dream, and it demanded a lot of research and creativity to realise," Van der Sandt says. "We've made many advances and that has only been possible within a consortium. As a commercial company, you can't do this sort of research alone. With BE-Basic, we have been able to share our expertise and knowledge and take the process on through our practical case studies." The new method is more cost efficient. "DSM considers the environmental impact of what we do to be extremely important. Experiments take a lot of time and energy. This new method generates better returns across the board. In addition, the quality standards demanded of products – both for biopharma and food applications – are higher. Having efficient purification processes which deliver pure products is becoming increasingly important."

From PET to PEF: the new generation of plastics

The FDCA (2,5-Furandicarboxylic acid) process makes it possible to produce alternatives to the standard PET bottle and other plastic packaging. Researchers involved in two B(E)-Basic follow up programmes have managed to make biobased building blocks for the production of sustainable resins and polymers. These new bioplastics will ensure we are less dependent on the petrochemicals industry. In addition, PEF based on FDCA offers something more: its natural components are more efficient at protecting the product and make it last longer. PEF has superior barrier properties to PET. It is 10 times more impervious to oxygen and four to six times more impervious to CO_2. PEF is now being developed worldwide by lactic acid market leader Corbion. Marc Lankveld, Project Director Corbion: "People are willing to pay for products with functional added value and that is what PEF offers."



See the interview 'Marc Lankveld sees commercial opportunities for bioplastics' on page 34

Maria Cuellar is fascinated by the microbial pathway to jet fuela

"What I like about scientific research is taking the time to look into processes from top to bottom," says Maria Cuellar. She is currently assistant professor of Bioprocess Engineering at Delft University of Technology and is working within BE-Basic on an alternative route to making jet fuel. "I found it hard to choose a profession when I was at secondary school. As a teenager I used to think I would rather be paid to study. That wish has come true," laughs Cuellar.

During her graduate degree course in food engineering in her home country of Colombia, Cuellar was introduced to biotechnology and decided to concentrate on this new field. "I started a two-year course in bioprocess design in Delft with the aim of going into industry. I got some experience at DSM which was fascinating – the link between science and industry, that feeling that in the factory they are waiting for your results. But I also saw that sometimes [in industry] you have to take shortcuts in research and development and that triggered the scientist in me. I would rather have the space to really get to grips with something, because that is the key to new ideas and optimisation. So I changed direction and decided to take a PhD position at Delft University, but still within the applied sciences."

Cuellar soon realised she would stay in the Netherlands. "I planned to return after the two years but on day two of my course I met a lovely Dutchman," she says. "In addition, I was able to further develop in my chosen field here, and that would not have been the case in Colombia. At the end of 2008 I began as assistant professor and four years ago the first PhD research within BE-Basic started." Currently Cuellar is working with a number of research students on a variety of topics within BE-Basic. "I am investigating the microbial production of oil-like molecules that you can use as diesel or jet fuel," she says. "You grow the microorganisms in a fermentation medium, a sort of broth made from water and nutrients. You can't simply use the molecules produced by the microorganisms because the mixture forms an emulsion, a bit like mayonnaise. In our research we are looking at the mechanisms which lead to the formation of the emulsion and how to develop an efficient recovery process."

We are testing a prototype reactor at the Bioprocess Pilot Facilty (BPF)

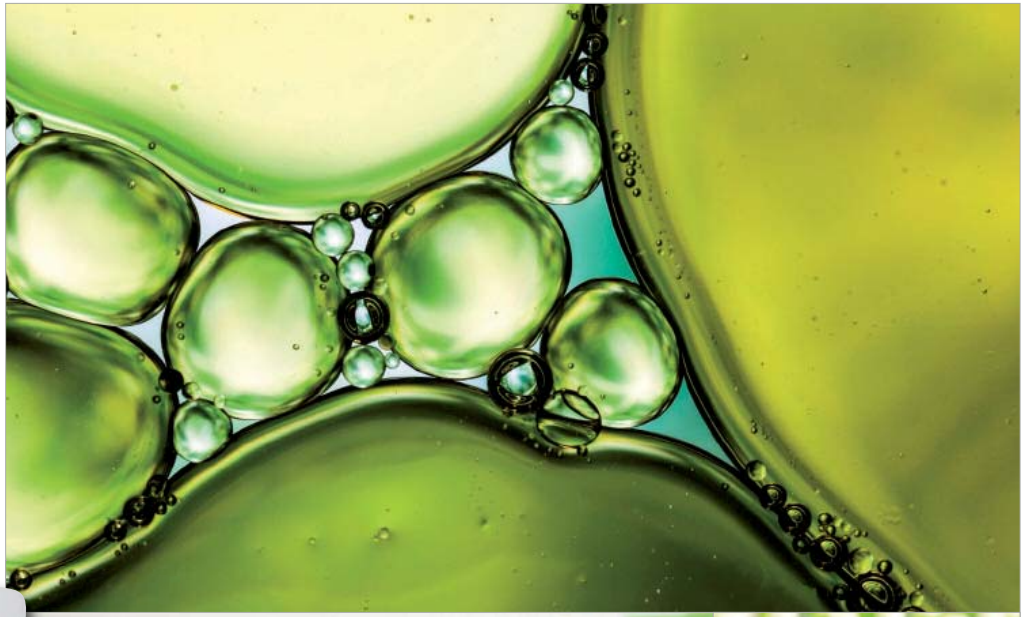
It is a promising project. "We are testing a prototype reactor at the Bioprocess Pilot Facility (BPF). The best option would be to let the entire process take place in a reactor so we can just tap the oil. Optimising the process of separating the oil reduces production costs. An early estimate indicates a cost reduction of 20% to 40%, which would make jet fuel production via this fermentation route an interesting market proposition. This fermentation route works and the forthcoming jet fuel has already been certified. The production method, however, is expensive and that is why we are working on improving the different stages in the process technology." This project has also led to the setting up of start-up Delft Advanced Biorenewables (DAB) which is taking over the project's entire upscaling and development, together with BPF.

Cuellar says she is too down to earth to celebrate every breakthrough. "Of course reaching each milestone is motivating and we are making useful advances, but there is always the next hill to climb," she says. "I am fascinated by how microorganisms work and what they can do, and by devising alternative production routes, because the petrol is running out." The assistant professor also enjoys lecturing and supervising PhDs and students. "It is very satisfying to get the best out of someone and to witness their personal growth from close quarters," she says. "Ultimately you form a real team with each other." By working closely with her team and project partners, Cuellar has high hopes for the future. "In five years time, we will be able to demonstrate that our technology is affordable and works on the right scale," she says. "As for myself, I will be involved in research. But I have an open mind and it would be dull to know exactly how my life will be in five years time. Sometimes good things just happen."

Marc Lankveld sees commercial opportunities for bioplastics

"I like to dive into the challenges in each project and then tackle them head on." And: "With any new scientific finding, commercial potential comes first." These comments typify the approach of Marc Lankveld, Project Director at Corbion. After graduating as a chemical engineer and working with various companies operating in the oils and fats market, he developed an eye for commercial potential. In 2009, as CEO of Delft University spin-off BIRD Engineering, Lankveld began to explore the possibilities offered by microorganisms. "It was too early for industry but I felt we were onto something with this one particular molecule. We went to B(E)-Basic in order to do more research and in that creative environment bio-FDCA was born."

Dr. ir. Marc Lankveld,
Project Director FDCA at Corbion,
Previously CEO and owner Bird Engineering
Educational background;
Chemical Technology/Bio Process Technology
at Delft University of Technology



The FDCA (2,5-Furandicarboxylic acid) process makes it possible to produce alternatives for the standard PET bottle and other plastic packaging. Lankveld's team managed to successfully make biobased building blocks for the production of sustainable resins and polymers. "When I saw the first product made of this bioplastic I was very excited," he says. "We had used something that basically looks like pea soup to make a nice little bottle with all the valuable properties you would want it to have. It was a real result. We had completed the cycle."

But Rome wasn't built in a day. "The groundwork was laid for the development of FDCA in the first programme (B-Basic)," he says. "You have to ask, how do certain bioroutes work and what are the best conditions to make this baby thrive? The second project (BE-Basic) was dedicated to finding out how we can make it better and whether or not particular sugars could be turned into FDCA. At this stage the company Corbion (formerly Purac) got involved." Lankveld stresses that many others around the world are thinking up clever ideas and applications. "It depends on what you do with your idea. You need the right people, the means and the environment to make it come to fruition. Without BE-Basic the development of FDCA wouldn't have happened."

So is Lankveld convinced this innovation will be a success? "The main consideration with any innovative product is its functionality. I realised FDCA's potential early on. The market for bioplastics is a large one and if lots of people want something, commercial success will follow. We all want to reduce our dependency on petrochemicals and promote a sustainable, green way of living. And bioplastic PEF based on FDCA offers something more: its natural components are more efficient at protecting the product and make it last longer. PEF has superior barrier properties to PET. It is 10 times more impervious to oxygen and four to six times more impervious to CO2. In other words, your soft drink or juice will have a longer shelf life. People are willing to pay for products with functional added value and that is, in my opinion, what will help biobased products find their place in the market."

Lankveld remembers the moment he first spotted the functional added value of FDCA. "In 2010 we produced the first kilo of material to see if we could get industry interested in its possibilities," he says. "I had a Eureka moment when we calculated the cost of the production process and found it made perfect economic sense. I remember exactly where I was at the time!" In 2013 BIRD Engineering was sold to worldwide lactic acid market leader Corbion and Lankveld took on responsibility for the business end of things. "It was exactly what I wanted: a chance to develop FDCA in a commercial environment," he says.

Experience has taught Lankveld that patience is a virtue in his field. "Take the development of bioplastics based on PLA which has an attractive outlook in terms of demand but a lower pace of growth than previously assumed. The demand for bioplastics is growing, but really widespread use will take the commitment of big companies with firm sustainability goals, like soft drink manufacturers. And governments can also play a role. Italy, for example, only allows bioplastic bags."

Lankveld is convinced it will happen. "The world market for alternative, non-petrochemical products is worth some € 60 billion. That tells me bioplastics will grow."

International alliances: added value through partnerships

Throughout its 10-year existence, BE-Basic has consistently looked for international alliances. This has resulted in partnerships in Brazil, Vietnam, the United States and Germany, and activities in Malaysia. Chairman Luuk van der Wielen: "The transition to a biobased economy is being explored worldwide. The Netherlands is an open economy. We are importing tonnes of oil and gas with which we make added-value products for export. The transition to a biobased economy is therefore having an enormous impact in the Netherlands. But we cannot make this happen on our own. If we want to contribute to a more sustainable world, and contribute to sustainable development as well as maintaining our way of life and level of prosperity, we have to collaborate with our colleagues abroad."

Brazil

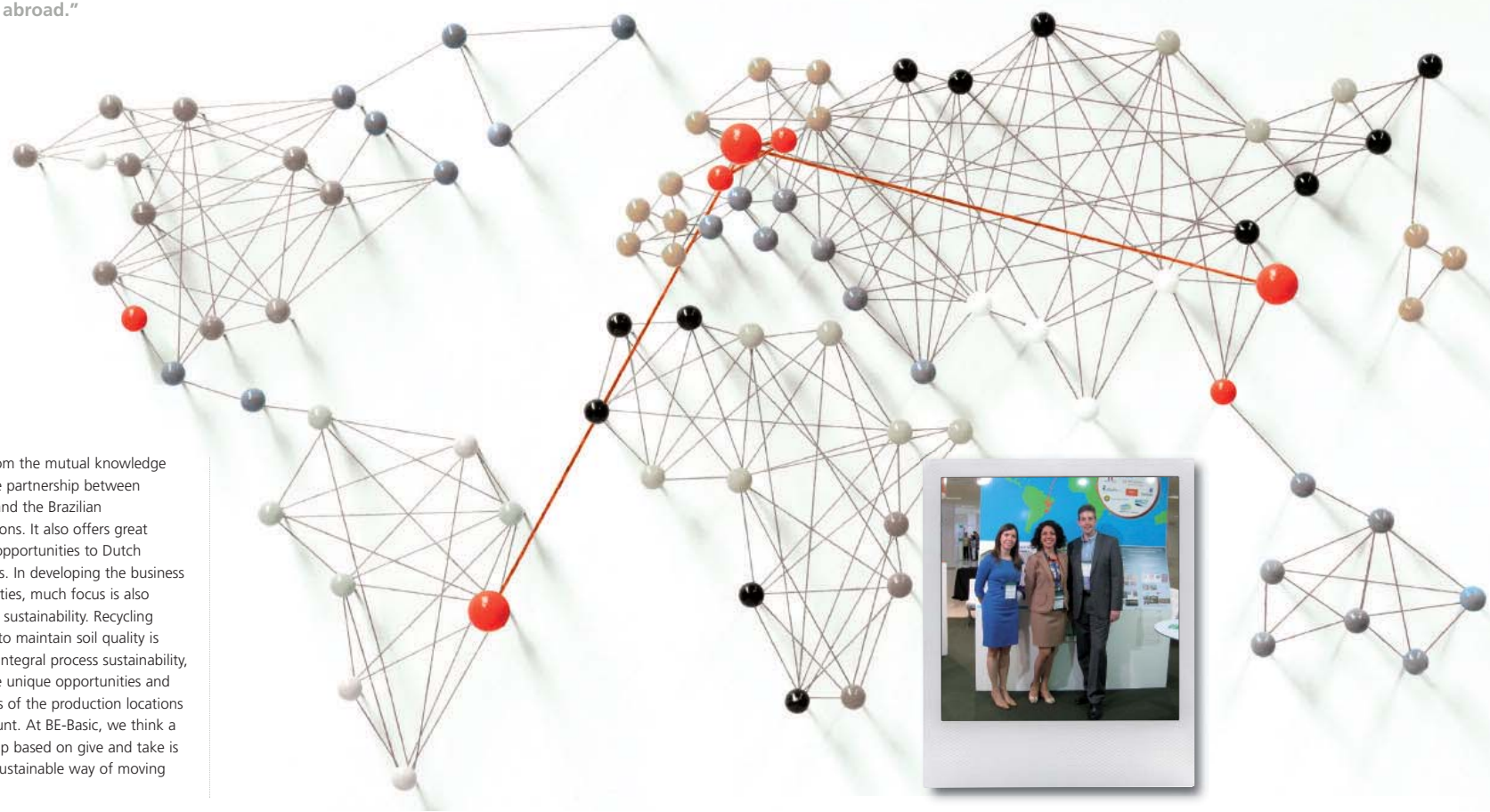
At BE-Basic, looking abroad means finding places where partnerships deliver added value for both parties. A good example is Brazil. "If you are looking for international partners, Brazil is an obvious choice," says Van der Wielen. "The country has been producing raw materials like sugar cane for years and has developed a great deal of expertise in the sustainable production of ethanol as a fuel. Brazil is an emerging economy and looking for opportunities to create more added value from its abundance of raw materials. When we started our preliminary explorations the Brazilians were looking in particular for support in human capital development, even more than R&D. So in recent years we have been focusing our efforts on the development of joint educational Master and PhD degrees with the best universities in the country. These courses also benefit from guest lectures by BE-Basic and Brazilian industry experts and are open to participants from industry. At the same time, joint research and development programmes bring Dutch technology together with the Brazilian genomics and agro-industry programmes, which are the biggest in the world. The fine-tuning for business development benefits greatly from the mutual knowledge within the partnership between BE-Basic and the Brazilian organisations. It also offers great business opportunities to Dutch companies. In developing the business opportunities, much focus is also placed on sustainability. Recycling nutrients to maintain soil quality is linked to integral process sustainability, taking the unique opportunities and challenges of the production locations into account. At BE-Basic, we think a partnership based on give and take is the only sustainable way of moving forward."

Reliable partner

It's a partnership that takes careful planning, Van der Wielen says. "In Brazil things are different. You have to invest in mutual understanding and trust. We found that the role of the community in Brazil is more central than in the Netherlands. The fact that we have shown ourselves to be reliable partners through the years has established a solid base for cooperation. We followed up the initial plans by establishing a BE-Basic office in Campinas. That made it possible to consolidate our relationship with Brazilian institutes, industries and the government. We are contributing to a federal bioenergy postgraduate programme, for instance."

Sustainable biojet fuel

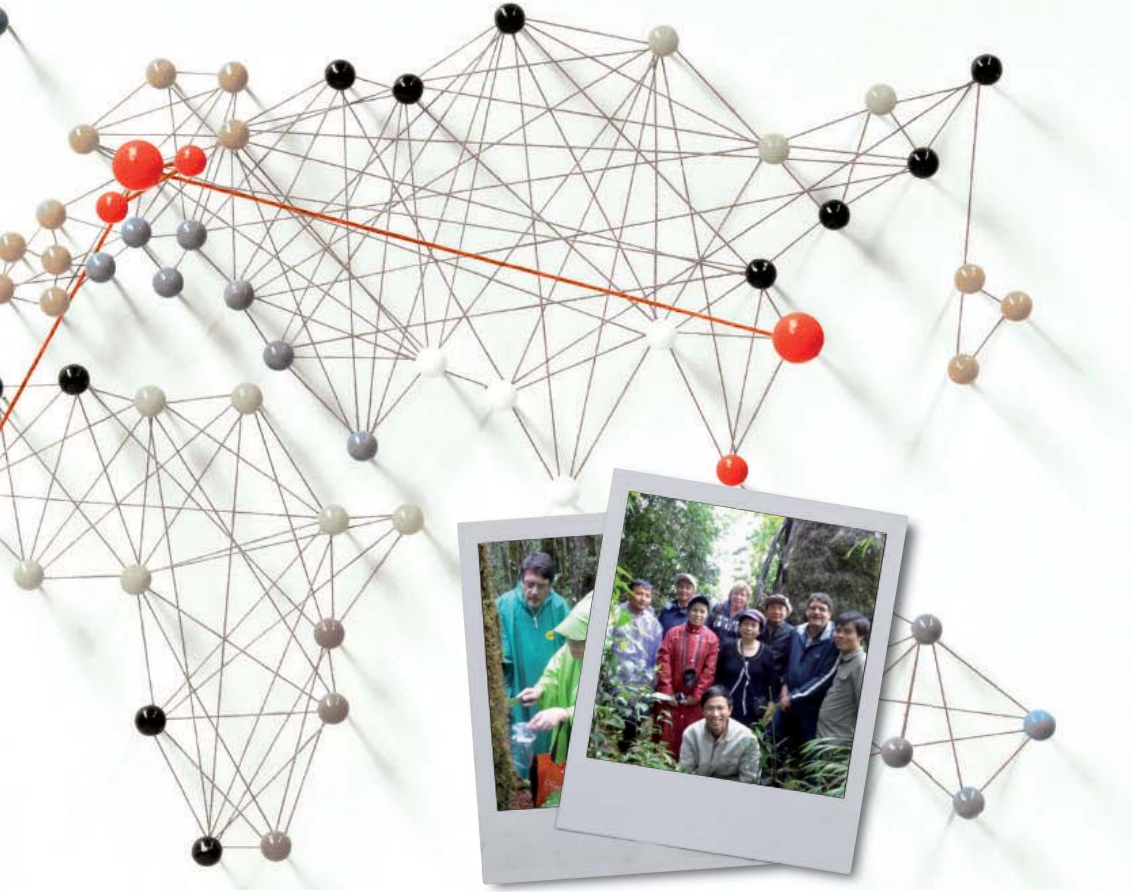
The partnership is all about creating opportunities. In 2014, BE-Basic, the Brazilian state Minas Gerais, KLM and SkyNRG announced a partnership to help develop a biojet fuel value chain. "Biojet fuel is the only way to a



sustainable future for the aviation sector," Van der Wielen says. "The public-private partnership gives us the opportunity to explore how we can achieve this in a sustainable way." A public-private partnership of this kind is new to Brazil. "In Brazil an alliance between industry and academic institutions is relatively unknown whereas the Dutch are used to thinking in terms of cooperation; it's in our genes. And it lies at the heart of BE-Basic too. Public-private partnerships give partners a chance to share innovations, work more efficiently and keep a tighter grip on risks. In order to create a value chain you need several partners, that is the basic principle. The key word is trust. That is a BE-Basic defining benchmark, not just in Brazil but everywhere in the world."

Vietnam

Perspectives for successful partnerships in Vietnam are promising as well. "We are not quite on the organisational level we have in Brazil," says managing director Bram Brouwer. "Two years ago we signed a cooperation agreement with the Vietnam Academy of Science & Technology and we have since come up with a clear set of plans. Now we are at the stage where we have to substantiate them: what will be the timeline? Who will be doing what? That takes time because our way of working doesn't necessarily match theirs, and vice-versa. We are lucky to be able to ensure 10 PhD students will spend part of their research programme in the Netherlands and part in Vietnam. How long they will stay in either country depends on the type of research project at hand. Vietnam has a rich biodiversity with potentially very successful cases and produces a lot of biomass. Their level of expertise needs to be brought to a higher level and that is where the dual degree PhD programme comes in. In addition, a large part of the technology is being developed in the Netherlands and the Vietnamese can become acquainted with it through training programmes, prior to investing in implementing this technology in their own country."



Bilateral agreements

The partnership between BE-Basic and the Vietnamese partners is supported by the governments of both countries. Brouwer: "The Netherlands and Vietnam now have some bilateral agreements in place concerning joint research activities. In 2014, the Vietnamese minister for Science and Technology Nguyen Quan came to the Netherlands to further support bilateral science and technology collaborations between the Netherlands and Vietnam." The research programme is made up of three parts. The first involves monitoring and bioremediation of Vietnamese soils, crops and biomass. The second focuses on the search for new probiotics, genes and bioactive compounds found in Vietnam's natural resources, and the third on exploiting raw materials for the production of chemical building blocks. Researchers have identified microorganisms which can break down recalcitrant contaminants, like dioxin in polluted soils. These can play an important role not only in bioremediation but, in the longer term, in the break down of lignin which will increase the volume of biomass that can be processed.

Germany and Flanders: BIG-C

The partnership with Flanders and North Rhein Westphalia is of a completely different order. In the spring of 2014 CLIB2021 (a German partner since 2012), BE-Basic and FISCH (Flanders) launched the Bio Innovation Growth megaCluster (BIG-C). Luuk van der Wielen: "The three states have a similar structure: advanced urbanisation and industrialisation around infrastructure including waterways, aviation, pipes, railways and roads. We share the same problems, one of which is the strong dependency on fossil fuels which brings in its wake a huge peak of CO_2 emissions from fixed and mobile sources. And all three regions have a solid knowledge base in the field of biobased alternatives. What could be more logical than to pool our resources to look for solutions?"

Regions of specialisation

BIG-C focuses on the most promising and concrete biobased solutions and wants to increase awareness of the necessity and urgency of a transition among stakeholders and the public. The cluster exemplifies the policy of the EU which favours 'regions of specialisation'. "There are very few places in the world where income, jobs, industry and people come together in such numbers in such a small area," says Van der Wielen. "Our region is comparable to Shanghai, Houston and Singapore. As BIG-C we can participate in and shape big European programmes. It is much more efficient for governments to invest in existing infrastructure. We explore government policy in other areas as well: how to link up our efforts with the SER energy agreement, for example. Ultimately the common goal is to reduce CO_2 emissions (and even better: reuse what we produce), create jobs and increase industry revenue through biobased and other circular processes."

Other activities

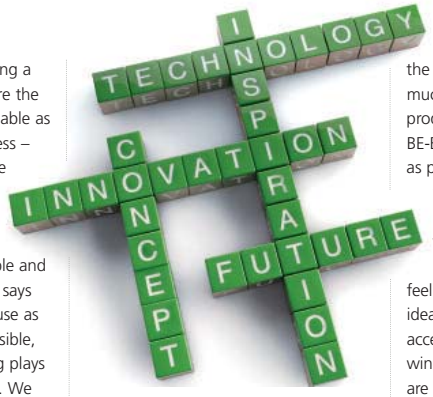
In the **United States,** Amyris has been a valued alliance partner for years, as has the Energy Biosciences Institute Berkeley. Luuk van der Wielen: "We are developing a joint vision of the biobased economy worldwide. We contributed to high level policy studies, including the high level, multi-author SCOPE (Scientific Committee on Problems of the Environment) report on Bioenergy and Sustainability which was hosted by Fapesp and the United Nations; and the Global Sustainable Bioenergy Project, along with partners worldwide, including EBI and others. We also work together with Amyris in the field of synthetic biology."

The alliance with **Malaysia** has not yet been formalised further because of the political situation. "The desire to work with BE-Basic was bottom up, from the biomass producers themselves," Van der Wielen says. "We remain in talks with them to determine what the options are. We see particular opportunities in the sustainable production of palm oil biomass residues. There is much to be gained from utilising the waste materials which are left behind, and substantially reduce emissions and increase possibilities for income."

From R&D to upscaling and implementation in a single decade

Biobased solutions are conquering the world

BE-Basic has come a long way in the 10 years of its existence. Luuk van der Wielen (President of BE-Basic Board) and Bram Brouwer (Board member and managing director) have a good idea of everything we can achieve in the coming years with the insights which have been gained. "We now have a fairly clear picture of the feasibility of biobased solutions," says Van der Wielen. "Thanks to the research we conducted in the early years, we know that the technology works. This year's annual report contains some striking examples of what is possible. Now we need to go on to the next stage, which is implementing the technology and creating a support base for it in society. To do this you need players who represent science, the market and government. BE-Basic Foundation is such a player and our next efforts will be geared towards exploring how our technical expertise, combined with our knowledge of society, can help pave the way for a biobased economy."



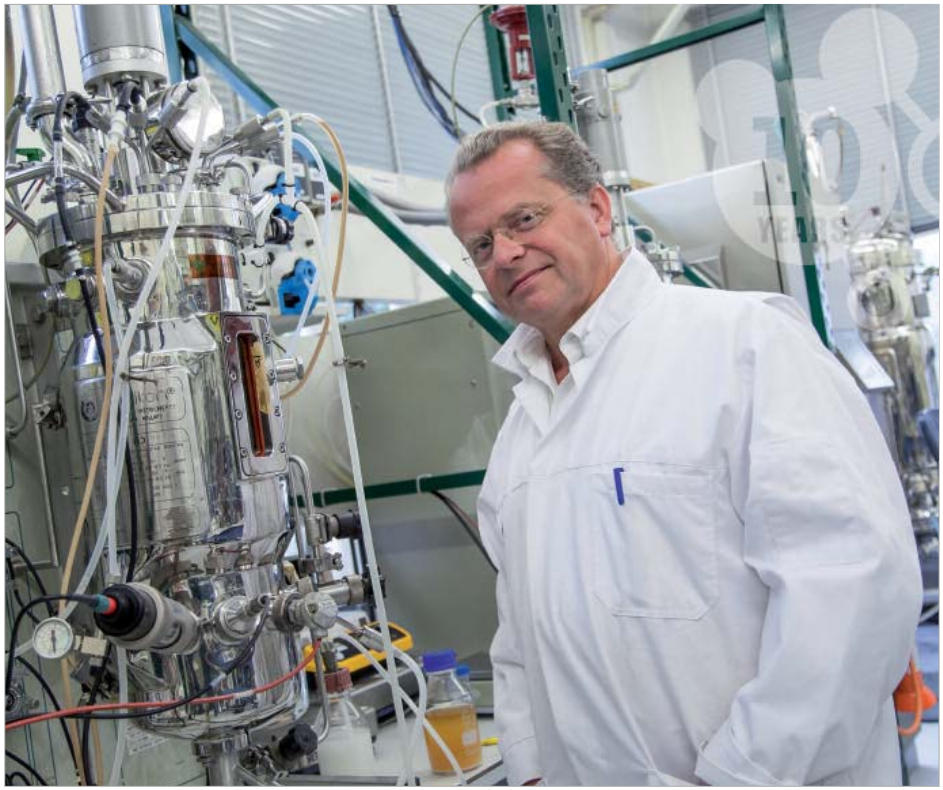
An important aspect of establishing a biobased economy is to make sure the biobased processes are as sustainable as possible. "Every step of the process – and this goes for every project we undertake – is evaluated for safety and environmental impact. We don't just look at targets and profits, we take people and the planet into account as well," says Van der Wielen. "Our goal is to use as much sustainable biomass as possible, such as residual waste. Cascading plays a part in every decision we make. We need to optimise the added value of biomass and only use it as fuel at the end of the line. We know that there are sectors, and aviation is one of them, which will always need liquid fuel."

Bioport Holland

This is why important players in the Dutch aviation sector, such as Schiphol, KLM and SkyNRG, the Ministry of Economic Affairs as well as Infrastructure and Mobility, and the Port of Rotterdam established BioPort Holland, just over a year ago. "The idea is to bring together the supply and demand of biojet fuel," says Van der Wielen. "A bioport located a short distance away from the users – in this case on the Maasvlakte 2 extension of the Port of Rotterdam – can enhance the security of supply. Large-scale production does mean we would have to improve conversion technologies. We will have to concentrate our efforts on the biochemical route, otherwise too much energy will be lost during production. That is something that the BE-Basic Foundation is going to support as part of the consortium. The great thing is that technologically we are more or less where we thought we would be when we launched BE-Basic. This was partly based on gut feeling but it is good to see how the idea of biobased solutions has gained acceptance in society as well. There is a window of opportunity there and we are going to do our very best to further the development and use of second generation biofuels."

Commercialisation

"Over the past few years we have shown proof of principle in various areas," says Brouwer. "So we've created the expectation that a biobased economy will become a reality. Certain elements are developed faster than expected while others are lagging behind. We are at a stage where the involvement of stakeholders and the public is becoming increasingly important. We are currently talking to problem owners, such as waste processing companies, to explain how our technologies can help them capture the value in it and to make their processes more cost effective. For this we use case studies. It is even more time consuming to explain the benefits of biobased solutions to the ordinary layman. The technology needs to be developed in such a way as to be affordable and easy to use. Start-ups represent another key element. They take the inventions from the lab and aim to prove their technological and economic value, and to de-risk the inventions to make them commercially viable."



'Luuk van der Wielen: We have everything we need to take the next step!

Technological revolutions

Advancing technology will do much to help the process. "We've come a long way," says Brouwer. "'We started by investigating microorganisms under the microscope and end up exploring the vast opportunities of the functional diversities discovered thanks to advancements in DNA techniques. Ecogenomics provides us with the opportunity to investigate the complex networks of microorganisms and how things hang together: the interaction of microorganisms in the soil, for instance, or the effects of stress and pollution. That broadens our scope enormously. I also think that the advances in nanotechnology will revolutionise how we do things. We can do more on increasingly smaller surfaces. This means that we can reduce costs significantly and with that the applications can be made financially accessible to private individuals."

Roll up those sleeves

All in all the BE-Basic Foundation is now preparing its plans for the next decade. Van der Wielen: "The sustainable biobased economy is coming and that means we will inevitably encounter technical and practical hiccups during the implementation process. It's a phase we have to go through. Upscaling is essential for the development of the perfect factory of the future, or the perfect process.So it's time to roll up our sleeves and get on with it. We have everything we need to take the next step!"

BE-Basic: scope and scale

Back in 2004, the B-Basic and Ecogenomics programmes each started out with approximately 10 industrial and academic partners and budgets of € 50 million and € 24 million respectively. They merged in 2010, combining their environmental and industrial biotechnology approaches into the BE-Basic programme. The newly-formed BE-Basic had an integral budget of over € 120 million and a flanking (yet independent) pilot plant with a budget of some € 80 million. In 2012, the Kluyver Center for Genomics came on board, further reinforcing BE-Basic's genomics programmes. The next stage involved setting up the BE-Basic Foundation to bring in various programmes (AMBIC, ISIM, EBD) attached to the Dutch government's top sector strategy and the IBPR project (cofunded by EFRO) with a joint integral budget of approximately € 27 million. This step also expanded the commercial partner pool by adding leading food industry firms to the energy and chemicals industry players.

The BE-Basic programmes were also instrumental in the partners acquisition of substantial EU funding as well as international (Brazil, Vietnam, Malaysian) programme grants. Today, the BE-Basic Foundation has over 50 partners worldwide and is connected to programmes worth €40 - 45 million per year. This makes the BE-Basic Foundation one of the largest, most active, visible and respected global public-private players with a focus on the responsible and sustainable production and use of biorenewables for food/feed, chemicals, materials, and the energy/fuels sectors. After all these developments, it is crucial to ask ourselves the question (again): Is this (or what is) the right scope and scale?

Scope

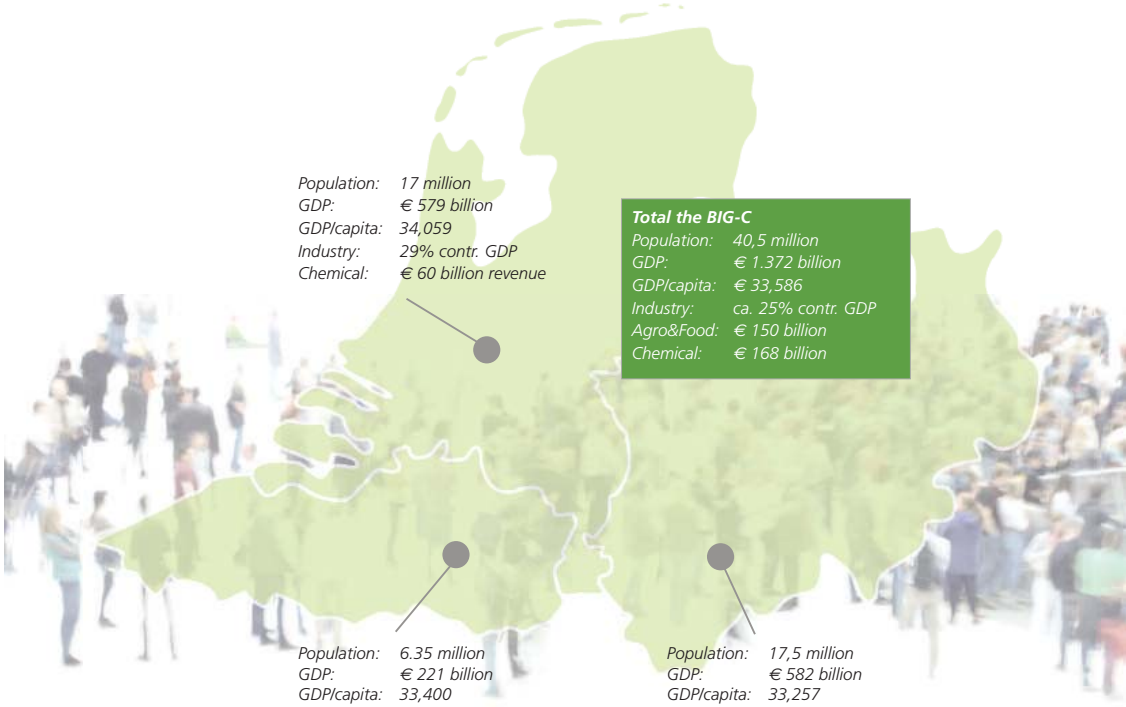
Let us look back at our objectives. *"The BE-Basic Foundation is an international public-private partnership that develops industrial biobased solutions to build a sustainable society. As we want to switch from fossil fuels to biomass in the near future, new technologies and insights are required for all industries that provide us with food, chemicals, materials and energy. The BE-Basic Foundation initiates and stimulates collaborations between academia and industry, between scientists and entrepreneurs and between the Netherlands and abroad."*

To reach these **objectives**, the BE-Basic Foundation coordinates and stimulates RD&I programmes for science and technology development, especially - but not exclusively - environmental and industrial biotechnology. BE-Basic stands for Biobased, Ecologically BAlanced, Sustainable Industrial Consortium. The focus is on **implementing** integral and sustainable biobased solutions that balance and optimise economic value and climate impact. Those balances are reached best by applying cascading and integral biorefinery concepts and prioritising high added value, non-energetic uses, while respecting energetic uses for those sectors without alternatives (aviation, marine and heavy road transport).

The key words are implementation, economic value and climate impact; even more than before. The BE-Basic Foundation aims to adjust the balance more towards implementation to stimulate sector and regional development, wherever useful and relevant. For example, in 2014 BE-Basic had a leading role in developing the aviation industry's Vision and subsequent Action Plan towards sustainable aviation biofuels industry in the Netherlands (part of SER Energieakkoord). One tangible result is the decision by BioPort Holland, a leading organisation set up by the Dutch aviation industry, to advance its activities in 2015 as a BE-Basic programme. BE-Basic also helps to explore large-scale biorefinery hubs around the Dutch port regions to better understand the business and climate cases. One of the preliminary findings is that **the projected economies of scale are larger than single companies can accommodate and that more collective, public-private action is required.** To achieve this, BE-Basic collaborates with regional platforms such as Biobased Delta, which includes the Port of Rotterdam and the emerging cluster around Groningen Seaports, as well as with partners in North Rhein Westphalia and Flanders (as BIG-C). From this perspective, it is logical that the BE-Basic Foundation partner composition develops more towards industrial players, although the involvement of academia remains critical to solving the technological challenges of this phase in the development of a biobased economy.

The scale of BE-Basic programmes the company intends to initiate for the period 2016-2024 should be in line with the size and scale of business and climate cases for the demonstration plants. For the Northwestern European (the BIG-C) region, the total numbers are given below.

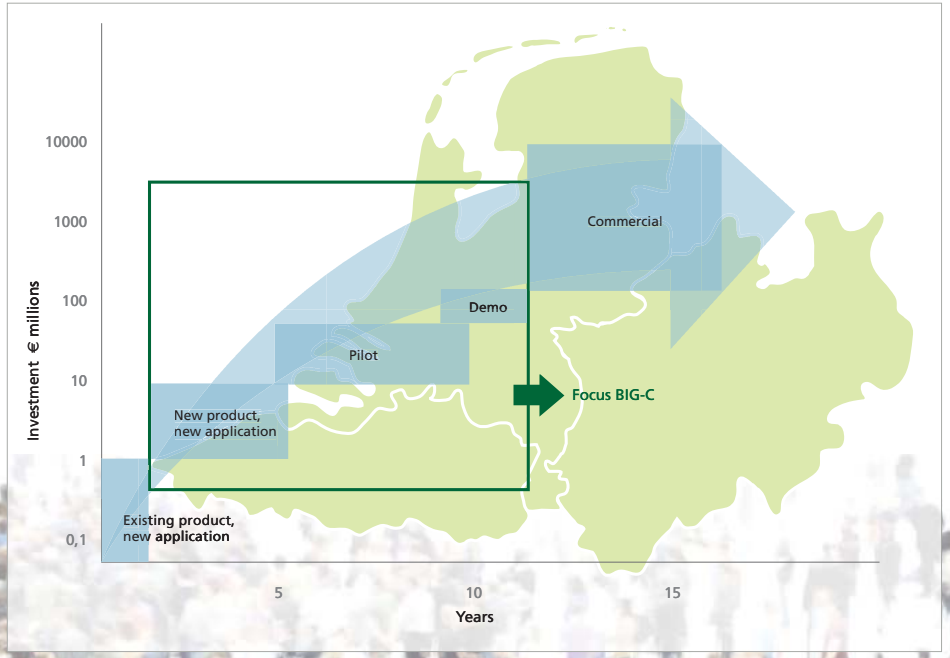
Various vision plans describe 10-30% biobased industries in these sectors over a wide range of years (2030 to 2050 window). There is a current debate on the underlying availability of biomass, but the government advisory Corbey Committee (supported by BE-Basic) concludes those numbers are possible, in principle. Whatever the final scale ends up as, BE-Basic believes there is a window of opportunity now, which can make a reality if we take action. Another aspect is the cost of RD&I programmes versus the CAPEX and OPEX of industrial operations.



The diagram below (Van Breugel and Van der Wielen, 2013) indicates development time and costs for various stages in the innovation chain for industrial processes. BE-Basic programmes fall typically become the category of new products and pilot scale operations (projects of €1-10 million), compared with commercial investments of €100-250 million. Industry return-on-investment is typically 20% – so low percentages of anticipated GDP-contributions of approximately €5 billion per year would be a reasonable programme volume.

Integral sustainability is a key driver. The BE-Basic Foundation spends roughly 10% of its budget on programmes that explore, investigate and communicate sustainability impacts (people, planet, profit) in broad national and global settings and develops sustainable solutions. This includes participating in, and contributing to, balanced, high level policy briefings and organisations.

Concluding on scope and scale:
BE-Basic's scope is being adjusted more towards implementation. As a national programme organisation, BE-Basic currently has the required scale for this phase in the development of the biobased economy, with a good leverage for each of the contributors: Dutch public support, industry and academic contributions and other support factors.



Progress update 2014 per Flagship

The BE-Basic R&D programme involves researchers from academia, industry and knowledge institutes collaborating on both fundamental science and technological, environmental and industrial challenges. We aim to bring about true innovations in biochemicals, biomaterials, bioconstruction concepts and biobased safety assessment and quality monitoring tools. This is supported by various activities to optimise the societal embedding of the products and processes developed by BE-Basic. These are the essential building blocks for our biobased economy. Within BE-Basic, the research is organised in 'Flagships'. Each Flagship addresses a major scientific, technological, environmental or socio-economic challenge.

Flagship 1

Second Generation Carbon-based compounds

The Flagship Second Generation Carbon-based Compounds aims to develop clean, efficient and sustainable industrial processes to create carbon-based chemical building blocks, mainly for the chemicals, materials and fuel industries. The research focuses on the conversion of lignocellulosic materials (first & second generation) and other biobased feedstocks (glycerol, alcohols, acids and furanics), including their contaminants, into relevant products.

All the projects are well under way and tremendous progress has been made, as can be seen in both the scientific and technological output and the plans to transfer the developed knowledge to the Bioprocess Pilot Facility (BPF) for scale up studies. In addition to publications, industrial partners are filing patents based on the scientific outcomes. One very successful recent project was the development of the biocatalytic FDCA process. FDCA (2,5-furandicarboxylic acid) is a biobased replacement for (oil-derived) phthalates in the manufacture of resins and polymers such as polyethylene terephthalate (PET). This process has been further developed together with BIRD Engineering and scaled up at the BPF. BIRD Engineering has been taken over by Corbion and the process is now being developed in an industrial environment.* Within Flagship 1 two new projects started in 2014: Omniyeast and a horizontal project led by Flagship 1 to develop label free in vivo measurement of enzyme activities.

) See the interview with Marc Lankveld on page 34

Flagship 2

Nitrogen-based Specialties

The Flagship Nitrogen-based Specialties develops novel technologies for the production of nitrogen-containing compounds from renewable feedstocks by using the advanced engineering of microorganisms. Research within this Flagship is focused on the design and optimisation of pathways for the production of unnatural compounds that can be used as pharmaceuticals or as building blocks for materials. In addition, this Flagship includes high throughput bio-pharmaceutical process development for the optimisation of protein production.

Over the past year, the most remarkable progress has been made in the development of Amoxigreen, involving two different routes for the fermentative production of the antibiotic amoxicillin. For both routes, two new enzymes have been created: one concerns a hybrid non-ribosomal peptide synthetase and the other is based on a re-designed CoA ligase that can handle the novel building block the team wishes to introduce. A proof of concept has been realised to produce amoxicillin but the compound does not entirely meet the qualifications yet.

Flagship 3

Sustainable soil management and upstream processing

The Flagship Sustainable Soil Management and Upstream Processing focuses on developing and testing scenarios for waste management from the perspective of closing cycles and prevention of negative side effects (spilling=spoiling). The Flagship was redesigned several years ago and its results are therefore mainly from the past 2-3 years. Furthermore, the Flagship uses and integrates methods and approaches developed in other Flagships (8 and 9). FS3 still sees many challenges ahead, for example in finding solutions for future waste streams coming from pre-treatment processes in FS1.

This Flagship is working on the project SURE/SUPPORT, which is testing the effects of recycling waste from the biobased economy into soil. This work will result in a support system that can be used by advisors and practitioners to decide which waste product will have the most positive impact on soil biodiversity and ecosystem services, depending on soil types, environmental settings, and land use. Work done in 2014 highlighted an interesting side effect with regard to methane. Soils with added recycled waste from the biobased economy are known to produce more greenhouse gases. However some waste products tested by SURE/SUPPORT resulted in a higher methane consumption by soils, which would be very good for counteracting greenhouse gas emissions and global warming.

Potential end users have also been asked about their needs and expectations with regard to the SURE/SUPPORT system. This work will result in an improved decision support tool with enhanced opportunities for providing adequate advice to farmers and others.

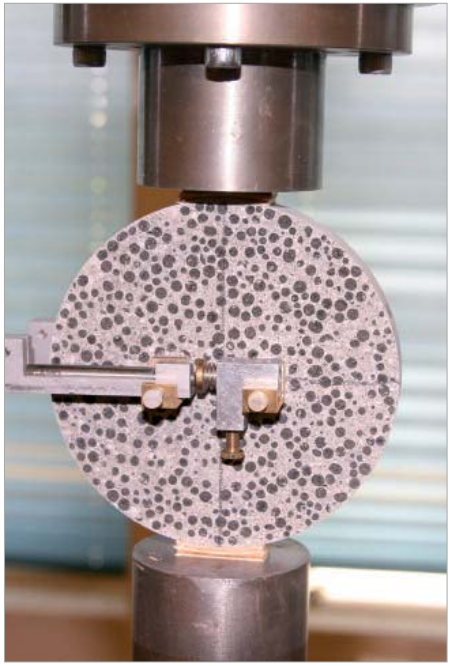
Another important development has been the approval of the Horizontal International Project (HIP) ASEAN/Brazil Biojet Fuels & Bioplastics, an integrated approach involving several Flagships (3, 5, 8, 11) to develop a sustainable and safe production system for biofuels and biomaterials. (See also Flagship 11).

Flagship 4

Bioconstruction Materials

The Flagship Bioconstruction Materials focuses on the development and testing of micro-organism-based solutions for developing self-healing bioconstruction materials.

Flagship 4 is working on turning self-healing concrete, developed by Delft University of Technology, into a profitable product for the building trade. The researchers are looking at how savings can be made on the healing agent production costs so they can sell the product for a competitive price. The researchers are also speeding up the process of concrete deterioration in the laboratory so they can prove concrete containing the healing agent lasts longer and needs fewer repairs. This is a key part of developing the business case. In addition, the healing agent has been added to cement used for repairs, which is currently being tested by the Limburg Water Board. Repairs made using the self-healing cement are being compared with those made using traditional materials. "We expect to be able to see the difference after just one winter," says Delft researcher Henk Jonkers. "If the tests proceed as planned, we may be able to launch the self-healing repair cement on the market at the end of 2016."



Flagship 5

Microbial Production of Biofuels and Biorenewables

The Flagship Microbial Production of Biofuels and Biorenewables focuses on the hardware (equipment) side of the development, scale-up and optimisation of (lignocellulosic) feedstock preparation and microbial-based process technology for converting biomass into biofuels and other biorenewables. The Flagship 5 programmes facilitate the transfer of other BE-Basic projects (especially those in Flagships 1 and 2) to the Bioprocess Pilot Facility. With a focus on implementation of novel technologies, it also ensures the training and education of BPF staff and others in using novel equipment and other pilot facilities.

At this moment, two projects are in progress: a dedicated and proprietary reactor (DIRC, *) for the production of advanced fuels and separating bioproducts, and the pretreatment project. The DIRC-project started its first pilot scale experiments in the BPF in 2014, and the pretreatment project started around the time of the BPF's formal opening in Spring 2015. Both projects link to the national implementation of a biobased economy, as well as to benchmarking the BPF to comparable world-class facilities elsewhere: there are biobased opportunities worldwide.

These projects also have concrete 'horizontal' elements: the DIRC-development is closely linked to the HIP-project looking into complete supply chains for aviation biofuels as well as chemical building blocks. The pretreatment project links to demonstrating the use of metagenomics technologies for fast fingerprinting and the prediction of pretreatment conditions in subsequent fermentation and environmental impacts (Flagship 7 and 8).

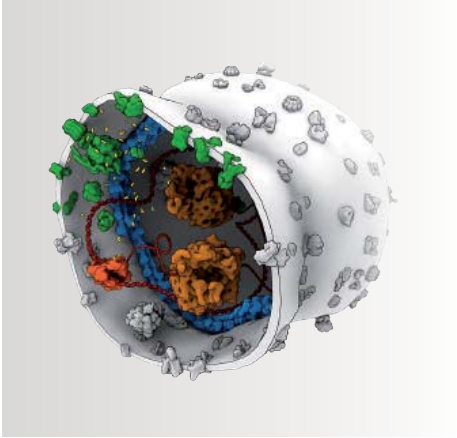
**) See the interview with Kirsten Steinbusch, CEO of Delft Advanced Biorenewables (DAB) on page 13*

Flagship 6

Synthetic Biology

The Flagship Synthetic Biology develops tools and techniques for the improvement of microorganisms. The design and optimisation of novel pathways to desired products is being complemented by unique cell membrane engineering aimed at the efficient product export and improved robustness of the production organisms.

After several years of investment, the first results of the project F06.004 around optimising the enzyme Acetyl-CoA have been published. This research uses results from Flagship 1. Acetyl-CoA is a building block in many metabolic engineering and synthetic biology projects. The fast and energy efficient formation of Acetyl-CoA is often a bottleneck in the production of heterologous compounds. Over the past few years, the cost of synthesising genes has fallen sharply. This, together with techniques such as in vivo homologous recombination (recombining genetic material from yeast cells) and CRISPR/Cas9 (combining DNA strands within yeasts), has dramatically increased the capacity to engineer and test genetically modified microorganisms with improved properties. These new techniques have recently been optimised and implemented in project F06.004.



Flagship 7

High-throughput experimentation and metagenomic mining

The Flagship High-throughput Experimentation and Metagenomic Mining develops and applies high-throughput approaches and tools to explore and mine the metagenome and the microbiome of a variety of environmental samples, including soils and fresh water systems. In addition this Flagship aims to engineer and screen enzymes and other products for improved properties.

Flagship 7's projects have been fully up and running since 2014 and several scientific and industrially interesting results have already been obtained. A range of novel microbial strains involved in (de)halogenation and the nitrogen cycle was discovered, isolated and analysed. The metagenomes of pre-treated and non pre-treated wheat straw converting mixed cultures have been extracted and are being analysed. Several new bioactive compounds with antagonistic activity against human and plant fungal and bacterial pathogens were extracted from environmental samples and from isolated bacterial strains and bacterial consortia. Some of these compounds were identified as novel products holding great promise for commercial applications. Of significant interest for the food industry, for example, is the discovery of the substantial production of exopolysaccharides by Acidobacteria, a bacterial genus that is abundantly present in a wide range of soils but of which only a few strains have been recently successfully isolated.

Methods

The first results from computational enzyme design holds great promise for the development of new catalysts while strongly reducing laboratory efforts. It employs modern computational methods and high-throughput in-silico screening to design small libraries of mutant enzymes that have improved stability and/or selectivity. This technology makes it possible to accelerate enzyme engineering projects. Furthermore, automated fluorescence microscopy methods have been developed that distinguish industrial yeast cells with different productivities, provided by DSM. The application of this to a selection of robust high ethanol producing strains will be explored next.

Flagship 8

Environmental Impact of Chemicals, Biobased Molecules and Processes

The Flagship Environmental Impact of Chemicals, Biobased Molecules and Processes develops novel and efficient methods for the evaluation and improvement of chemical safety in the biobased economy. Research is focused on assuring and promoting environmental and human safety in the transition to, and implementation of, a biobased economy, as compared to existing industrial activities.

The E from B(E)-Basic started out as the public-private partnership Ecogenomics and has undergone a clear transition. The focus has shifted from strongly ecological and soil-orientated research with various applications to an integrated project to develop the safe and sustainable use of biomass to produce chemicals in the biobased economy. For example, the company BioDetection Systems (BDS), world leader in the use of bioassays for the safety assessment of substances and complex compounds, has published more than 10 papers on novel applications and has made clear steps towards increasing the acceptance of bioanalysis, without the use of animal testing.

In addition, results have been booked in determining the causes of the greenhouse gas emissions stemming from the use of the sugar industry bi-product vinasse as a fertiliser. Researcher Wim van der Putten has published an article in Nature giving an overview of the influence of below-ground biodiversity and ecosystem functioning. Researchers at the VU University Amsterdam and Wageningen University have also been working to highlight the importance of a system biological approach to microbial ecology.

Flagship 9

Societal Embedding of a Biobased Economy

The Flagship Societal Embedding of a Biobased Economy studies the societal embedding of the products and processes developed by BE-Basic for optimal innovation. The Flagship focuses on the identification of socio-economic aspects and sustainability issues and the development of adequate systems to monitor and model these. The Flagship develops effective and efficient education, communication and societal valorization programmes.

In 2014 BE-Basic launched a completely new educational programme. This follows an inventory of the educational needs throughout the entire chain, from primary to post-graduate level, which was carried out in 2013. The new programme focuses on a broad and international audience. Activities have been developed for different educational levels (secondary, tertiary and post-tertiary). These include a successful free MOOC (massive online open course) which has been followed by 8,000 people around the globe. *

) See the interview with Isabel Arends on page 52

Flagship 10
Genomics for industrial fermentation

The aim of the Flagship is to deliver improved fermentation processes for bioconversions and the food industry focusing on the selection of natural strains or strains resulting from directed evolution or (non)-genetic modification. The Flagship is in the process of starting up the research programme and setting up initiatives to ensure optimal collaboration between research partners and industrial partners.

Project 1 of the AMBIC programme of Flagship 10 started one year ago. The researchers have identified potential regulators of fungal cell factories that are involved in the conversion of lignocellulosic material into simple sugars. These simple sugars can be used to feed microbes for biofuel production. The regulatory genes that are identified in this project will be targets to improve the cell factories for the production of enzymes for biofuel production. This should result in reduced production costs for these fuels, making them more competitive when compared to non-sustainable energy resources such as oil.

Flagship 11
EBD Programme: Economy, Policy and Sustainability

The Flagship EBD Programme: Economy, Policy and Sustainability focuses on the societal preconditions for the economic and sustainable introduction of biorenewable chemicals, materials, fuel and energy production. A major effort of the Flagship is to provide insight into the likely macro-economic and sustainability impact and policy conditions for the large-scale use of biomass in Dutch industry. The programme involves many partners of BE-Basic, including NGOs and industry, contributing to stakeholder meetings and studies. The EBD Programme is supported by the government-backed foundation TKI-BBE (Top Consortium for Knowledge and Innovation, Biobased Economy). The Dutch government's top sector policy focuses on organising the applied R&D scene in the Netherlands towards demand (industry & society) driven consortia.

Important steps in 2014 were the delivery of a study comparing biomass needs and availability in 2030, carried out for the government advisory Corbey Committee, and concluding the Societal and Innovation Roadmap for analysing non technological barriers to implementation of biobased innovations. Horizontal projects in collaboration with other Flagships have been launched which look at the integration of socio-economic and sustainability aspects in innovation designs for biobased production in different contexts. Such horizontal projects also relate to international collaboration with ASEAN and Brazil and in the BIG-C (Netherlands, Flanders and Nord-Rhein Westfahlen) consortium. This demonstrates how BE-Basic is contributing to the overall and integrated assessment of biobased innovation, paving the way for a strong science-based transition to a biobased economy, and helping industry to select and develop the optimal business cases.*

) See the interview with Patricia Osseweijer on page 22

Flagship 12
Isobutanol Platform Rotterdam (IBPR)

The Flagship Isobutanol Platform Rotterdam (IBPR) focuses on cascading the conversion of lignocellulosic feedstock into products such as isobutanol and the further valorization of derivatives. At the moment isobutanol is extracted from petroleum but this green energy project is looking for alternatives with economic potential. The research involves using the Organosolv extraction/bio-refining process to separate lignin and other useful materials from biomass. The lignin fraction will be converted into high quality chemicals. The (hemi)cellulosic sugars will be fermented into isobutanol which can be further converted to aromatics such as solvents, jet fuel, diesel, and GTBE as diesel additive.

Wood pellets a likely alternative

A desk research study was completed last year and the lab phase has now started. The research process involves attempting to extract isobutanol from rapeseed waste, sugar beet, fruit juice concentrate and beet pulp. None of these currently offer an economically worthwhile alternative. Cellulose-based waste materials, such as wood pellets, do appear to offer potential and are currently being researched in the lab. These raw materials are being prepared and fermented to develop the lignocellulose which isobutanol can be extracted from.

Commercial production in 2020

The lignin fraction of biomass is not suitable for the production of isobutanol. This is currently burned but research scientists are also looking at whether it is possible to give the lignin added value so that it can be used in, for example, coatings or bunker oil. Flagship manager George Brouwer says the aim is to complete the lab phase in 2015. "Then we can start the first production at pilot level in January 2016. That could ultimately lead to commercial production from 2020."

educational

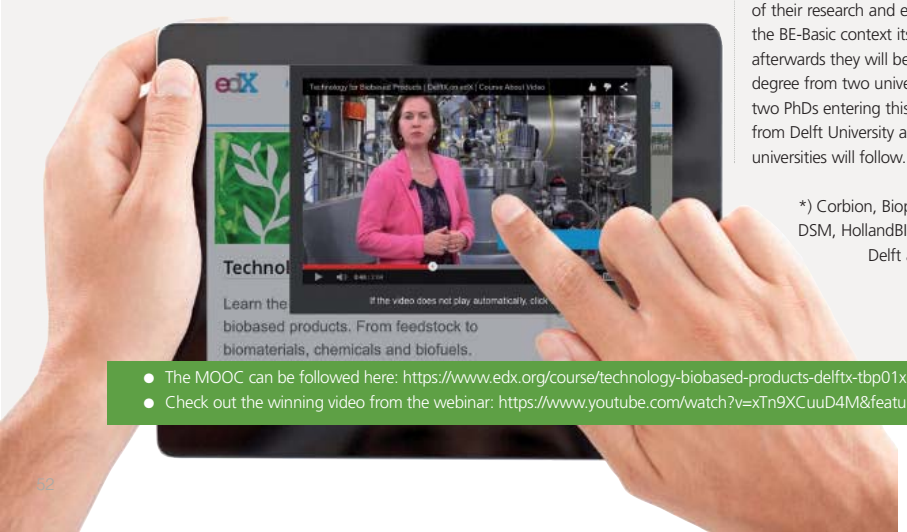
8,000 registered for the MOOC

Educational programme has a successful start

"Education about technology for biobased products is essential to build-up an adequate human resource capacity, which is crucial for the development of a successful biobased economy. It is crucial to involve people," says Isabel Arends, who is responsible for the development and implementation of novel educational and training modules within the BE-Basic programme. "In 2014, 8,000 people all over the world registered for our MOOC about the basics of process design for biobased products. This is a great success for our free online programme, which was set up and launched by Delft University in collaboration with Brazilian partners and industry. The MOOC platform also allowed us to challenge the international public to play an active part. In cooperation with six partners* we organised a webinar during the European Biotech week to promote the launch. There was a debate with stakeholders and we asked students to make videos to capture their ideas about biobased applications. That generated some good discussions and exposure for our biobased education programme."

In 2013, an inventory of the educational needs throughout the entire educational development chain was drawn up, from primary to post-graduate level. This resulted in the launch of a new education programme, including the MOOC, and was an important step forward. "One of the outcomes was the need to set up a life-long learning programme for SME-partners in the biobased industry. Groningen University is developing a sub-programme to cover this for the coming years," says Arends. The focus has widened considerably since B-Basic began its educational programme 10 years ago. "Part of our outreach is to introduce children to the idea of a biobased economy at a young age and get them interested in it. We have mobile DNA laboratories in which secondary school pupils can take lessons about, say, bio-ethanol. We also run the Imagine competition involving secondary school students in their final year project, in which they devise a biobased product for a developing country."BE-Basic organises courses and lectures all over the world, in conjunction with Delft University, Groningen University, Wageningen University, NIOO-KNAW and with industry. A number of successful MSc/PhD courses have already been set up in collaboration with local staff at UNICAMP, the leading university of technology in Brazil. These courses are also attended by people from industry, so professionals benefit as well. The course developed by professor Henk Noorman in China on bioreactor design is another example. "An additional positive development is the double degree programme we have managed to set up for PhD students," says Arends. "In this way Brazilian students can conduct part of their research and education within the BE-Basic context itself, and afterwards they will be able to obtain a degree from two universities. The first two PhDs entering this programme are from Delft University and hopefully other universities will follow."

*) Corbion, Bioprocess Pilot Facility, DSM, HollandBIO, Biotech Campus Delft and Delft University of Technology



- The MOOC can be followed here: https://www.edx.org/course/technology-biobased-products-delftx-tbp01x
- Check out the winning video from the webinar: https://www.youtube.com/watch?v=xTn9XCuuD4M&feature=youtu.be

who is who

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IPRC panel composition

The IPRC members involved in the evaluation process of the BE-Basic programme are:

- *Prof. dr. Urs von Stockar, Ecole Polytechnique Fédérale de Lausanne, Switzerland*
- *Prof. dr. Matthias H.C. Reuss, University of Stuttgart, Germany*
- *Prof. dr. Sven Panke, Department of Biosystems Science and Engineering, ETH Zurich, Switzerland*
- *Prof. dr. Martin E. Feder, University of Chicago, USA*
- *Prof. dr. Mark J. Bailey, Centre for Ecology & Hydrology, NERC, Oxford, UK*
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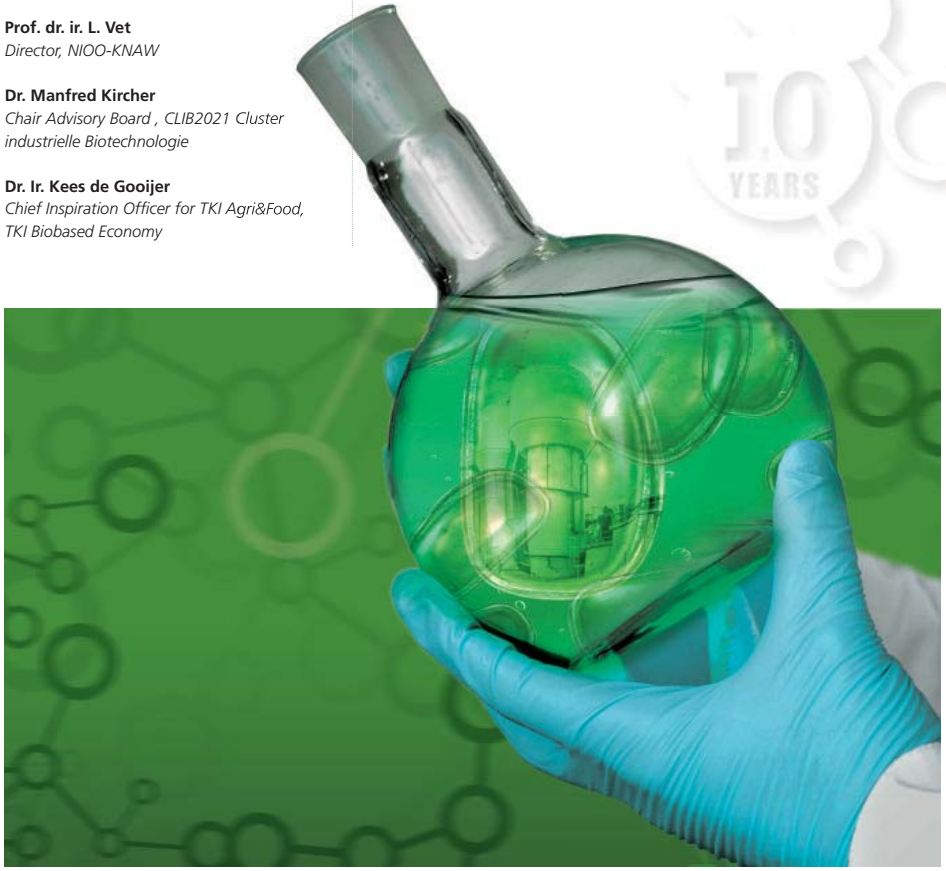

BE-Basic Foundation Annual Report 2014

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