BE-Basic Annual report 2012

BE-Basic

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We thank all scientists and parties involved for their cooperation

March 2013

Foreword

Dear reader,

We are proud to present to you the popular version of the second Annual Report of the BE-Basic Consortium. Our partners have given an overview of the research and other projects carried out within BE-Basic. Here we present only some of the highlights of the full research programme of the BE-Basic consortium.
BE-Basic, Biobased Ecologically Balanced Sustainable Industrial Chemistry, is a public-private partnership that develops industrial biobased solutions for a sustainable society.
BE-Basic has an initial R&D budget of more than 120 million euros. Half of this is funded by the Ministry of Economic Affairs, Agriculture and Innovation (a FES grant). BE-Basic was founded early 2010 and builds on the recognised breakthroughs of the B-Basic and the Ecogenomics consortia. The official ending date of the BE-Basic programme was 2015 but we have received a positive response upon our request to prolong the date until mid-2017.

The year 2012 has been an exciting year for BE-Basic. As of October 2012, BE-Basic has become BE-Basic Foundation. This new legal structure offers more options of cooperation with new (international) partners but also gives us more and additional (financial) means to focus upon the deliverables of the BE-Basic programme, especially for innovation and SME's. The structure of BE-Basic Foundation is explained in the last pages of this report.

Within BE-Basic Foundation we can also focus more on the societal extension of the programme. The 'softer side' of the Biobased Economy is providing hard constraints for implementation, a reality that is understood more and more by industry, academics and politics worldwide.

We are very proud that mid 2012 the Bioprocess Pilot Facility (BPF) has opened its doors as a national open access facility. The BPF was initiated by BE-Basic and partners. In this facility, process development research can be facilitated over the entire field of biomass pre-processing, biomass pre-treatment, fermentation and downstream processing. The BPF is open to both BE-Basic partners and other companies, universities and institutes. Another highlight was the opening of the joint Brazilian Office of BE-Basic and TU Delft in Campinas by His Royal Highness Prince of Orange to better support the wide range of existing and new initiatives with our Brazilian partners.

We hope you will find this Annual Report interesting and inspiring. BE-Basic keeps on building the Biobased Economy in The Netherlands and worldwide through our collective efforts, and we are proud to present our progress.

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

FS1 Carbon based compounds

tackling every step in the production chain

The compound called FDCA is a very promising biobased building block that can be used for a wide range of application areas such as biopolymers for packaging, plasticizers and resins. That is why a large BE-Basic consortium of academic and industrial partners is currently working on an integrated production process for producing FDCA from renewable resources.

In the list published by the US Department of Energy of biobased building blocks that can replace fossil fuel-based chemical equivalents, the compound FDCA (2,5-furandicarboxylic acid) has been placed in the Top 12. "If you look at the ranking in terms of potential, in the past decade FDCA has risen to the Top 3", says Marc Lankveld, CEO of the contract research organization BIRD Engineering and project leader for the FDCA-project within BE-Basic. "What is even more interesting is the reason why it gets so much attention: FDCA is the only compound with a ring structure. All the others are rod-shaped, aliphatic building blocks. In terms of chemical properties FDCA has many, many more benefits than all those eleven lookalikes together. Cyclic compounds are known for their ability to make polymers more rigid, for example."

The BE-Basic project is a follow-up to a lead from a previous B-Basic project on the detoxification of hydrolysates (biomass) for second generation bio-ethanol. "It was during this project that researchers of TNO and TU Delft discovered that the pathway for the breakdown of furanic inhibitors in the bacteria Cupriavidus basilensis went via the compound FDCA. The responsible enzyme was identified and subsequently expressed in Pseudomonas putida", adds his colleague Tom Elink Schuurman.

Pure bio

Since the Top12 list was published everyone has been trying to produce FDCA chemically. Only a tiny percentage of the research worldwide focuses on bioconversions. Lankveld: "For chemical synthesis you need a very pure sugar stream to produce FDCA. Since microbes are capable of dealing with impure biomass flows, the biological route is much more attractive economically. We can reach overall yields of 80%. That is the beauty of biotech", says Lankveld, inspired. Another advantage is that there are no other interfering by-products, which makes the desired FDCA relatively easy to recover. The yield of the chemical route for FDCA production is hardly 30%, which means an energy-expensive distillation processes needs to be used for recovery.

Chain processes

BIRD Engineering has organized the project as a chain of sub-processes. Wageningen University Research is starting with the raw lignocellulosic biomass such as miscanthus, in order to synthesize the basic compound HMF (hydroxy methylfurferal) required for the FDCA-production. BIRD Engineering is optimizing the next bioconversion step of HMF into FDCA, and also bringing in their improved Pseudomonas strain. "The role of the University of Groningen is more fundamental. They characterize and optimize the enzyme system that is responsible for the actual conversion reactions", explains Elink Schuurman. The research group of TU Delft provides the downstream processes needed to recover and purify FDCA from the fermentation broth. DSM, finally, is focusing on Life Cycle Assessment (LCA) and process integration matters. Lankveld: "All the parties carry out their piece of the chain, and if you put all the pieces together you have a working process. To me this is an open innovation model avant la lettre."

Soon the time will be right to integrate the separated processes and test them on a pilot-scale. Proposals for pilot tests have already been submitted. "We are looking for opportunities to do this within BE-Basic, making use of the Bioprocess Pilot Facility in Delft. That is the most logical step to take", thinks Lankveld.

no more trial and error, no more black boxes

By combining the power of high-throughput experimentation with a model-based design approach, Marcel Ottens and his team have a unique tool in hand for developing purification processes for the biopharmaceutical industry that are fast, accurate and robust. "What we can offer is not yet available worldwide."

The development of purification processes in the biopharmaceutical industry is often the result of trial-and-error. "Processes that run at a laboratory scale are linearly scaled up to production scale. But what works on a small scale for obtaining a few milligrams of product is not necessarily the most efficient method on a production scale", says Dr Marcel Ottens, Assistant Professor of Micro BioSystems Technology & Process Chromatography at TU Delft. "Moreover, high-throughput screening is used to find the optimal conditions for the purification process. However, this black-box approach gives no insight into the underlying mechanisms."
Ottens advocates a structured design approach based on rational modelling and knowledge of the molecular properties of proteins (or biologics) in a separation process. "We use high-throughput in such a way that we gain a mechanistic understanding of the separation dynamics. Together with our in silico models we can design a more efficient purification process on a large scale."

Model-based approach

A rational design starts with the analysis of the basic raw material that contains the biopharmaceutical: the filtered fermentation broth. "We fractionate the mixture as far as possible, and characterise all the different proteins or protein fractions so we know exactly how well they adsorb to resins in separation columns and how well they dissolve in the liquid phase."
With the information about the molecular properties, together with computer models that describe the behaviour of proteins in chromatographic separation columns, Ottens can make a reliable prediction of what the best sequence of separation techniques will be, plus optimal conditions. Tests in practice with monoclonal antibodies from crude cell culture supernatant to validate the predictions have demonstrated that the approach works successfully. Ottens: "We have great confidence in this approach. We are going to apply it to other case studies, for instance for our two industrial project partners DSM Biologics and Synthon."

Miniaturization

During the next few years Ottens, together with four PhD students (Hanke, Hoon, Iannacone and Kittelman), is going to improve the analysis stage by using high-throughput robotics and microfluidic systems. This means he will be continuing his earlier collaboration with B-Basic (DSM, Dr van de Sandt; Synthon, Dr Eppink; TU Delft, Professor Verhaert and Professor van der Wielen), along with the MESA+ Institute for Nanotechnology of the University of Twente (Professor Gardeniers) for their expertise on microchips, and with the Karlsruhe Institute of Technology (Professor Hubbuch) for their expertise on robotics. The big advantage of these techniques is that the whole fractionation step in principle can be done on the scale of a microchip, especially as very little protein material is available at the beginning of the development of biopharmaceuticals. "By miniaturization and automation, we are able to determine all the relevant properties of the starting material, and can directly design the process on a large scale. That is the beauty of mechanistic models - the scale dependence is incorporated", explains Ottens.
This year, Dr Ahamed started as a business developer who will finalise the initial business plan, will look for further investment opportunities, and approach clients. "We have the robotic infrastructure established in Delft, and can offer this to other industrial parties together with consultancy services for process development. What we offer is very specific and not yet available anywhere else in the world. In about two years we can decide whether it would be viable to start a spin-off company."

matching organic residues with agricultural soil needs

Maize is an example of a biomass crop. The residues of the entire plant can be used for e.g. biogas production. This might lead to the decrease of the organic matter. Whether the remains of the plants are re-usable for agricultural purposes is being examined within Flagship 3.

Large amounts of residual organic matter resulting from biomass production are not optimally utilised, even though agriculture requires such organic matter in order to stay sustainable and maintain a good soil quality. To match this supply and demand of organic matter a dedicated decision tool is now being developed by the BE-Basic consortium.

"To be able to grow biomass for food, energy and non-food products year in, year out it is of the utmost importance that the agricultural practice is sustainable", says Aad Termorshuizen, Senior Agronomic Soil Scientist at BLGG Research. "Sustainable agriculture means that yields are optimal, provided that soil quality is maintained and that environmental effects are minimal. This implies that there is no decline in organic matter content, no accumulation of pathogens or toxic substances and no more than acceptable losses of nutrients or greenhouse gases. However, the high removal rates of biomass typical in the biobased economy will ultimately result in decreased levels of organic matter in the soil. And that is very risky."

Organic matter matters

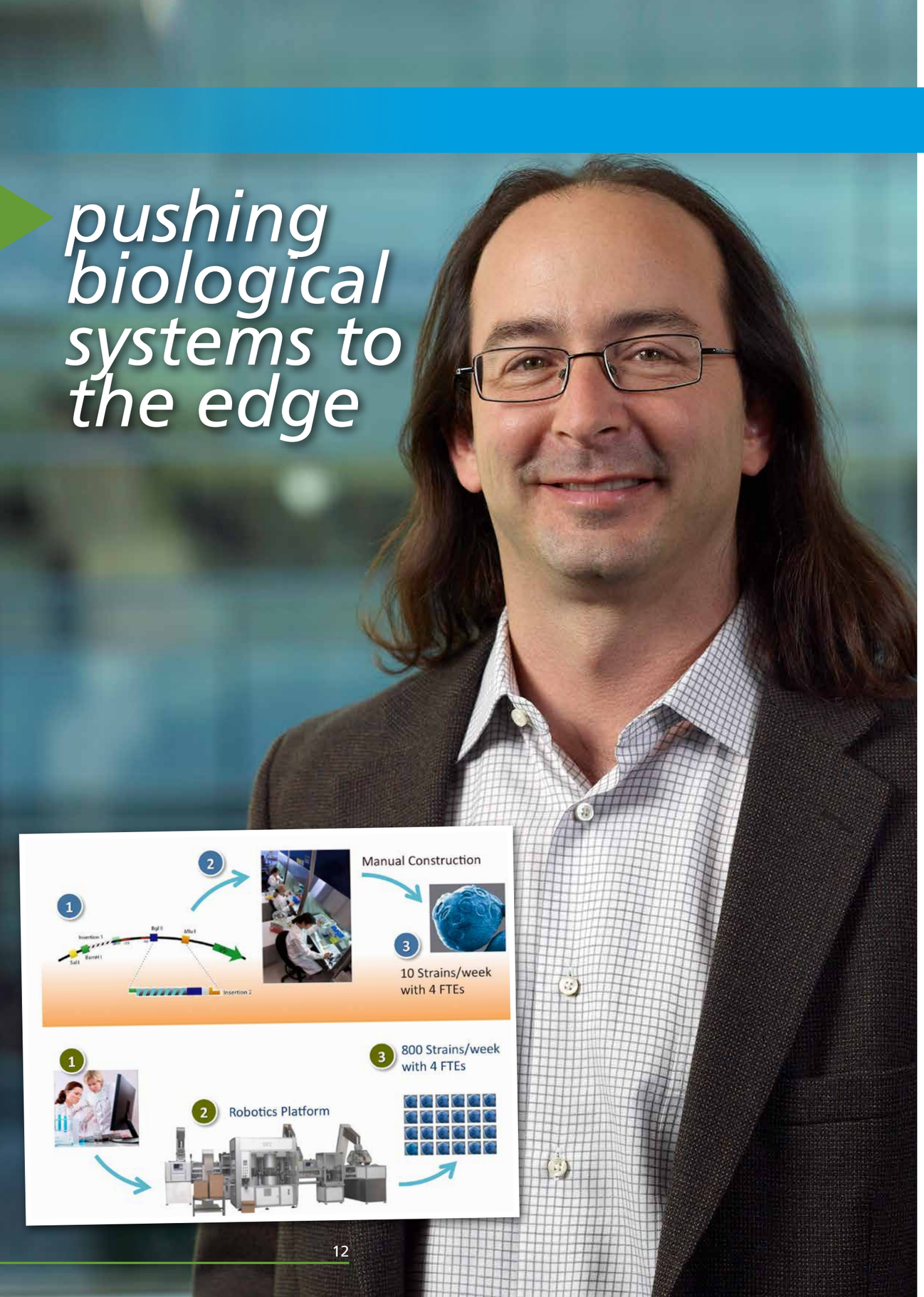
Organic matter fulfils three essential functions in terms of supporting soil quality. First, it contains nutrients such as nitrogen, required for the healthy growth of crops. These nutrients become available when soil organisms decompose the organic matter. Secondly, organic matter aids the natural suppression of soilborne plant pathogens by stimulating common soil fungi and bacteria. And thirdly, organic matter is capable of absorbing large amounts of water which it can release to the plant roots in drier periods. Its water absorption capacity also prevents the loss of nutrients through leaching or runoff after heavy rainfall. "The trick is to find the right type of organic matter for the right type of soil", says Termorshuizen. "A good source might be the many different kinds of residues, ranging from harvest waste to high-tech residues that are produced in the course of bioplastic production and which are now often incinerated."

Matching

"What we need is a methodology to assess whether a particular organic residue is suitable for use in agriculture, and to which soil/crop location it can be best applied. This depends on the soil requirements and the kind of crop that is grown", Termorshuizen continues. He is leading the consortium that recently started to develop such a toolkit. Therefore BLGG Research collaborates with the Netherlands Institute of Ecology (NIOO), the Laboratory of Nematology of Wageningen University and the Systems Bioinformatics department at the VU University Amsterdam. The first thing on the agenda is to draw up an inventory of all the residues resulting from production processes in the biobased economy, including their composition and volume. All BE-Basic partners will be involved. The industrial project partners Bioclear, BioDetection Systems and ClearDetections will develop techniques to identify the biotic and abiotic contaminants in residues, such as the presence of pathogens or toxic substances. Termorshuizen: "That is the most important thing that needs to be checked first. Only after that can the agricultural application can be considered."

The end result of the coming years of hard work will be a tool that is able to match the available organic residue with the needs of agricultural soil in terms of nutrients, soil structure improvement and disease suppression. Termorshuizen: "What we are about to do is really new. The tool will not be restricted to potatoes in the Dutch clay, it should be applicable globally."

pushing biological systems to the edge



Synthetic biology makes it possible to design and program microbes and turn them into efficient, living cell factories that are capable of producing chemicals from renewable feedstocks. The challenge is to combine high-tech genetic engineering with large scale fermentations. "We should start thinking about what is needed to build this sector."

Flagship 6 of BE-Basic uses synthetic biology as a tool for improving the performance of industrial micro-organisms by designing and incorporating new functionalities. "Amyris, one of our industrial partners, is one of the companies that is leading the way in both the development and application of synthetic biology for industrial strain engineering", says Ton van Maris, Associate Professor of Industrial Microbiology at the Delft University of Technology.

It was their shared interest in the industrial yeast Saccharomyces Cerevisiae that brought Amyris and BE-Basic together to work on the efficient utilization of carbon sources by the yeast. "Delft, BE-Basic and its microbiology is pretty unique in the world", says Jack Newman, Chief Science Officer and co-founder of Amyris. "There are very few research environments that appreciate both the high-tech aspects of synthetic biology and the industrial emphasis of large scale fermentations.'

Limitless possibilities

Amyris's first major achievement in synthetic biology was the development of microbes that produce artemisinic acid, a precursor of the anti-malarial drug artemisinin. The next step was to use their technology platform they had developed to create microbes that efficiently produce farnesene, a long-chain, branched, renewable hydrocarbon that forms a basic building block for industry. Today Farnesene is produced from plant sugars on an industrial scale, in the millions of liters. "Once you realize that you can control the chemistry in living organisms by reprogramming their DNA, the possibilities are in principle limitless. But you have to figure out what the technology is ready to deliver today, while pushing the field to make strides over the next decade."

One way of doing that is using high-throughput processes to create and test microbes. "The act of programming the DNA of microbes is really an information technology: you have to understand the existing programs within an organism, and be able to write new programs", explains Newman. "We developed a way to program microbes on our laptops. The actual genetic engineering is done by a dedicated professional group at Amyris, who have automated that process. That way we have more time to do the science and see if our programming has the desired effect on the metabolic routes of yeast."

Ecosystem of companies

Another important aspect is to build on a synthetic biology sector in the coming years. Therefore it is not only essential to explain synthetic biology to the public, it is also essential to explain to the science community what is needed to build up this industry: what will the ecosystem of technology companies look like? As a board member of the BioBrick Foundation Newman invests a lot of time in talking about these issues. "What we need is specializations in each unit operation. For example, DNA-sequencing is a very mature technology sector, but many more are necessary to allow the sector to grow. DNA-synthesis is one field that is currently emerging: half a dozen companies are in operation and new companies are being launched." As the sector is built up further Newman also sees a need for companies dedicated to high-throughput screening. On the industrial side, however, there is a tremendous need for low-cost, aseptic fermentation. "So when you put your engineered bug into that huge fermentor, you need to be able to exclude all other microbes. This is an area that is ripe for innovation and a highly desirable discipline in the biobased world", Newman concludes.

AMYRIS

FS7 High -throughput experimentation and metagenomic mining

In the red sludge of wastewater treatment systems for nitrogen removal, Mike Jetten and his team are searching for new microbes, genes and enzymes for biobased applications. Meanwhile, the performance of the treatment plant is being studied and optimised.

discovering new microbes in wastewater treatment systems

There is still a lot of microbial life to be discovered, even in more cultivated environments such as microbial wastewater treatment systems. "We have learned a lot about the nitrogen cycle and nitrogen removal from wastewater in the past ten years, but we are still discovering new bacteria with new traits that are involved in ammonium and nitrite conversion. We are therefore going to make an effort to find these micro-organisms", says Mike Jetten, professor of Ecological Microbiology at Radboud University Nijmegen, who has recently awarded the NWO Spinoza Prize for his breakthrough science on the anammox process and the role of bacteria in the global cycles of nitrogen, sulphur and carbon.

"It will be primarily a voyage of discovery of new organisms, genomes and genes. Based on our experience, I am confident that we will find many new useful enzymes or proteins that can be applied in the biobased economy. This will be done in collaboration and consultation with groups working in other BE-Basic flagships. For example, if they are looking for new enzymes of nitrogen metabolism or redox enzymes, we may be able provide the genetic information."

Genome assemblies

The final challenge of the project is to map the metagenome of the entire nitrogen-removing community of a wastewater system. "That will be the icing on the cake", Jetten says. "And we have a specific system in mind - the wastewater treatment plant in Olburgen, in which nitrifiers and anammox bacteria work together to remove nitrogen from wastewater."

That will be a major task, as it was not easy to put the anammox genome together in the first place. "We have mastered that now, but a whole wastewater treatment system is still a few steps up. We did some initial scans on a few sludge samples with our new high-throughput sequencer", Jetten says proudly, given that the BE-Basic project has been a catalyst for his group to purchase the sequencer. "It is likely that we have already found two new anammox species. The genomes were not related to those of the species in our lab. That means we have a lot more sequencing and analysis to do."

The research by his group will give an insight into the variation in anammox species and ammonium oxidizers. The genomic mapping of the nitrite oxidizers will be the task of TU Delft.

Optimizing performance

In addition, the response of the microbial community to incidents in the treatment plant will be studied. "We gain a lot of extra knowledge about the performance of the wastewater treatment by also looking at the mRNA levels, which are a measure of how active genes are. That way we can see what happens when microbes get stressed by too much oxygen or when the nitrite levels rise above their threshold value", explains Jetten. Since it is impossible to predict when things go wrong at Olburgen, Daan Speth, a PhD student in Jetten's group, has set up a lab-scale bioreactor in order to mimic the incidents. Jetten: "This gives us a greater understanding of the response mechanisms, which can lead to a more sustainable one-step anammox reactor."

With more than three years to go, the first harvest of four publications by Speth and Jetten is remarkable. This has been made possible by an investment in a high-throughput sequencer, in bioinformatic tools and by genome databases. "And above all, anammox is a rewarding object of study. There are still so many secrets to discover", says Jetten.

effect-based monitoring of environmental safety

Chemical analysis alone is not sufficient to determine the effect of industrial or agricultural activities on the aquatic environment. Even if it was possible to determine all components it would not give a balanced indication of their biological effect. That is why BE-Basic is developing effect-based monitoring tools that screen for the biological effects of complex mixtures of chemicals.

The current guidelines for water quality and chemical safety are based on assessing individual components and their maximum acceptable concentration. "The problem with an environmental, feed or food sample is that you don't know its exact composition, let alone that toxicological information on all the substances present in these mixtures is available", explains Sander van der Linden of BioDetection Systems located in Amsterdam. That was the reason to start research on biological-effect based methods. "With a bioassay it is not necessary to determine the identity of substances in your sample, you only have to see if these substances can cause an undesirable effect when combined", he says. By determining the combined activity of complex mixtures in relation to natural background activities, you can get a realistic indication of the safety of the afore mentioned processes.

Finding the pathways

BioDetection Systems already uses effect-based bioassays for environmental monitoring. In the coming years Van der Linden aims to explore which additional bioassays are applicable, thereby aiming at a comprehensive screening system for monitoring water quality. Meanwhile his colleague within BE-Basic Flagship 8, Barbara van Vugt-Lussenburg, is mapping all the relevant pathways that are known to be linked to adverse effects and the safety of pure components. Van der Linden will be using this toolbox in his evaluations.

Another important aspect of his research consists in developing efficient methods for the pre-processing of the samples. "Because we use human cells in culture, currently we cannot use our bioassay and environmental samples such as wastewater directly. Non-specific effects may mask the effect on important toxicity pathways that are more relevant to human toxicology. It is therefore common practice to first make an extract. These methods are further developed for different types of assays and samples. What we are ultimately aiming at is using very simple methods that can be used by non-specialized personnel, preferably in a kit-like format", explains Van der Linden. Finally, he wants to determine how many assays are minimally required to conduct a proper safety assessment of a waste stream.

Monitoring waste streams

Bioassays can also be used directly for the rapid and efficient optimization of a waste management or purification process, ensuring that the environmental impact will be as low as possible. "Bioassays not only test if a single toxic substance in a waste stream has disappeared, but also screen the activity of its degradation products in against the background of the levels of the environmental effect. That is the added value of bioassays compared to chemistry", states Van der Linden. "Besides, our technology gives industries the opportunity to distinguish themselves. How nice is it to be able to say: not only does my biobased production process have a smaller carbon footprint, it is also environmentally safe and much less toxic for the environment than the traditional process."
Until now, however, one thing that stands in the way of acceptance of the technology is the limited regulatory acceptance of its use. According to Van der Linden the acceptance of a bioassay is a very long process. "The problem does not lie in developing new methods, the problem is: how do we adapt the old rules that are based on technologies and insights of the past? That is a long-term project, and that is why we are actively engaged in this process, which will be further intensified within BE-Basic."

overcoming barriers by staying connected

The implementation of new environmental and industrial biotechnologies that help in the transition towards a biobased economy, often encounters obstacles, resulting from restrictive patents, burdensome regulations or opposing pressure groups. BE-Basic is investigating how a dialogue between science and society can contribute to a higher societal valuation of these innovative technologies.

"We learned a lot from what went wrong with the introduction of genetic modification in Europe in the last century. Scientists, the industry and policymakers forgot to include citizens in the debate about the application of this technology", says Tjerk Jan Schuitmaker, a researcher at the Athena Institute of the VU University Amsterdam. "A well timed dialogue between science and society can solve that problem and ensure that more aspects and more actors are included in the innovation process. To enhance the implementation we are going to develop and refine the dialogue process and see how it runs."

Schuitmakers' research builds on the experience of the Dutch Ecogenomics Consortium, which piloted the dialogue process. "Although they improved the process and created interconnections within their network of scientific and industrial partners, in the end they ran into all sorts of policy and legislation barriers. That hindered the introduction of novel, more accurate biological detection tools, for example", Schuitmaker explains.

Nailing down barriers

According to Schuitmaker, improving the societal valorization of new technologies involves two aspects. First of all, the technology that is developed has to be able to solve the problems that society is faced with. In the case of the biobased economy, it should focus on tackling climate change, the depletion of fossil fuels and pollution problems. Secondly, the technology has to be received well by society. The successful introduction of promising technology is, however, often hampered by obstacles such as patent limitations, social resistance and discrepancies with existing legislation and policies.

"By introducing the dialogue process in an early stage of the development we try to nail down the systemic barriers for implementation", he explains. "It would be a pity if good scientific ideas that can help to solve sustainability problems are not applied for reasons that have nothing to do with the product or idea itself." To improve the implementation process Schuitmaker is going to introduce methods from the field of transition thinking to the dialogue process. "This can help to find out why good ideas get off track and how systemic barriers and institutional structures work against them."

Mapping and focus groups

Last year Schuitmaker, together with colleagues from the Athena Institute, mapped out the barriers that researchers and industrial partners within a selected program of BE-Basic encounter when they start to develop their ideas. "We followed the possible development routes and also visited approval authorities and investigated the OECD-guidelines to identify the existing regimes and barriers", he says.

The next step, now he has completed the inventory, is to organize focus groups with relevant stakeholders to discuss the findings within the group and evaluate strengths, risks and opportunities. "Then we will broaden the dialogues and invite other relevant societal actors such as NGOs and policymakers, as we don't want to impose anything on society. Our goal is to make connections and initiate collaborations between the actors."

How these connections can be sustained after the dialogue process has finished, is still a question. Schuitmaker: "That is something we will find out in the coming years. Creating 'communities of practice' so that the collaborations endure might be an option. Solutions do not work if, after the dialogue process, people return to their business as usual. It helps if they integrate the results in the way they work and think."

from idea to product to start-up

BE-BIC: BE-Basic's Business and Innovation Centre

The Business and Innovation Centre is setting up a course series to generate innovative ideas and stimulate entrepreneurship. PhD students, postdocs and senior researchers will be challenged to think about inventions, products, clients and business plans. ClearDetections – which recently joined the BE-Basic consortium – will share its experiences as a start-up company.

Business ideas sometimes simply present themselves: the 'only' thing one has to do is recognise and grab the opportunity. And that is precisely what Dr Renske Landeweert did. She is now managing director of the start-up company ClearDetections, a joint initiative of Wageningen University and the Dutch agricultural service laboratory BLGG AgroXpertus. ClearDetections offers DNA-based test kits for the detection of plant pathogenic nematodes.

Ten years ago, Landeweert joined BLGG AgroXpertus to set up a molecular laboratory for plant health and to develop new DNA-based tests together with nematologist Dr Hans Helder from Wageningen University. There, she implemented a new test that had been developed at the university by highly-trained people for just a few samples, into a routine laboratory staffed with less well trained employees handling 40,000 soil samples a year. She then started getting regular requests from foreign laboratories to try the DNA-based tests. Landeweert: 'I always sent the tests free of charge, but meanwhile we had to pay the Technology Foundation STW royalties because they'd financed the research that resulted in the DNA-based tests in the first place. So we realized it would make sense to charge for these services. And our business case was born.'

Prizes and momentum

Winning the Netherlands Genomics Initiative's Venture Challenge in 2010 was a crucial event in the final step towards creating a start-up. Landeweert: "During that event, our ideas were thoroughly challenged. But we came out as the winner and with a business plan, a name for our company, 25,000 euros in prize money and, most important, the strong notion that we had to start a company no matter what. The only question was, how and when."

A big hurdle was to obtain the intellectual property rights from the university. Landeweert: "We got caught up in a lengthy discussion about shareholders, patents, licences and conflicts of interest. But after the Food Valley Award in 2011, we could no longer wait around, or we'd lose the momentum. We founded ClearDetections with BLGG as the only shareholder on the last day of December 2011." The following year, they won third prize in the Rabobank's Herman Wijffels Innovation Award.

Another tough job is finding new customers. Since Landeweert had sent test material around earlier, the first clients were present on day one. "Most important is that our tests ended up in the protocols approved by the European Plant Protection Organization and in the French National protocol for plant diseases. So every French lab must use our tests for these diseases."

Landeweert is continuously looking for project opportunities to further develop ClearDetections' knowledge and product portfolio. "We're very pleased that we, as a small high-tech SME, could join a BE-Basic project, as there are still some fundamental nuts to crack. In addition, we recently brought the biobased economy right into our lab, as we replaced our Styrofoam boxes with boxes made of BioFoam!"

Breeding ground for new businesses

Not all business ideas are clear from the start. We spoke to Prof. Bram Brouwer, who is responsible for the Business and Innovation Centre (BE-BIC): "BE-BIC's aim is to identify innovative ideas and inventions, and to stimulate scientists to transform those ideas into real products and businesses. So we need ideas and we need entrepreneurs."

BE-BIC has therefore developed three modules for PhD students, postdocs and senior scientists to give them a basic training in entrepreneurship and what that means within the biobased economy.

The first module – Defining the Business – will be a 1-day workshop that provides an introduction to business development. Prof. Brouwer: "It basically comes down to learning which questions you need to answer when you start thinking about business ideas. This training can also increase the job opportunities of trainees when they join start-ups or bigger companies."

The second module – Action Lab – will be a 2- or 3-day workshop that helps the scientists to create a draft business plan. The emphasis will be on how to create value from an innovative product. The third module will be similar to the Venture Challenge competition. The scientists will draw up their final business plans, and the winner will get a grant to carry out a feasibility study. Prof. Brouwer: 'The aim is to create a larger pool of innovative ideas and potential entrepreneurs, from which pearls like ClearDetections may arise.'

International cooperation

The strong International focus of BE-Basic is reflected by the membership of the consortium of leading institutions in the EU like Imperial College from the UK. Moreover BE-Basic puts its international focus into practice through strategic partnerships in a selected number of countries: Brazil, Germany, Malaysia, the U.S.A. and Vietnam.

We have expanded our activities with our American partner Amyris. Amyris is applying an industrial synthetic biology platform to provide high-performing alternatives to petroleum-sourced fuels and chemicals. More information about the work of Amyris can be found on page 14 and 15.
Besides the cooperation with Amyris, BE-Basic has selected the Energy Biosciences Institute (EBI) at Berkeley and the Oak Ridge National Laboratory (ORNL) as partners. They were selected for their excellence in research and the opportunities they offer other BE-Basic partners. EBI and ORNL are leaders in investing in research programmes for Bio-energy and biorenewables.

USA

BE-Basic and Germany's Cluster for Industrial Biotechnology (CLIB2021) signed a memorandum of understanding to cooperate in developing the bio-economy. The cooperation will focus on the bilateral exchange of educational programmes, the alignment of societal programmes around feedstock sustainability, a joint approach to third-party international partners, and the facilitation of joint technology development by organizing targeted joint workshops.
Other fruitful German cooperations, such as those with Technische Universität Dortmund and Karlruhe Institute of Technology, illustrate our joint strengths within several BE-Basic projects.

Germany

Brazil

The article on the productive partnership with Brazil can be found on pages 24 and 25.

Malaysia

The memorandum of understanding with the Oil Palm Biomass Center (OPBC) was officially signed on 22 March 2012 in the presence of the Malaysian prime minister. OPBC is a Malaysian public–private partnership in which BE-Basic and several BE-Basic partners participate. Under this memorandum, BE-Basic has explored various initiatives.
BE-Basic was strongly engaged in Malaysia's National Biomass Strategy and Macro-economic Impact Study, both of which were executed under the supervision of AIM (Agencia Inovasi Malaysia). Both studies underlined the clear opportunities of a higher added value industry (chemicals, advanced biofuels and bio jet-fuels) based on sustainable biomass, rather than focussed use for power production.
A detailed study on Mill Integrated Conversion of Palm Biomass to Commodity Intermediates (MICCI) was completed as a techno-economic model for large-scale tropical crop residues by TU Delft, University Putra Malaysia and Universiti Teknologi Malaysia (UTM), in close collaboration with various small and large palm players and chemical industries.
The study evaluated the integral scale effects of biomass logistics and downstream conversion to commodity platforms. MICCI's results provide an initial step towards a planned horizontal programme titled 'Sustainable Biobased Products in ASEAN'.

Vietnam

As a follow-up to the letter of intent signed in March 2012 by BE-Basic and Vietnam Academy of Science and Technology (VAST), an International VN-Basic Workshop was held in Hanoi last June. Ten participants from BE-Basic and about 35 from the VAST organization were involved. During this 3-day meeting, the R&D programme and topics for joint collaboration were defined. An overall volume of activities of around 4 million euros (2 million from each party) was agreed upon. It was also agreed that all topics defined would be converted into project proposals for the BE-Basic submission call at the end of September 2012. The Vietnamese part of the proposals will be subject to the Vietnamese project approval systems; they are expected to be approved at the end of 2012/beginning of 2013.
To discuss the progress of project formulation and submission, a delegation of Vietnamese scientists and representatives from the Ministry of Science & Technology, the Ministry of International Affairs and the VAST institutes visited BE-Basic in September.
Two VN-Basic cluster project proposals were submitted and evaluated by international peers and received very good scores. BE-Basic granted them funding in December.

beyond bio-ethanol

Productive partnership with Brazil

Brazil now has 30-odd years of experience of producing bio-ethanol from sugarcane and is moving towards a biobased economy. HRH Prince Willem-Alexander boosted collaboration with our Brazilian partners when he officially opened the joint TU Delft-BE-Basic office in the state of São Paulo.

The Brazilian office of TU Delft and BE-Basic was officially opened on 21 November 2012 during a Biobased Economy Seminar organized as part of the state mission of Crown Prince Willem-Alexander and Princess Maxima. According to the Crown Prince: "The transformation towards a biobased economy is imperative to sustain life and development on this busy planet. But it also offers great opportunities."

BE-Basic and TU Delft are seizing these opportunities. In 2011 TU Delft and BE-Basic jointly decided to invest in the establishment of an office in Brazil to strengthen the relations in the field of Biobased Economy research and education. With a start-up grant from TU Delft an office manager was appointed and negotiations on the location were started alongside establishing agreements with universities and research organisations. BE-Basic invested in the organisation of joint workshop to boost the research program. The choice for location was the campus of the University of Campinas, UNICAMP, in the state of São Paulo. The university has a strong base in science and technology and is one of the most prestigious in Latin America. São Paulo's 40 million inhabitants produce 35 per cent of Brazil's GDP, making the state a major industrial and economic powerhouse. "This is a unique opportunity for BE-Basic and TU Delft. It is the first foreign office on the campus of UNICAMP, where we are well positioned to roll out our plans for joint research and education, also with the other universities in Brazil", says Luuk van der Wielen, Director of BE-Basic and Distinguished Professor Biobased Economy for the TU Delft.

Cooperation with academic and industrial partners in Brazil started in 2004 with the B-Basic consortium (predecessor of BE-Basic), but has intensified over the last few years with the launch of the first joint projects and formalised agreements. Patricia Osseweijer, BE-Basic account holder for Brazil: "In 2010, a memorandum of understanding was signed between FAPESP – the research organization of the state of São Paulo – and BE-Basic. For a period of 5 years, 8 million dollars are being made available for joint projects in the full spectrum of biobased research, from soil improvement to bio-refinery and the socio-economic impacts. We are now reviewing the submitted projects of the second Call."

Flagships sail to Brazil

Several BE-Basic Flagships have already set sail towards Brazil. Examples include: sustainable soil management, where NIOO and USP are looking for bio-indicators for monitoring soil quality; development of macro-economic models (LEI-WUR, ICONE) for the biobased economy; assessing sustainability of biomass supply chains (Copernicus Institute, CTBE) and process technology for biofuels (TUDelft, UNICAMP).

Ernst-Jan Bakker, director of the TU Delft-BE-Basic Brazil Office since September 2012: "The collaboration, which is initiated by workshops on the joint development of projects, is quite successful. So much so, in fact, that we mutually agreed to extend the period of the memorandum of understanding with FAPESP to 2018 with equal additional input in funding. The Dutch investment in research collaboration is highly valued by our Brazilian counterparts. We complement each other's scientific knowledge and work together on valorising our research."
Osseweijer added: "That's why our Brazilian colleagues also have a great interest in BE-Basic as a programme. The concept of public–private partnership in research and innovation is new to them, but they're very eager to learn how it works."

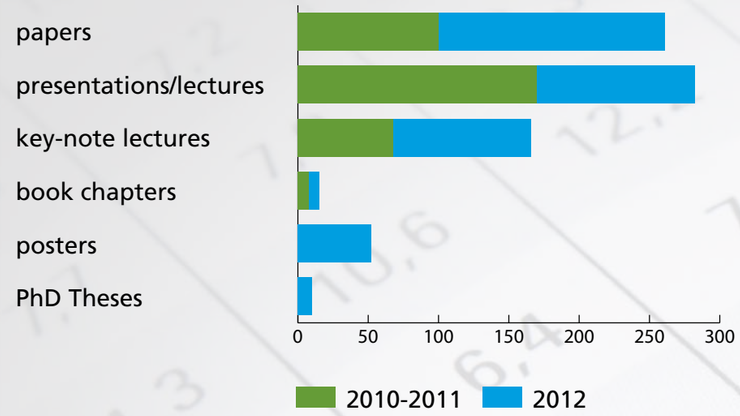
New products and processes

BE-Basic Brazil also cooperates with CTBE. In 2011, an agreement was signed for a 4-year cooperation programme. In 2012, two PDEng (Professional Doctorate in Engineering) students did their process design project at CTBE in close collaboration with BE-Basic industrial partners.

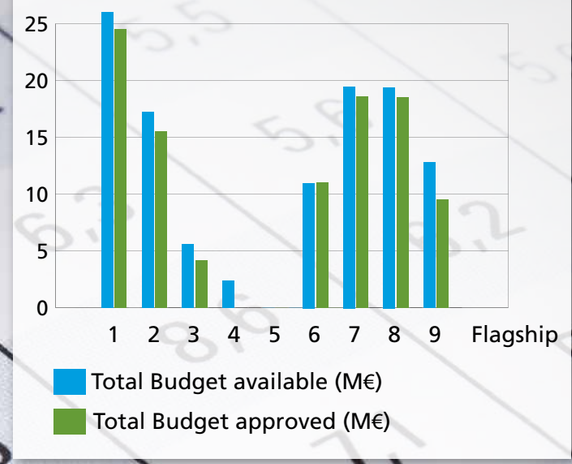
To further develop business opportunities, BE-Basic also initiated a partnership with FIESP, the industry federation of the state of São Paulo. Bakker: 'Industry leaders are very keen on developing the biobased economy by converting scientific results into new products and processes. Hence, our collaboration focuses on the exchange of knowledge and the development of human capital. Education in entrepreneurship is also part of our agenda'

For the coming period, an investment of 3 million euros of joint projects per year is anticipated, which puts Brazil at the top of the list.

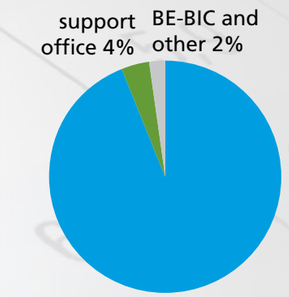
Cumulative Scientific Output



Total available and approved budget per Flagship per end 2012

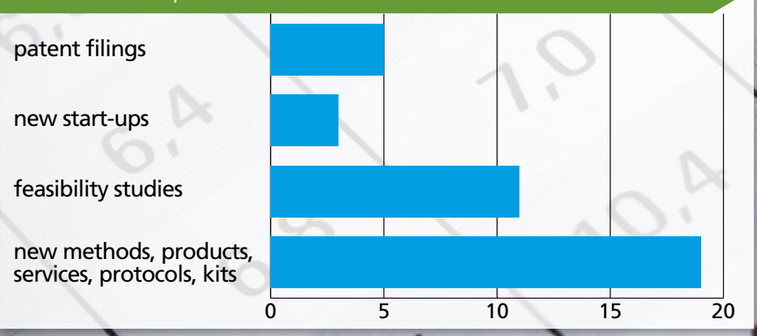


Distribution of BE-Basic funds

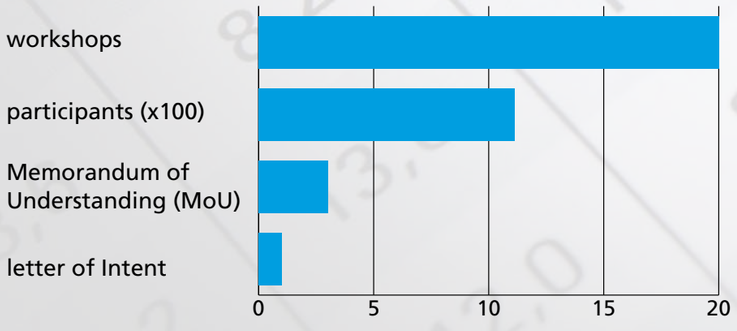


(Total Budget 120 M €)

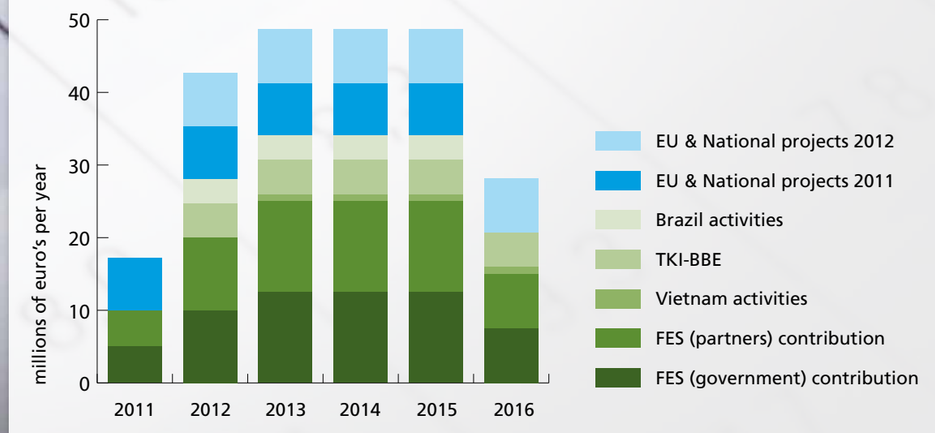
Valorization output 2012



International activities 2012



Size of different funds acquired in addition to BE-Basic



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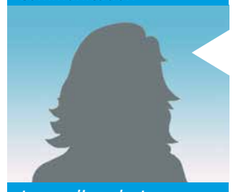

Jacqueline de Jong
Finance

The future as a BE-Basic Foundation

Last October, the BE-Basic programme was officially established as a foundation. BE-Basic is now able to respond more dynamically to developments in the national and international arenas, for instance the Dutch 'top sector policy'. Another challenging ambition is to play a leading role in the technological advancement of and innovation through synthetic biology.

"The basis of our existence is that private companies and academics can significantly accelerate the innovation process by joining forces and sharing capacity, costs and risks", explains Luuk van der Wielen, Distinguished Professor of Biobased Economy at Delft University of Technology and Chairman of BE-Basic Foundation"s Board. "And to make that possible, BE-Basic Foundation offers a professional framework with solid and accepted agreements on intellectual property, confidentiality and finance."

Because of the scale of BE-Basic (it spends approximately EUR 45 million (US$ 60 million) per year), it is able to take and support significant scale initiatives. For example, BE-Basic and its partners initiated what is now the Bioprocess Pilot Facility, which allows both larger and smaller businesses and knowledge institutions to carry out large-scale testing. It also supports programmes on innovation, public communication and international macro-economic impact studies, and the establishment of offices and collaborations within Brazil, ASEAN member states and the USA.

Apart from science and technology developments, BE-Basic has a significant impact on the Dutch strategy towards a biobased economy and is a key player in the international sustainability debate through the Global Sustainable Bio-energy Project, as well as Brazilian and UNESCO programmes for large-scale Bio-energy.

Van der Wielen: "One of our latest achievements is our contribution to the establishment of the Topconsortium for Knowledge and Innovation for the Biobased Economy – or TKI-BBE – of Topsector Chemistry, Energy and Agri-Food through an ambitious 1-billion euro, 5-year plan."

Need to change

Now that BE-Basic has become a Foundation, the BE-Basic programme is no longer coordinated by TU Delft but by the BE-Basic Foundation as a separate legal entity. "There are good reasons for this transfer", says Van der Wielen. "One of them is a clearer demarcation of responsibilities and risks. Although the coordination has been transferred, the connection with TU Delft as initiator and coordinator remains, although it is now more formal and at a distance." Another reason was a strong desire to be able to reprogram annually to anticipate developments in policy, market and technology. In the old setting, some changes were possible, but only limited ones and within the original budget.

"For our partners, nothing changes concerning the rights and obligations laid down in the Consortium Agreement, which remains the legal basis of the BE-Basic Foundation," he explains. The forthcoming enlargement with key players in the food industry will complete the range of industrial sectors that are served by industrial and environmental biotechnology.

Van der Wielen: "Of course, we are always open to new project ideas from our partners. New entries are welcome, but we examine them on complementarity and quality."

New standards

In the coming years, the BE-Basic Foundation will focus on consolidating national and international programmes that are already running. Another objective is to stimulate innovation especially in smaller companies, spin-outs, start-ups and high-tech SMEs, for which the ties with the financial sector have been strengthened.

"We have the ambition to realize some other facilities that are closer to science and can help in matters such as the worldwide standardization of synthetic biology," Van der Wielen says. "To draw a parallel with micro-electronics, that technology was boosted when all the leading electronic manufacturers reached an agreement on global standards. We are strong in industrial biotechnology and metabolic pathway engineering, which is very close to synthetic biology, so we are able to play a leading role in this process." That is why the BE-Basic Foundation has developed Flagships for the top science fields of synthetic biology and high-throughput metagenomics. "This is fundamental research, so it"s actually a challenging task for the Netherlands Organisation for Scientific Research – and less so for BE-Basic, with our focus on application and implementation. We hope to inspire them, as the programme of the Netherlands Genomics Initiative is ending. Now that they have acquired additional research funds amounting to 100 million euros a year, perhaps BE-Basic can transfer this task," Van der Wielen concludes.

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