

Essenscia and the International Year of Chemistry

Chemistry and the life sciences count more than ever in the Walloon economy and a lot of hope rests on their growth.

This industrial sector currently represents 220 companies, employing 25000 people and generating over 3 billion euros of added value. With nearly 50% of the employment in the sector, health sector biotechnology plays a dominating role, in Walloon Brabant, the Charleroi region (principally the Biopark), the Liège region and also in west Hainaut. The importance of health biotech is due both to the growth of companies set up a few decades ago and to the emergence of new enterprises putting into practice the results from research carried out in the universities.

The Biopark Charleroi Brussels South is a good example of the coexistence of university research centres and biotech SMEs side by side.

Essenscia is the federation of employers in this sector where, as well as health biotech companies, others involving basic chemistry, parachemistry and transformation of plastics are also present. Almost all the member companies have a common objective: to assure the sustainable development of our society by developing innovative products and putting them on the market, and by developing applications or services which enable us to cope with the societal challenges of health, use of energy and natural resources, and provision of food and water.

Innovative research in biotech and other areas is crucial to ensure a continuous improvement in everyone's life.

The first objective of Essenscia, with its regional divisions (Essenscia Wallonie for the Walloon Region) and product divisions (Bio.be for biotechnology) is to defend the interests of companies.

To a large extent, intervention by Essenscia has enabled companies and universities to benefit from a reduction in social security contributions for the researchers they employ. This can only be beneficial for the development of research activities in our country.

Essenscia also provides a variety of services to member companies, including permanent information on regulations, political orientation, and personalised advice in different areas such as social matters, aid, environment and safety, not forgetting promotion of the image of the sector and community services. Essenscia Wallonie was at the origin of Cefochim, a training centre in the sector, which provides training for production technicians in the biopharmaceutical industry, just as Biopark Formation/Training does for laboratory technicians.

2011 is of crucial importance to the sector as it has been declared the International Year of Chemistry by UNESCO. This not only concerns chemicals companies but also any company based on chemical science, and therefore includes biotech enterprises and all university chemistry and biochemistry departments.

A whole series of events marks this special year (the agenda can be consulted at www.iyc2011.be) but the highlight of the year, the culmination of the visibility of the sector, will be on 21 and 22 May, during the «Open weekend» in which the Biopark is par-

ticipating, when chemistry and life science companies and educational institutions will open their doors to the public.



Bernard Broze
Managing Director
Essenscia Wallonie
and Essenscia Brussels

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Sustainable collaboration

Even though they're not in the majority in IBMM, chemists are nevertheless present, even at the head of several departments. Among these chemists, is Véronique Kruys, manager of the Molecular Biology of the Gene Laboratory. Since this year she has headed the Department of Molecular Biology of the ULB Faculty of Science.



> You're a chemist yet you work at the Institute of Molecular Biology and Medicine. Do chemistry and molecular biology go well together?

Véronique Kruys : Of course, and if you're not convinced, just look at the Nobel Prizes in chemistry awarded in the last ten years. They all show the direct link between chemistry and life sciences. In IBMM, we don't think about whether we're biologists or chemists. We need each other, we each have our approach and our exchanges are very enriching.

> More precisely, what characterises a chemist at IBMM?

Véronique Kruys : Chemists work mostly in vitro, on a nanometre scale, the size of a molecule. They're interested in small details, in aspects of biochemistry. They have the experimenting spirit, they like to work in the lab, create tools, develop techniques, methods... Chemists bring the dimension of smallness, knowledge of the aspects of mechanisms of molecular reactions. On the other hand, they don't have the aspects related to the living world. This is why interactions between chemists and biologists are rich.

> Is this interest in «coeducation» new?

Véronique Kruys : No, at the beginning of molecular biology at

ULB, there were already a lot of chemists in the laboratories and it was a scientific strength. Twenty years ago around 40% of the students did their PhD in biochemistry in the Department of Molecular Biology or at the Institut de Recherche Interdisciplinaire en Biologie Humaine et Moléculaire. However, in recent years, following the reorganisation of the education system with the Bologna reform, biochemists have become scarcer in our laboratories. This is a pity because chemistry is everywhere in life sciences. And with the development of technologies, its role is more and more important. Let's take the example of high-throughput sequencing. It's based on chemical processes. Likewise, we find chemistry from the classic microscope to small animal imaging.

> Are chemists interested in different questions from biologists?

Véronique Kruys : The main difference between them is the way chemists are trained in science, their affinity for small dimensions, their attraction to experimental aspects... In IBMM, chemists study the molecular aspects of the working of proteins or enzymes. They also study the metabolism of RNA. When we study a protein, we're interested in its different domains and their functionalities. We like to refine the knowledge of different functions, their activity, their location, etc. But science can't

live compartmentalised, limited to one discipline. Our laboratory, for example, recently published an article on the function of an RNA binding protein during embryogenesis. This research wouldn't have been possible without collaboration with the biologists who brought us their knowledge of in vivo models. Our expertise is different, it's up to us to use it in sustainable collaboration.

Open Day at the Biopark

The Biopark Charleroi Brussels South is participating in the International Year of Chemistry Open Day in collaboration with Essenscia. The IBMM laboratories open their doors to the public at 13h00 on Sunday 22 May.

Information at :
<http://www.essenscia.be/iyc2011/>
 071 600 300 or info@biopark.be

The ribosome «machine»

In 2009, the Nobel Prize in Chemistry was awarded to Venkatraman Ramakrishnan, Thomas A. Steitz and Ada E. Yonath for the study of the structure and function of the ribosome. This is a question which is also being studied in IBMM.



The ribosome is the little machine in our cells which manufactures all our proteins. In other words, where there's life there are ... ribosomes. Parents give their children DNA, the genetic information which needs RNA to express itself and so become

the active information translated into proteins by the ribosome. As a consequence, a genetic or proliferative disease can be due to a fault in the DNA or a malfunction in the ribosome. This subject merited the Nobel Prize in Chemistry in 2009, awarded to Venkatraman Ramakrishnan, Thomas A. Steitz and Ada E. Yonath, who discovered the structure of the ribosome on the atomic scale.

For almost 15 years, the Laboratory of RNA Metabolism (Faculty of Science) has been trying to understand how the ribosome is manufactured. They are interested in the nucleole, the compartment of the cell where the ribosome is made.

After working on a yeast model, the IBMM laboratory has just turned the corner. It is now focussing on ribogenesis in man. «The idea came during an international congress. I understood that if our laboratory wanted to progress in its comprehension of the ribosome it had to move over to man. I trained at the Swiss Federal Institute in Zürich and in Lyon, then it was the turn of my team, composed mainly of molecular biologists, but there were also some chemists, from Belgium, France, Greece, Lithuania and Canada. Our research has a biomedical perspective even if we're still working in basic biology. The human nucleole is, in fact, an indicator of the health of our cells. If it isn't well, it grows, multiplies, becomes irregular, etc. Finding an inhibitor which would regulate the rate of manufacture of the ribosome would be interesting in the context of different diseases. We're just at the beginning but it's clear that the nucleole has a large potential as a biomarker», explains Denis Lafontaine, head of the Laboratory of RNA Metabolism.

The ribosome is composed of around a hundred pieces which organise themselves in a logical way, a mechanism well defined in the nucleole. The researchers are trying to penetrate these instructions and the assembly process which, when it fails, can cause different cancers. Highly structured, the organisation of the layers of the nucleole is sometimes affected. The laboratory is trying to identify the mutations which influence this organisation. To do this, it is going to examine closely the 20 000 genes of the human genome, inactivate them one by one and try to answer a key question - is the inactivated gene necessary for the manufacture of the ribosome? And where does it act in the nucleole «factory»? For this high throughput examination, the IBMM laboratory is going to use the CMMI expertise and equipment, especially in the section «Automation and Quantitative Morphometry» coordinated by Denis Lafontaine.

ARC Biology-Chemistry

There are many research projects which associate biology and chemistry, for example, the concerted research action (ARC) «Structural, biochemical and physiological analysis of amino acid transporters and sensors» which unites the Laboratory of Molecular Cell Physiology (Bruno André, IBMM) and the Structure and Function of Biological Membranes team (Cédric Govaerts and Martine Prévost).

Membrane transport proteins exist in all living cells and their malfunction leads to several pathologies in man. The aim of the project is to understand how they work down to

the last detail. How do they link to their substrates, the amino acids? Why do they associate in two in the membrane (dimerisation)? The researchers are also studying the molecular dynamics of these proteins since this is key to the way they work. They want to understand the influence of membrane lipids on the structure and function of the proteins and hope to elucidate their different regulation mechanisms. All these questions have been studied in yeast proteins, a cell model which has great advantages.

Set up in autumn 2010, this ARC associates molecular biology and che-

mistry. Bruno André's laboratory has gained wide expertise in the function and regulation of yeast amino acid transporters, studying them using molecular genetic techniques. Cédric Govaerts is specialised in the study of the biochemical and dynamic properties of membrane proteins while Martine Prévost has expertise in the modelling of their spatial structure. It's the combination of these two complementary skills which make this research original and should lead to a better understanding of pathological situations linked to the malfunction of amino acid transporters in man.

Quality Control

Marc Massaer, a chemist, is the Quality Control Manager in Henogen-Novasep. We met the man who assures quality control in production and environmental control.

Specialised in the contract development and production of new biopharmaceutical substances, Henogen-Novasep helps their customers with their research and development activities, from process development and the manufacturing of products in accordance with GMP (Good Manufacturing Practice) to Phase III clinical studies. Quality control has, of course, an important place in this Biopark spin-off.

At the head of a team of around twenty people, Marc Massaer has been Quality Control Manager for 11 years. A chemist with a specialisation in biochemistry, he says «I could have done the same job if I had studied biology or agronomy. However, I think that being a chemist is a plus. Chemists understand and interpret phenomena in a particular way, we have the capacity to go into a subject in depth, to wonder what the cause of a phenomenon is, to find a solution by reasoning».

In Henogen-Novasep, Quality Control has two facets: the control of production and of the environment. «We have to verify quality at all steps of production, from incoming materials such as chemical reagents (for which the supplier's certificate

of analysis has no official value in the eyes of the Minister of Health) through intermediate production steps to the finished product, ready to be administered to man. We can also do accelerated and long-term stability testing on the finished pro-



duct. This requires setting up a series of tests to be done at each production step and developing them in consultation with our customers and in accordance with regulations», explains Marc Massaer.

The second part of Quality Control is environmental control. Since they have GMP areas, Henogen-Novasep must monitor the air, surfaces and fluids at all times and the microbiological burden on the garments worn by the production operators.

Composed of high school and university graduates, his team members are chemists and also biotechnologists, agronomists, biologists... «When we recruit, being a chemist is not absolutely essential but it is a plus. Among applicants of similar age, experience and skills, I would certainly choose a chemist because I've seen the meticulous, autonomous, conscientious, methodical character of the chemist on the job. And these are precious qualities in a Quality Control team like ours», emphasises Marc Massaer.

Alain Van Bierbeek, biotechnologist

Industrial engineer in chemistry, university graduate in organic synthesis, Alain Van Bierbeek followed the course «Versatile biotechnologist» organised last summer by Biopark Formation/Training. He now works in Henogen-Novasep.

How did you arrive in Quality Control in Henogen-Novasep?

I've always been attracted by innovation. I worked seven years in the IT sector but in the end I started to miss laboratory work. I decided to get some training in biopharmaceutics, a sector oriented towards human health. I followed the «Versatile biotechnologist» course which Biopark Formation/Training organises for job seekers. At the end of this, I did a traineeship in Henogen-Novasep and this led to an employment contract.

Was your training as a chemist an asset?

I've now got several strings to my bow - the analytical vision of a chemist and the knowledge of life sciences and techniques of a biotechnologist. My way of trying to find answers, developing my activity in the Quality Control laboratory, linked to this double training is very much appreciated.



Chemistry, a must in imaging !

Robert Muller, a chemist by training and Scientific Director of CMMI, the new Biopark Centre for Microscopy and Molecular Imaging, emphasises the utmost importance of chemistry in the centre, and in imaging in general.

Chemistry is present in all imaging techniques, its role is therefore essential to stay in the forefront of the technology. To cite only a few examples: the development of new reporter molecules (which allow us to see specific tissues and cell types), radio-isotopes used in PET and SPECT scans (radiochemistry), and the development of «intelligent agents» which only act on the image if the critical threshold of a physiological parameter has been reached and an anomaly can therefore be «mapped».

At CMMI at the moment, they're developing contrast agents, used especially *in vivo*, but their use can be extended to *in vitro* if necessary. The production of these agents needs a lot of development work and a certain know how, which is undeniably CMMI's strength. Its state-of-the-art equipment and the specialised personnel in the ULB and UMONS laboratories mean this type of compound can be produced on a larger scale. From this perspective the plan is the-

refores the creation of a first spin-off which is now ongoing. A First Spin-off project has been submitted to the Walloon Region (project AGECHO). Impressive, when you think that the building of the new centre isn't yet finished and that all this has happened in temporary university laboratories located far from each other! But such an opportunity can't be missed, the demand is certainly there. It often happens that companies from abroad

contact the Scientific Director of the CMMI to obtain this or that agent cited in a publication. At present, it's not possible to satisfy all the demands, as the synthesis of some of these agents sometimes takes over six months. However, if they can directly produce on a larger scale, there's a really interesting potential. We can therefore say that chemistry promises CMMI and the future spin-off a prosperous short-term future...

Sabrina Bousbata, Head of the Proteomics platform

«Protein chemistry is the nerve centre of proteomics. Mass spectrometry instruments were first developed for small chemical molecules and only took off when they were used for proteins. In 2002 this was worth the Nobel Prize in Chemistry for two inventors of protein ionisation, Koichi Tanaka and John B. Fenn. Today, chemistry continues to support proteomics in different ways: to give only the two examples which have had the greatest impact, the introduction of tags for the enrichment of subclasses of proteins and peptides, and the study of post-translational modifications and stable isotope labelling strategies for the quantification of proteins».

IN BRIEF

IBMM-CMMI collaboration

The IBMM Bacterial Genetics and Physiology Laboratory (Laurence Van Melderen) is participating in a COMICS project supported by the ESA. The objective? To look at how bacteria and bacterial mobile elements evolve in semi-closed systems such as the International Space Station, ISS. In this project, the IBMM laboratory is studying bacteriophages i.e. viruses which only infect bacteria. Through a collaboration between the proteomics (Sabrina Bousbata) and electron microscope (David Perez-Morga) platforms of the Biopark, Pierre Smeesters from Laurence Van Melderen's laboratory has managed to characterise a virus of *Bacillus cereus*, a bacterium responsible for food poisoning. The research was published in the journal *Research in Microbiology* in March.

SBIA delegation

In the context of the partnership of the competitiveness cluster BioWin with the Shanghai Biopharmaceutical Industry Association (SBIA), BioWin received an SBIA delegation in Wallonia on 10 and 11 March. In collaboration with the SPoW (the Association of Scientific Parks in Wallonia), a programme of visits for the Chinese Walloon tour was organised, one of which was to the Biopark Charleroi Brussels South. After a presentation of the Biopark by its director, Dominique Demonté, the delegation visited Delphi Genetics in the company of its CEO, Cédric Szpirer.

Sabrina Bousbata

«ULB was one of my first expatriation choices»

This year Sabrina Bousbata became a tenured lecturer at ULB. The career path of a researcher now at the head of the proteomics platform in the Biopark...



«As a child, I was fascinated by Pasteur. When I read his biography, I said to myself « That's what I'd like to do later» admits Sabrina Bousbata half-jokingly. After secondary school in Petite Kabylie where she lived, she took the entrance examination for medicine but finally decided to study biochemistry. «I said to myself that sounding patients, waiting for researchers to perhaps find a drug I could prescribe wasn't what I wanted to do. I wanted to work earlier in the process. I was convinced that, as a researcher, I could answer biological questions, find solutions to improve human health, that's what interested me» she explains.

Algeria

Sabrina Bousbata did a master's in biochemistry at the University of Béjaia, with one idea in mind, to go abroad to become a researcher. «Unfortunately, the year I graduated, Algeria had political problems. Terrorism increased, travelling abroad became difficult» she remembers. She dreamed of going to the US or to ULB (already) «I applied to ULB as I was attracted by the excellent reputation of its research, impressed by its Nobel Prizes» she says. She was

taken on in Algeria in a ceramic enterprise and for two years was in charge of quality control.

However, the young woman still had one desire, to do research. She applied to the Mediterranean Agronomic Institute of Chania (MAICh in Crete). She left for Greece to do a master's in plant molecular biology. She then got a grant for Germany where she joined the biology department in the Westfälischen Technischen Hochschule (RWTH) in Aachen. This is where she met her husband, a Dane she followed ... to Denmark.

As a member of Professor Peter Roepstorff's team, she did a doctorate at the University of Southern Denmark of Odense, in a proteomics laboratory among the most reputed. She then did a post-doctorate, also on proteomics, at the INRA in Montpellier. After, she returned to Denmark and got a job in the Technical University in Copenhagen.

Biopark

She then applied for the post of manager of the proteomics platform in the Biopark Charleroi Brussels South and got the job. Direction Belgium... «It's amusing to think that in 1993 when I

was a student, ULB was already one of my first expatriation choices and that in 2008, via Greece, Germany, France and Denmark, I finally arrived» she smiles.

In 2011, she became a tenured lecturer at ULB. «Proteomics is a new research tool which appeared in the mid-90s and really took off at the beginning of the 2000s. Today the different techniques have become obligatory tools in molecular biology» she explains.

Innovative

«Our platform provides services to third parties and develops new techniques in close collaboration with ULB research laboratories, from bacteria to mouse and man. It's really fascinating, you have to find new techniques to answer new questions. This means you have to keep yourself informed and trained all the time, you have to have an inquiring mind and be innovative» insists Sabrina Bousbata.



Queen Elisabeth Medical Foundation Cerebral cortex and the DMRT5 gene

The IBMM Developmental Genetics Laboratory has won the support of the Queen Elisabeth Medical Foundation. We met the head of the Laboratory of the Faculty of Science, Eric Bellefroid, who presented his research project on the cerebral cortex to us.

> What is your laboratory studying at IBMM?

Eric Bellefroid : Our laboratory is interested in the mechanisms controlling neurogenesis and uses the amphibian and mouse embryo as models. Following the work done a few years ago by Virginie Moers during her PhD, we became particularly interested in the mechanisms controlling neuron specification in the cerebral cortex. We're studying the DMRT5 gene which codes for a transcription factor expressed in gradient in the progenitor cells in the cerebral cortex. We've shown that it's expressed particularly in the posterior medial part of the cortex and that it plays a key role in the regionalisation of cortical progenitors.

> Is the research project supported by the Queen Elisabeth Medical Foundation on the DMRT5 gene ?

Eric Bellefroid : Yes, this three-year project aims to lead to a better understanding of how the expression gradient of DMRT5 is established in cortical progenitors and how this transcription factor controls the early regionalisation of the cerebral cortex. Our goal is to use this factor as an entry point into the better understanding of the development of the cerebral cortex, one of the major challenges in neurobiology today.

> Could you explain to us ...

Eric Bellefroid : The cerebral cortex is

one of the major regions of the brain, responsible for the coordination of cognitive, motor and sensorial functions. It's a complex structure, made up of hundreds of neurons of different types, organised in six layers and in different areas carrying out distinct functions. The size of these different cortical areas varies from one species to another. It also varies within the same species, from one individual to another, which leads us to think that it could affect the behaviour of individuals. Better knowledge of the mechanisms controlling the formation of cortical areas should therefore have primordial implications in our understanding of certain neurological malfunctions and pathologies.

> You're interested in one particular gene, DMRT5. Why?

Eric Bellefroid : Today we know that the formation of these different areas is initially controlled by signalling centres located at the periphery of the cortex. Before these signals, only some of the transcription factors controlling the formation of cortical areas have been identified and the way they interact is not well known at present. We know that the DMRT5 gene is essential for the development of the cerebral cortex. DMRT5 mutant mice have a smaller cerebral cortex, don't have a hippocampus and the molecular analyses we've done show displacement of the cortical areas towards the back and medial regions of the cortical

areas. At the moment we're trying to understand how this factor controls the regionalisation of the cortex, by studying its relationship with other known regulators and analysing the consequences of overproduction of the factor in transgenic animals. We're working with different groups, like those of Dr David Zarkower of the University of Minnesota, a specialist in genes of the DMRT family, and Pierre Vanderhaeghen of the IRIBHM, ULB.

> «DMRT5» is one area of research of your laboratory. Are there others?

Eric Bellefroid : Yes, at IBMM, our laboratory is also studying the formation of the neuronal circuits of the spinal cord involved in the rhythmic movements of locomotion. Better knowledge of the formation of these circuits should contribute to the development of new therapeutic approaches to the treatment of spinal cord lesions. Finally, a third area of research, coordinated by Jacob Souopgui, is the study of the mechanisms controlling the specification of ectoderm cells during the formation of germ layers. Here the researchers are particularly interested in Seb4R, an RNA binding protein which plays an important role in the first choice cells from fertilisation of the egg must make.

DNAVision

A complete human genome for €7500 !

Complete sequencing of the human genome is now available at an accessible price to the players in pharmaceutical and medical research. DNAVision, the European leader in this technique, is located in the Biopark.

With around three billion DNA bases and 3 million variations between each individual, the human genome contains several billions of pieces of information. The first human being to be entirely sequenced was in the United States. Since then, the US has led research in this area, followed by Asia to a lesser extent... but Belgium, and DNAVision in particular, is not to be outdone. In 2008, eight people in the world had been sequenced, in 2009, the figure of a hundred was reached.

In 2010, DNAVision invested in resources to succeed in what some think is the next scientific revolution on the same scale as the Internet...and the number of people sequenced in the world reached 2500...

Like the big American and Chinese centres, DNAVision chose to invest in «Illumina Hiseq 2000» and «Life Technologies Solid 5500XL» platforms. This equipment is expensive but its acquisition would enable the company to stay the European leader in this technique.

100 gigabases per patient

The equipment already provides a sequencing capacity of eight complete human genomes a week and this will soon increase to twenty - an impressive figure given the billions of pieces of information in question. This consists of around 2 terabytes of data per patient which have to be stored for 20 years as they are medical data... We can suppose that DNAVision is the company which produces the most data in Hainaut!

The DNAVision team has increased in size and 10 IT and bioinformatics specialists have joined the existing team. Another sign which shows the current stakes are high, Laurent Alexandre, an emblematic figure of the medical Internet, decided to invest with DNAVision in what he considers to be an essential step forward in European research.

DNAVision now provides sequencing of the human genome for 7500 euros. This is the lowest price on the market

because the company does it from only one sequencing. There's therefore no need for a customer to be a big company and to order in large quantities. When we know the cost of this type of analysis was up to 3 billions of dollars in 2003, there are reasons to suppose the practice is going to become more common and therefore more accessible in the coming years. Today it costs the same as a small car, one day it might cost the same as the analysis of a blood sample... and we can perhaps imagine that all newborns could one day be sequenced at birth, or even before, in order to assess their risk factors.

<http://www.dnavision.com>

IN BRIEF

Bone Therapeutics raise €9500 million

Bone Therapeutics, a Biopark spin-off, is specialised in cell therapy for bone diseases. In February they announced they had raised funds of € 9500 million which will enable them to continue their development programme and start Phase III clinical studies, the last step before commercialisation of their products for bone reconstruction.

www.bonetherapeutics.com

Biopark Formation/Training

The Biopark Formation/Training 2011 programme of is out: short modules (0.5 to 2 days) in Molecular Biology, Imaging, Flow Cytometry and Cell Biology.

Find out more at www.biopark.be/formations

Biopoly

Following on from the success of its first edition, the training course «Biopoly» ('Versatile biotechnologist') is once again on the agenda in 2011. Organised by Biopark Formation/Training and Forem, Biopoly provides a customised transdisciplinary programme for job seekers . Next cycle: from 16 May to 16 September 2011.

Information at www.biopark.be/formations

Scientific Film

From March 22 to 25 will be the first edition of Scientific Film Festival in Brussels on the Solbosch campus of the ULB in Brussels. Program : 15 films, 2 previews, presentations of PhD students to give a taste of wonder and discovery ...

Information: www.ffsbxl.be