En Route to the Knowledge-Based Bio-Economy

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Knowledge-Based Bio-Economy (KBBE) can be concisely defined as “transforming life sciences knowledge into new, sustainable, eco-efficient and competitive products”. **(1)** Renowned experts from academia and industry were invited to contribute to an expert paper which outlines the perspectives of a KBBE within the next 20 years.

The resulting so-called ‘Cologne Paper’ was published on 30 May 2007 in Cologne at the conference ‘En Route to the Knowledge-Based Bio-Economy’ hosted by the German Presidency of the Council of the European Union. It presents the findings of six workshops which were held between January and March 2007. The participants (see page 19 ff) discussed the following aspects: 1. Framework, 2. Food, 3. Biomaterials and Bioprocesses, 4. Bioenergy, 5. Biomedicine and 6. New Concepts and Emerging Technologies.

The visions, forecasts and recommendations presented are intended to assist policy-makers in identifying priorities and adopting measures. The findings of the paper reflect the view of the independent experts and should not be regarded as the official position of the German Presidency of the Council of the European Union.

En Route to the Knowledge-Based Bio-Economy (KBBE)

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Summary

Visions and Trends

Biotechnology will be an important pillar of Europe´s economy by 2030, indispensable to sustainable economic growth, employment, energy supply and to maintaining the standard of living. It will be increasingly used in labour-intensive sectors, e.g. industrial processing, pharmaceuticals, agriculture and food. By 2030, the **products of white biotechnology and bioenergy** will have an estimated one-third share, worth €300bn, of industrial production.

Biotechnology is expected to help **meet the most urgent global challenges** – growing and ageing populations, limited resources of raw materials, energy and water, the threat of global warming – by facilitating the development of a sustainable economy built on bio-based industrial processes. On a global scale climate change is regarded as one of the most challenging issues to be addressed right now.

Combined with advanced bioprocess engineering the development of **high performance crop plants** is the key to this vision becoming reality. Crops will serve as factories for enzymes, amino acids, pharmaceuticals, polymers and fibres, and will be used as renewable industrial feedstock to produce biofuels, biopolymers and chemicals. Green biotechnology will be employed since conventional or smart breeding alone will probably not be able to provide the required increase in performance. It is anticipated that already by 2020, in addition to the then mature gasification technologies, the conversion of ligno-cellulosic biomass by enzymatic hydrolysis will be standard technology opening up access to large feedstock supplies for bioprocesses and the production of transport fuels.

The coming years will see the advent of tailor-made, **personalised nutrition** providing better food with improved health attributes. The authors expect **personalised medicine** to be a reality by 2030. Thanks to novel biotech drugs and regenerative medicine a number of serious diseases will be treatable by then. Many severe chronic diseases are expected to be treatable by transplanting industrially produced stem cells. Organ replacement will be a therapeutic option and future medicine is expected to succeed in generating fully functional organs, including teeth. Novel vaccines will also prevent and combat diseases like cancer, multiple sclerosis and Alzheimer's disease.

The ambitious quest for answers to several **fundamental scientific 'big questions'** (Can we understand brain function? Are we more than the sum of our genes? What determines cell fate? Can we describe cell functions and cellular communication by computer programs?) will continue to drive the development of novel technologies while technological innovation will continue to accelerate basic research. **Biotechnology will have matured from a discovery science into an engineering science.** For example, the coming years will see the construction of synthetic cells, capable of selectively producing defined products. Systems biology, brain research and computational neuroscience will inspire technological innovations, e.g. intelligent prostheses, neuromorphing computer chips, and functional models that consolidate our knowledge of the brain from the level of molecules to psychophysics.

Hurdles to overcome en route to the KBBE

The number of qualified people will not keep up with demand. Measures should be taken early, e.g. by increasing the share of science courses at primary and secondary school level. In order to counter the strong international **competition for talented scientists** European public research institutions need to receive adequate funding and to provide more reliable and attractive career options with competitive salaries and positions. There will be a **growing need for interdisciplinary education and joint research** that is closely entwined with technological development. For example, the experts suggest building a pan-European network (Pan-European Institute of Technology) of about two dozen small excellent interdisciplinary institutes scattered across Europe which are focused on the 'big scientific questions' and visionary ideas.

An at least two-fold increase in agricultural yield will be needed within the next two decades. This must be achieved in an ecologically sustainable way employing plant biotechnology. Future conflicts resulting from limited arable land for **food versus non-food** production need to be solved by innovation, e.g. by high tech crops, and by efficient regulation on an international level. The production of industrial crops on irrigated land should be discouraged in favour of food crops. While the production of biomass, possibly with export potential, is expected to translate into higher income, local independence and greater political stability of developing countries, the import of biomass/biofuels at the expense of food security and the environment must be avoided, the conservation of ecosystems, such as rainforests, being mandatory.

Agriculture thriving without subsidies is another vision for Europe in 2030. Shifting subsidies from the Common Agricultural Policy (CAP) to support innovation through science and research programmes is suggested, especially since the heavy dependence on agricultural subsidies as under the current CAP is expected to decline thanks to profitable integrated production of food, fibre and energy.

Competitive **tax incentives** will be needed to attract private capital. European and national **funding programmes providing seed money** will be indispensable for a long time. The founders of early-stage companies should be encouraged, e.g. by means of tailored funding and by affordable access to external expertise. **Public-private cooperation** in industrial biotechnology should also extend more downstream, in particular to validate new concepts by pilot and demonstration

plants, e.g. a 'zero-waste biorefinery'. Initial public procurement will be necessary to stimulate the development of novel technologies in Europe.

Eventually, a single European Community Patent (one language, one agency) will help to reduce the cost of intellectual property (IP) protection. Common European **standards for biotechnological research**, i.e. stem cell research and field trials with GM (genetically modified) plants, and for the protection of inventions should be implemented. The present high European standards of safety and approval regulations for GM organisms should not be extended to the detriment of R&D.

The **co-ordination of European and national programmes** related to KBBE should be improved. A high-level representative of the Commission ("KBBE Co-ordinator") should be in charge of implementing KBBE.

Science needs the support of society. A well-informed public aware of the opportunities and risks of biotechnology is considered a competitive edge in global competition. The public involved in developing the agenda of European research policy is a clear vision for the future. The acceptance of green biotechnology – especially when applied to the generation of non-food products – is expected to increase. Advanced technologies with controversially discussed ethical and legal implications, like interventions with brain functions or genetic testing, the latter regarded as indispensable to personalised medicine, will need transparent, balanced and feasible regulation. As biotechnologists will be able to manipulate the human brain/mind with increasing precision, we must be realistic about what is achievable and deliberate about what we actually wish to achieve.

A Knowledge-Based Bio-Economy in 2030

Driving forces

The growing demand for a sustainable supply of food, raw materials and fuels is the major driving force behind the KBBE. A giant leap in agricultural production and yields – at least by a factor of 2-3 – will be needed within the next two decades. This must be achieved in an ecologically sustainable way, e.g. by avoiding large losses.

The most urgent and challenging issue is climate change which calls for effective measures to reduce the release of greenhouse gases and to promote the transition from conventional fossil fuels to alternative and renewable sources. It has already resulted in political initiatives supporting the development of appropriate technologies. Regulations limiting carbon dioxide emissions are already in place in energy-intensive industrial sectors (power production, oil and gas refining, pulp and paper, steel and aluminium) and are expected to be extended to other areas of economic activity.

A challenge of equal order is the anticipated increased demand for energy in the next decades while fossil fuel reserves, particularly oil and gas, will continue to decline. The demand for transportation fuels is likely to rise even though the energy efficiency of transport is expected to improve.

Moreover, the highly productive European agriculture industry needs future markets and Europe's still leading engineering sector should not miss the business opportunities from the potential growth of commercial bioenergy projects.

Clearly defined lead markets could help to pave the way. A sustainable, competitive European agriculture, less dependent on subsidies, will have to grow into new markets. Industrial crops are one such opportunity. If equally priced, products derived from sustainable production should have a competitive edge over conventional products with respect to acceptance by consumers.

The high standards of health care and the ageing of the population in industrialised countries are key drivers of medical research as the need for treatment of degenerative and lifestyle-related diseases is on the increase.

Growing knowledge, bioinformatics, and the strong interaction of engineering sciences with life sciences – already bearing fruit in the -omics sciences, systems biology, and nanobiotechnology – will find medical application and will open avenues to new diagnostic and therapeutic options.

Valuable biomarkers, derived from epigenetics and the -omics sciences, will revolutionise drug discovery. As powerful methods, e.g. from stem cell technology, provide more reliable data and far-reaching forecasts, preclinical studies will become more important in the approval process.

All sectors of biotechnology will continue to grow globally; developing countries will benefit from new vaccines and therapies and will see the highest growth of green biotechnology. Europe's agrobiotech sector will face stiff competition from the emerging industrial countries (e.g. Brazil, India, China).

Biotechnology is, and will be, an international industry, based on international business models. Europe's biotechnology has to intensify cooperation, especially with the emerging industrial nations. Cooperation with US researchers and US companies will remain of high value in the next two decades, however, business opportunities arising in emerging markets should be exploited and our strategies adapted accordingly.

Biotechnology is a fast, highly competitive race and scientific breakthroughs will continue to happen everywhere in the world. Concentrating all its strengths and efforts, Europe has to take the right measures now and to allocate the appropriate resources to catch up and take a leading position in the race to the Knowledge-Based Bio-Economy (KBBE).

Bioproducts and bioprocessing

The authors agree that the combination of plant breeding and industrial (white) biotechnology will serve as the basis of a KBBE by 2030. **(2)** Roughly one third of the chemicals and materials then produced will stem from biological sources and advanced biocatalytic processes. The forecast revenues, including those from biofuels, would amount to a volume of € 300bn. **(3)** The production of small molecules by white biotechnology is expected to grow significantly. White biotechnology will contribute to all sectors of industry, e.g. providing biomaterials including novel biopolymers and bioplastics for the construction and engineering sector. Toyota, for example, which has been producing bioplastics for its own use since 2003, expects its 2020 production of biodegradable plastics to be 20m t worth $40bn. Although starch and sugar will still be key substrates the efficient biocatalytic degradation of lignocellulose fibres will be standard technology by 2020 and will have increased the volume of available feedstock.

The coming years will also see the development of powerful engineering tools (e.g. systems biotechnology, synthetic biology). Biorefineries of the future will be able to extract novel, value-added compounds, like fine chemicals, and convert the remaining biomass into energy or building blocks for chemical synthesis, leaving only small amounts of waste whose inorganic components could be recycled for use as fertiliser. Process technologies required for a zero waste biorefinery will be available by 2020, at least at the level of semi-commercial demonstration plants.

Progress in these fields will rely on the availability of novel high tech plants designed to provide high yields and properties well suited for industrial processing. Such smart plants would enable the biosynthetic production of specialty chemicals, intermediates, and more complex chiral molecules. Conventional breeding, employing methods from molecular biology, e.g. genetic markers for selection, is expected to increase crop yields significantly. Besides providing novel traits, genetic engineering will be necessary to further boost the yields. Genetically modified (GM) high tech plants for industrial use will have become standard crops of European agriculture. These 'industry plants' will be derived from either traditional crops like maize or from special non-food crops like switch grass which allow co-existence with food crops. As arable land and water supply are the limiting factors of global agriculture, low-input drought-tolerant and pathogen-resistant plants will be grown in regionally adapted crop rotation systems. To achieve this, a deeper understanding of plant metabolic network regulation and plant-environment interactions is required. In addition, novel breeding approaches and powerful tools for the genetic engineering of plants will be needed.

The KBBE is the most promising of all efforts to keep production industries in Europe: a mature bioeconomy will see the alignment of different types of companies along the value chain. Much will depend on the smart coupling of chemical and biotechnological processes. Europe is still the world leader in key biotechnology sectors like the production of industrial enzymes. It cannot afford to miss the opportunity to defend its position.

Bioenergy

Sustainability is a clear goal when building the bioenergy pillar of a KBBE: a more secure energy supply, efforts to counter greenhouse gas emissions, minimised production of waste, as well as the conservation of ecosystems, rural social structures and employment. All these goals need to be obtained cost effectively.

Early action on the issue of climate change is mandatory as it is the only cost-effective strategy. **(4)** Biotechnology is considered capable of providing adequate and highly valuable means to meet the challenges. The production of 'bioenergy' (a term comprising bioheat, bio-electric power and biofuels) from biomass will become essential to the energy mix of the future – in addition to the reduction of energy consumption, increased energy efficiency and the development of other sources of renewable energy and novel technologies for carbon dioxide capture and storage. Bio-energy production is an outstanding example of integrated RD&D combining green and white biotechnology, agricultural production, conversion technologies, materials sciences and others. It is noteworthy that the production of bioenergy does not always involve biotechnology, e.g. the thermochemical pathways of biomass-to-liquids (BTL) using gasification and catalytic processes to derive biosynthetic fuels and chemicals from biomass.

Theoretically, 5% of the earth's land is sufficient to meet the world's total energy demand, given a conversion efficiency of 1% of sunlight into bioenergy. In Europe annual yields of 20-30 oven dry mass tonnes per hectare (odt/ha) from conventional plants are the limit that sunlight and climate would permit given adequate water and nutrient availability. In tropical regions yields of up to 50 odt/ha can be achieved.

There are distinct areas of bioenergy: the liquid fuels area, where biomass is transformed into combustible chemicals such as ethanol, butanol and biodiesel, and the heat and power (primary) energy area, where biomass is directly used as combustible raw material for heating and/or electricity generation via combustion or gasification. Today, heat production has the largest share of bioenergy from biomass, while power and fuel generation are growing sectors. This should be recognised for future strategy. Recent studies, e.g. found in the EU Biomass Action Plan, also forecast a growing market share of biogas that will be distributed through the existing natural gas pipeline networks, and require higher investment in infrastructure (biogas filling stations).

The IEA predicts that by 2030 today's 1% share of biofuels (based on energy content) of the global transport fuel market could have risen to 7%, with other projections even higher. The EU has recently agreed on a target of 10% biofuels by 2020 with a 30% share produced from local resources possible by 2030, assuming that "second generation" biofuels, such as biogas, BTL or ethanol from ligno-cellulosic biomass, will have become commercially viable some years earlier.

The development of novel crops and the integrated use of whole plants is the key to all solutions based on biotechnology. By 2030 energy crops that store more energy (in terms of GJ/ha) and can be used in their entirety will have become available from advanced breeding technologies, including genetic engineering. Varieties of energy crop plants adapted to different local conditions should achieve an additional increase of biomass, e.g. due to the prolonged uptake of nutrients. Plants considered as weeds in some regions could be cultivated and improved to deliver annual biomass yields above 30 odt/ha. The increased efficiency of nutrient uptake should reduce the use of fertilisers which partly have to be imported from outside Europe and are generally expensive and energy-consuming to produce and transport. The need for agri-chemicals may also have declined due to improved breeding methods. In the long term the diversity of agricultural plants will increase due to energy and industrial crops.

Food and fibre crops currently contribute to the supply of feedstock materials for energy supporting the vision of decentralised energy production. It is anticipated that by 2020 or earlier the conversion of ligno-cellulosic biomass (straw, wood etc) by enzymatic hydrolysis will have become standard technology and will open up access to large feedstock supplies, thus avoiding direct competition with food production. Straw, wood process residues and vegetative grasses will be the feedstock of choice for enzymatic processes, but short rotation woody biomass crops could also be grown for an additional market. Europe's forest industry will provide a significant share of ligno-cellulosic biomass and will mature into a bioenergy supplier. In order to retain its competitive edge the industry will have to implement genetic engineering and develop GM trees for an efficient raw material supply.

The US is already investing large sums in ethanol production from ligno-cellulosic feedstock. Over the next four years the Department of Energy (DOE) will spend US$385m on six biorefinery pilot and near commercial scale projects which – if all implemented – are expected to produce more than 500 million litres of cellulosic ethanol per year. Combined with industry's cost share, a total of more than US$1.2bn will be invested.

New technologies are continually being developed. Subject to the specific process employed and the use of additional non-biomass sources of energy, BTL technologies being currently developed could yield 1.0 t of bio-synthetic fuel per 2.2 - 6.0 t of biomass feedstock, retaining 64 - 45% of the energy stored in the feedstock and reducing CO_2 emissions by up to 91% compared with fossil fuels. However, a sufficient, continuous supply of biomass is a challenge requiring sophisticated logistics, especially where local production is insufficient. New harvesting and pre-conditioning technologies which yield easily usable and storable materials could contribute towards solving these problems. There are opportunities for growth: the vegetable oil share of the transport fuel market is only expected to grow by a moderate 2% per year, whereas, once fully commercialised in the longer term, BTL fuels could possibly deliver around 20% growth per year. For BTL production the use of most kinds of biomass is possible, but woody biomass is the most efficient and also offers logistical advantages. Short rotation wood crops can be harvested every 3 to 10 years and, in the case of coppicing species, they eventually regrow from the roots. Presently available tree species, such as *Populus*, *Salix* and *Eucalyptus*, already produce more than 10-20 odt/ha/yr under temperate conditions. Under tropical conditions 30 odt/ha/yr can already be achieved from plantations with specially bred and adapted tree species.

Alternative routes, like the fermentation of butanol or the production of glycerol as a by-product of biodiesel inter-esterification, may also have matured into competitive supplementary sources of biofuels.

By 2030 the production of lipids and/or hydrogen from engineered algae may be feasible and probably profitable in sunny parts of Europe. In addition, biomimetic artificial systems based on nanotechnology and porphyrin chemistry may be capable of performing artificial photosynthesis to supply hydrogen and/or electricity.

Food and nutrition

Concurrent with changes in our lifestyle in recent years (less physical activity, higher food intake, intake of convenience food and fast food), an increase in lifestyle-related diseases can be observed. Nutrition is one of the keys to prevention, which requires innovative products. The coming years will see the advent of tailored, personalised nutrition (nutraceuticals, functional foods) providing better food with improved health attributes. The authors expect that food will be designed for special consumer groups, e.g. elderly people, to promote health and prevent illness, and for therapeutic support. One priority is the development of foods and nutraceuticals for groups with defined risk factors or diseases (diabetes, obesity, cardiovascular diseases), linking diet to treatment. The production of food with less allergenic potential will clearly reap benefits for the consumers concerned, e.g. children. Novel technologies and tools (nanotechnology, biosensors) will provide safe new products with added value for consumers. These innovations in the food industry will result in the European food markets being split up into conventional food products and targeted or personalised foods.

The food industry is one of the largest sectors of the European economy, with a turnover of €800bn and roughly 4m employees. Biotechnology already plays an increasingly important role since many traditional foods, food ingredients and enzymes are produced by means of engineered microorganisms and bioprocess technology. Biotechnology is essential to the production of high quality, mildly preserved convenience food. Biotechnology has an impact on the entire value chain, including food safety. The future will see the development of highly flexible production systems addressing the demands of a diverse spectrum of consumers with a correspondingly large variety of ingredients. Smart packaging of products to retain freshness will also permit control of shelf life and better food chain management. Improved quality management systems will reduce the growth of microorganisms or toxins (e.g. mycotoxins), thereby increasing consumer safety. Thanks to biotechnology valuable ingredients and nutrients will be increasingly extractable from residues of conventional food production.

Personalised nutrition relies on sound, non-invasive diagnostics which is expected to become available from advances in biomarker research, genetic testing, and from advanced imaging and biosensor technologies. Information on the interplay of individual genetic makeup and the physiological response to food is already being collected in genomics projects.

European skills in food biotechnology and automation of agriculture could be the drivers of the food supply in developing countries. R&D on the production processes of food for developing countries, e.g. employing indigenous microorganisms and raw materials, should also be supported in the future. Food processing by controlled fermentations and the application of new food raw materials will reduce post-harvest losses and develop new markets and thereby significantly alleviate poverty by income generation.

Biomedicine

Closer to the ideal of maximum treatment outcome and minimal side effects, biomedicine in 2030 will see a great repertory of therapeutic options. Novel efficient drugs and therapies will be available and diagnostics will have made great advancements. It will be possible to treat the underlying causes of diseases that are not curable today, especially cancers and neurodegenerative diseases. Some cancers will, at least, have become a chronic disease. Cystic fibrosis is likely to be curable by then.

Even molecular interventions to prolong human life may have become a reality, as it is already possible today to significantly extend the life span of animals. New powerful imaging technologies will allow non-invasive monitoring of body functions and physiological states at high resolutions.

The integration of molecular and cellular biology into clinical medicine will certainly make a change. Instead of detecting macroscopic disease symptoms too late, future diagnostics will reveal the emergence of a disease at the molecular and cellular level as well as its genetic predispositions. Genetic testing will be a key technology essential to pharmacogenetics and gene therapy as well as to regenerative medicine and the development of novel drugs. Biomarkers for early detection and disease susceptibility will be the basis of personalised therapies tailored to the specific molecular basis of a disease. For example, knowing about the genetic makeup and/or the biomarker patterns of tumours will help physicians in the choice of appropriate therapeutic options.

Biochips, i.a. cDNA microarrays measuring gene activities, will allow a hitherto unknown degree of diagnostic precision and a reduction in costs due to targeted treatment. Diagnostics of the future will be mainly based on specific genetic markers and biomarkers derived from protein analysis. A combination of these will be well suited for accurate characterisation of a disease state and for prognosis.

Preventive medicine will play a more prominent role in the future. Therapeutics and diagnostics will benefit from insights into epigenetics and other subtle mechanisms of genetic regulation. Although improved diagnostics could increase the costs of prevention there will be huge savings from cost-efficient early intervention as well as from the delayed onset of diseases due to preventive measures.

The advent of personalised medicine is expected to transform the pharmaceutical sector. Specific molecular therapies – more efficient and associated with fewer side-effects – will dominate the medicine of 2030. Small specialised companies, resembling think-tanks and close to academia, will feed big pharma's drying pipelines with new medicines.

The therapeutic value of biopharmaceuticals will continue to increase. By 2030 they will have doubled their present share of 25% of the pharma market. Today's large pharmaceutical companies, still relying on the blockbuster business model, will have to diversify their strategies. In general, drugs are limited with respect to their therapeutic scope: a significant percentage of patients do not benefit, and even suffer, from the adverse effects. There will always be room for blockbusters, but awareness will grow that blockbusters alone do not resolve the issue of "difficult-to-treat" patients. Therefore more specialised and targeted medicines, including proteins, antibodies and siRNAs, will emerge as the weapons of choice in fighting severe diseases. Engineered with a sound knowledge of the links between genomic information, protein structure and function, these drugs will home in on their molecular targets. Directed post-translational (glycosylation, hydroxylation, etc.) and specific chemical modifications will enable the quality of drugs to be improved.

As stem cell research is still in its infancy, by 2030 regenerative medicine will have revolutionised medicine. Most, if not all, severe chronic diseases, e.g. cardiovascular diseases, neurological disorders, diabetes and degenerative conditions of joints and bones, will be treatable by transplanting industrially produced stem cells; this will avoid organ transplants and therapies to treat the long-term secondary consequences of chronic disease. Treatment with stem cells will be cheap and efficient. The authors also expect stem cells to be applied for organogenesis. Methods will be available for heart repair, neural regeneration and the regeneration of islet cells for the treatment of diabetes. Tissue regeneration will be widely used as a source of organs suitable for transplantation. Future medicine is expected to succeed in building three-dimensional organs, like livers, hearts, kidneys – and teeth.

By 2030 pluripotent stem cells will be obtained from re-programming adult, differentiated cells; this may reduce the need to use embryos to derive embryonic stem cells. Stem cell research will result in the enhanced efficacy and fewer side-effects of future therapies. Specially constructed stem cell lines will be useful for screening new drugs and for predictive toxicology, which will result in a reduction in attrition of compounds failing late stage development due to unexpected side effects. Genetically modified stem cells, targeted against tumour epitopes, will be available as one of the many options of gene therapy. Malfunctions and degenerative diseases of the brain will be amenable to therapeutic intervention.

Advances in nanobiotechnology will enable the development of biomedical implants and man-machine interfaces, providing the technological basis for smart, computer-controlled prostheses which will be available to compensate severe somatic deficiencies.

The availability of miniaturised devices will allow practically non-invasive treatment with almost no damage to tissue and the potential to address regions as small as 500 cells. Combinations of bioimaging technology and electrical brain activity measurements will enable the visualisation of activity patterns within the brain while we are thinking, mourning, happy or asleep. Directed electrical stimulation of certain brain regions will be useful for the treatment of Parkinson's disease and its prevention by the induction of a neuroprotective effect. However, these therapies will require sound knowledge of brain functions since targeting brain areas with electrodes affects a number of circuits and it is not exactly known how these various circuits with all their ramifications might weave through different neuroanatomical structures. Electric stimulation to help patients with diseases of the spinal cord may also be envisaged.

The development of medical devices will probably be an important economic driver as the merger of pharma, biotech and medical device companies will open new opportunities for value generation and devices will complement drugs as therapeutics, in some cases with the sales potential of blockbusters. Novel vaccines will not only prevent severe threats to the public (HIV, HCV, Malaria) and potential future epidemics, but will also prevent and combat diseases like cancer, multiple sclerosis and Alzheimer's disease. Even metabolic diseases (obesity) and behavioural disorders (nicotine addiction) are likely to be amenable to vaccination.

New concepts and emerging technologies

The ambitious quest for answers to some fundamental 'big questions' will drive the development of novel technologies. Moreover, the important forces mentioned previously, e.g. ageing of the populations in industrialised countries, limited raw materials and energy resources and the threat of global warming, are pushing technological developments.

The Big Scientific Questions

Can we combat human disease more efficiently?

Much as for normal cell type specification (see below), there will be reference networks for detailed key regulatory pathways and how they are perturbed in most human diseases. This knowledge combined with sound diagnostics will eventually pave the way to personalised medicine, providing patients with optimum therapies.

What determines cell fate specification and cell type identity?

Despite the great insight gained by the genome sequencing projects, complex gene regulation is still not well understood. Basic research on a variety of model organisms is required to reveal the interplay of the diverse mechanisms controlling genetic, protein and RNA networks that dictate cell fate specifications. By 2030, the molecular makeup and key regulatory processes determining stem cells and fully differentiated somatic cells will be known. There will be reference networks and interactions of distinct hierarchical pathways that discriminate the diverse cell types. These reference networks will be important for tissue engineering, ageing, and other currently unresolved questions (see previous chapter on Biomedicine).

Are we more than the sum of our genes?

The impact of the environment on gene activities has yet to be elucidated. Research (epigenetics, proteomics, metabolomics) will shed light on the interplay of the diverse mechanisms controlling the flux of genomic information and its interactions with the environment. To what extent behaviour is dictated by DNA sequence, by epigenetic differences and by distinct neuronal cell-cell communications is a related, equally challenging question that will be addressed.

Can we describe cell functions and cellular communication by computer programmes?

The ultimate goal of quantitative biology is an understanding of the interactions among biological networks across hierarchies, e.g. an understanding of the pathways of decentralised communication as in plants and centralised neuronal communications (brain directed) found in animals. Efforts in both fields will deliver essential information on the biochemical networks and their dynamics. It will be valuable for biomedical research as well as for an understanding of the interaction of living systems with the environment. Computational biology will evolve from modelling hierarchical interactions to cellular models. The quantitative analysis of complex genetic and phenotypic data will be of crucial importance to the field.

Such data will, for example, provide the necessary link between plant performance in the laboratory and in the field and will thus make the enormous advances in plant genetics and molecular biology applicable to improving plants, e.g. for the production of renewable resources.

Can we understand brain function and plasticity?

The brain offers the biggest challenge to science in this century. Synaptic plasticity, axonal connections and wiring networks demonstrate the importance of cell-cell communications that lie beyond the description of isolated genes. High-resolution imaging will reveal the physical templates and connectivities of how the brain works to translate perceptions, emotions and knowledge. We need to look beyond isolated genes to understand the more complex neurochemical mechanisms and how they are the key to the processes of neurodegeneration and other neurological disorders.

The future will see the breakdown of interdisciplinary borders. It will boost technological innovation which in turn will accelerate basic research, e.g. by miniaturisation and automation. As progress in research and technology is growing exponentially, projections 20 years ahead are at best guesswork. The exponential advancement of semiconductor technology is a model for other technology-driven research areas, the Human Genome Project being the best example: it took more than 10 years and hundreds of millions of euros to sequence the entire human genome. Today, it requires just some months at the cost of about a million euros, and within the next few years chip-based sequencing is expected to take no longer than two days at a cost of roughly 1000 euros.

Technology trends:

Personalised medicine

The authors expect personalised medicine to be a reality by 2030. Reliable diagnostics, including genetic testing, will help optimise therapies with tailor-made drugs and biotherapeutics suitable for defined subgroups of patients. Better diagnostic tools will help to individualise diseases manifesting the same symptoms, but caused by different mechanisms and sometimes only detectable by their subtle genetic variations. High blood pressure is a well-known example. Despite the high costs of drug development, research in this field will continue to grow. The advances in diagnostics and sound knowledge of individual responses to food will also enable personalised nutrition promoting health.

Integration of plant biosciences and microbial biotechnology for the development of a sustainable bioeconomy

The emerging technologies in plant sciences will open new routes: genome sequences of a wide range of wild relatives and hitherto unused plant species combined with bioinformatics will become the basis of smart breeding. Knowledge of the genomes of major plant pathogens will allow us to find novel resistance mechanisms to be employed with various crops. Signalling pathways within plants and between plants and their environment will have been elucidated, *i.a.* by employing methods from chemical biology, and will be applied to optimise plant interaction with their biotic and abiotic environment. High-throughput phenotyping of plants using novel instruments based on nanotechnology and robotics will pave the way towards predictive systems biology in plant sciences.

The expected rapid development in plant biosciences will greatly facilitate the transition to a renewable, resource-oriented economy in the areas of energy, chemicals, and materials – especially when combined with microbial biotechnology. On the one hand, plants will be highly potential sources of new enzymatic functions applicable to microbial biotechnology and will provide specifically designed raw materials for microbial processing. On the other hand, enzymes of microbial origin will be increasingly used in plants to optimise their function (for bioenergy and biorefinery applications), range of products (e.g. bioplastics) and yields under unfavourable conditions that are not suited to food crops.

As our understanding of microbial metabolism improves, there will be more opportunities (employing metagenomics, metabolic engineering, protein engineering, advanced fermenter design, etc.) to modify bacteria, yeasts and fungi to produce new products and increase yields and to develop biocatalysts for novel applications.

Systems biology – from a reductionist view to holistic understanding and construction

The coming years will also see the development of powerful engineering tools such as systems biology and synthetic biology. Modelling, e.g. for designing experiments, will become an indispensable tool of scientific research and will boost R&D. Systems biology will help us to understand phenomena inaccessible to reductionist approaches and will become the key to understanding the mechanisms behind drug activities in mammalian cells and to the construction of minimal organisms. The authors expect systems biology to provide the sound knowledge base that is required for biotechnology to mature from a discovery science into an engineering science. The future vision of a virtual cell, i.e. the *in silico* modelling of cell functions, will remain one of the biggest challenges.

However, the model of a minimal cell, containing only a subset of genes and able to efficiently produce a defined product or to provide a certain physiological output, may not be far away. Robust cellular factories generating hydrogen could contribute to the supply of energy. The first approaches to reconstituting artificial cells from purified components and synthetic cell walls have already been reported. The coming years will see the construction of 'synthetic genomes' coding for the makeup of artificial cells.

Nanobiotechnology and biomimetic systems

Within the next 20 years, the development of synthetic nanosystems will make major strides. Although it may not be possible to fully reconstitute autonomously reproducing systems, advances in nanobiotechnology will enable the development of biomedical implants and man-machine interfaces. These will provide the technological basis for 'smart prostheses' to compensate severe somatic deficiencies. Especially nano-scale mind-machine interfaces connecting brain cells with computers would allow the construction of biorobotic systems fully controlled by the brain. Autonomous bio-mimetic robots emulating the behaviour of humans will be an inherent part of the ageing society. Special service robots will increasingly replace human services at various levels of our everyday life.

Nature will continue to inspire ideas for materials science. The next years will see more biomimetic materials combining many advantageous properties.

Miniaturisation and automation will also continue to drive technological advancements, especially the construction of devices for parallel experiments. Progress will be made by the combination of nanodevices with living cells. This will enable the routine detection of single molecules as well as quantitative imaging in living systems. The performance of miniaturised tomographs and magnetic resonance spectrometers will eventually arrive at microscopic resolutions. Nano-devices will be the key to improving the speed and accuracy of medical diagnosis.

The impact of brain research

Studying the brain by simulation will be a key factor for understanding brain function and dysfunction. In order to devise models that accurately link cellular and subcellular mechanisms to emergent phenomena, computational neuroscience will merge with systems biology for functional models that consolidate our knowledge from the level of molecules to psychophysics. The growth in computer power will allow the exploration of whole brain models for the purpose of drug discovery.

Similarly, biotechnology will be increasingly applied in brain research within the context of brain function and dysfunction. Neuroscientists have already shown that in several brain areas neurogenesis can be stimulated with small chemical molecules, opening the opportunity to produce new nerve cells with drugs.

An implant of a microelectrode array into the brain has enabled a quadriplegic patient to 'will' a cursor to move on a computer screen, and as such offers hope of restoration of function to those with spinal cord damage. In fact, we now know that isolated neurons will function on integrated circuits by interfacing readily with electronic components on microchips. This work will have two major implications for biotechnology: an increased use of implant therapy and the development of man-machine interfaces. Information science will also benefit from research in this field: the need for more energy-efficient computer architectures will drive research on neuromorphing chips which will eventually be the basis of a bio-inspired IT sector.

Nanotechnology will help to develop drugs which can overcome the specific problem of crossing the blood-brain barrier, for example delivering drugs to fight brain tumours.

Any changes in brain function will translate to a change in the individual mind. There will be an increasingly blurred distinction between 'curing' a disease, and changing the type of thoughts and feelings an individual might experience. There is a need for programmes spanning the different levels of brain operations from the genetic to the cognitive level. As biotechnologists will be able to manipulate the human mind with increasing precision, we must be realistic about what is achievable and deliberate about what we actually wish to achieve.

Obstacles and recommendations

The development of a thriving future KBBE faces some serious challenges and obstacles. The workshop participants gave their views on what they regard as the most pressing deficits and made recommendations for priority actions.

Public acceptance

Currently biotech applications in healthcare, industrial and environmental protection enjoy strong support by the European public **(5)** while GMO food and feed are still linked to negative perceptions. Obviously, a better understanding of the potential, the benefits and the value of green biotechnology needs to be supported and actively promoted.

Early analysis of ethical, legal and social implications of emerging therapy options from biomedical research as well as public education is a key issue to be addressed. Scientists have to be more involved in informing the public about the opportunities and the risks of novel technologies.

A well-informed public aware of the opportunities – and the risks – is considered a competitive edge in global competition, and a public involved in developing the agenda of European research policy is a clear vision for the future. The key to improving public acceptance is to demonstrate the value and discuss both the pros and cons of biotechnology in various applications. As there are impressive success stories from biotech research with clear benefits for the consumer - the number is rising at an increasing rate **(6)** - the interest of the media in communicating such success stories is likely to grow; this will help to raise public awareness and acceptance. The case of today's biotech drugs has already proved that this is possible.

However, the following remedies still seem very relevant: intensify the dialogue with the public, address the problems, and stick to the facts. The key persons are scientists, farmers, NGO experts, and opinion leaders who are essential to building trust. It should be accepted that in Europe there will always be two schools of thought about biotech: a more progressive one vs. a very cautious one. Too aggressive campaigns aimed at changing public opinion can be counterproductive.

In the authors' opinion the public debate on GM crops is likely to lose its intensity within the next few years and the acceptance of green biotechnology – especially when applied to the generation of non-food products – is expected to increase. However, a communication strategy and the clear commitment of politicians to raise awareness of the potential and necessity of biotechnology and the KBBE are desirable.

Besides a lack of funding the climate for innovation in the consumer (food) goods sector is not very encouraging. Public acceptance is still an obstacle to the commercial success of personalised nutrition concepts in Europe. Recent polls found that about 80% of US consumers think positively about personalised nutrition, while roughly 50% of Europeans would accept it. These figures are likely to drop when the debate on GMOs comes into play. However, as personalised nutrition will provide individual benefits and is regarded as a matter of personal responsibility, acceptance is likely to increase. As recent polls indicate, even the acceptance of GM plants is expected to grow with the younger generation, whereas resistance to GM animals is expected to remain for a long time. Novel food products that come with clear benefits for the consumer are expected to obtain acceptance due to good performance and safety.

Consumers should be informed of achievements in nutrition research through balanced and transparent information campaigns by industrial and academic researchers.

Making science attractive by increasing public awareness: although there are teaching programmes in place, a better dialogue with the public is needed to explain big questions and benefits/problems in lay terms. The mass media, particularly TV, as well as weekly articles in leading newspapers would be very helpful. It is essential that scientists play a major role in the communication with the public. They should be trained to be able to spark the fascination for science with the young. Through increased communication it would not be unreasonable to establish a new 'science communicator' career path.

Education and research

Despite the exciting perspectives of bioscience research there is a decline in student numbers in Europe which will eventually result in a lack of a trained workforce in the future. Science must become an attractive career option, regain its attractiveness as a main subject at early school levels and be promoted by European top-level research centres that 'breed' Nobel laureates. The lack of attractiveness also correlates with the low ranking of basic science on the political agenda.

The authors suggest increasing the share of science courses in school education at primary and secondary level. These courses need to deliver hands-on experience through the active participation of the pupils and it is believed that they will spark fascination and enthusiasm for science with the young.

A skilled workforce is already a scarce resource today. In the US the number of qualified people looking for biotech jobs has not kept up with demand, according to the US National Science Foundation. For more than a decade only about 11 percent of US college graduates have been taking up science and engineering jobs. Almost 50% of global biotechnology research capacities, in terms of headcount, are located in China, and multinational companies will continue to locate their research at centres of excellence wherever they are.

In order to counter the strong international competition for talented scientists (brain drain) European universities and academic institutions need adequate funding from both the public and the private sector. The current rigid framework of salaries and positions in universities must be overcome in order to win over the brightest students to a scientific career. As biotechnology is a cross-cutting subject university education should bring together engineering and scientific disciplines. Interdisciplinary interaction between subjects must become a natural part of teaching without altering the core of important subjects like chemistry and biology. The university education of scientists should also comprise business-related subjects.

Today, European researchers are usually appointed to more structured and tenured positions when they are almost 40 years of age. This is clearly a deterring signal that will continue to prevent many students from going for scientific careers. Consequently, there should be sounder career options in both academic and applied research that offer competitive salaries and positions.

National or regional initiatives, harmonised by improved ERA-Net-like instruments, should be the nucleus of European research programmes. Research at the European level should be funded only according to scientific excellence, not national quotas.

The concept of the European Research Council (ERC) is considered very helpful in promoting scientific excellence in the future.

Research focused on great scientific challenges dependent on interdisciplinary projects should become the standard in academic life science research. There will be a growing need for joint research that is closely entwined with technology development, CERN and EMBL being successful models in countering the brain drain and lack of well-trained scientists.

The authors' vision is to build a pan-European network of about two dozen small excellent interdisciplinary institutes scattered across Europe (pan-European Institute of Technology, pan-EIT). While not duplicating efforts, the research should focus on the 'big questions' and visionary ideas, be interdisciplinary and integrate the best minds on a competitive basis. Each institute could offer positions for about 6 senior and 12 junior scientists, recruited on the basis of scientific excellence. Employment would be on the basis of flexible, pan-European tenure-track contracts where the selection criteria and evaluation would depend on external peer review.

In comparison to the future network, large-scale research institutions are considered either very hierarchical, framed within national programmes or, in some cases, simply too big. Providing exposure to top-level research, less hierarchical pan-EITs would offer a structured European career path in science to young talented researchers at the PhD student and postdoc level. For example, researchers could do a PhD in Madrid, take on a postdoc position in Munich, hold a junior position in Rome and accept a senior position in Stockholm. Funding for the pan-European EIT network could come from three sources: funds from the member states, the European Commission (50%) and the private sector. Each of the 25 pan-EITs with a staff of around 200 would require an annual budget of roughly €20m. For a 10-year programme, this would amount to €5bn. The EU contribution would then equal €2.5bn, or €250m per year. Replacing the projected central EIT by a pan-EIT network and converting some funds from 'virtual' networks to a real and physically existing network would allow this vision.

A great number of different, well defined, homogeneous populations gives Europe an advantage over the United States. The authors suggest a Europe-wide collaborative effort to identify biomarkers in large studies. Clinical studies and approvals should be adapted to the requirements of new, personalised therapies with smaller numbers of stratified patients. A European centre of excellence in clinical research should be created which would be in charge of benchmarking and the comparison of clinical studies.

More research is necessary to add value to agricultural products and food ingredients, such as enzymes and starter cultures. Research priorities should be food safety, food quality and flexible manufacturing, sustainable production and food chain management. More detailed recommendations are found in the ETP Food for Life Strategic Research Agenda **(7)** Another obstacle is the limited comparability of studies on the physiological effects of nutrition. A long-term strategy for generating and analysing data from large test groups and improved analytical tools for the prediction of markers is a high priority. More precise scenarios and models of food consumption and production will facilitate the development of sustainable food production and also contribute to healthy nutrition. Currently available data are often not adequate for sound analysis and the extraction of valid biomarkers, for either pre-disposition or ingredient efficacy. The application of high-throughput platform technologies and systems biology approaches will make breakthroughs possible. The development of reliable, ready-to-use, and non-invasive diagnostics will support this trend on the consumer side. The foundation of a European Food Research Institute and a network of the few existing institutes is recommended. Such networks should be supported by national co-funding programmes. These centres should advise on, for example, standardisation procedures for clinical nutrition studies and be open to co-operation between academia and industry.

Technology transfer

The main task is the translation of knowledge into products. We need to support a 'culture of commercialisation of ideas' which is – with the exception of some member states - largely lacking in European research. However, a climate stimulating entrepreneurial spirit is essential. Key measures to improve the situation should be taken: promoting university research while raising awareness of the opportunities for patenting and commercial application of the results. The founders of early-stage companies should be encouraged, e.g. by means of tailored funding and by affordable access to the expertise of consultants and lawyers, including outlicencing on fair terms.

Public-private cooperation should also extend more downstream, in particular to enable the development of flexible, research-oriented pilot and demonstration plants to validate new concepts (e.g. integrated and diversified bio-refineries). Europe-wide harmonised IPR protection (see chapter on legal framework below) is needed to overcome hurdles in public-private co-operations.

Compared to their global competitors, European pharmaceutical companies are lagging behind in stem cell research and regenerative medicine. Strong efforts to catch up are needed - in strong alliance with academia and small start-up companies. Research on all categories of stem cells should be supported in order to keep expertise and technology development in Europe.

Funding priorities in the bioenergy and biomaterials sector should include the development of new crops, logistical arrangements in the supply chain for delivered biomass feedstocks, and advanced bioenergy production pathways (BTL, ligno-cellulosic ethanol, co-refining of biofeedstock with fossil feedstocks) at the level of demonstration plants as well as reliable support of first commercial activities.

Financing

Biotechnology is a global technology which competes for financing, as money is the fuel for innovation. Investors need to see the upside potential and have exit options. This requires Europe to bring about improvements: competitive tax incentives will be needed to attract capital from outside the EU and keep European venture capital here. The French and Belgian Young Innovative Companies initiatives (YIC) are good models to adopt. Tax incentives would help to extend the time horizon of investors according to the life cycles of bioindustrial products. As spin-offs from academic research are indispensable to sustaining a biotech sector, they should have priority access to funding. European and national funding programmes providing seed money will be indispensable for a long time.

Besides attractive exit options, capital investors require professional management skills and industry experience of the executives. In particular, VC still shies away from investing in young companies from the white biotechnology sector where business models are often immature and so far not much value creation has been evident. Instead, financing in this sector will continue to come from the big companies of the chemical, pharmaceutical and food sectors – be it through collaborations, partnerships or M&As.

In order to increase the supply of risk capital it seems necessary to match private capital with public funds and loan guarantees through existing instruments, e.g. EIF/EIB and the Competitiveness and Innovation Framework Programme (CIP). The European Investment Bank (EIB) is ready to take higher risks in the financing of growing companies.

Initial public procurement will be necessary to stimulate the development of novel products and technologies in Europe, market incentives should serve to stimulate the commercialisation of bio-based products (temporary pricing measures, labelling). Bioenergy/biotechnology applications can be made more cost-competitive by targeted RD&D, possibly boosted by government support mechanisms, such as loan guarantee programmes to support technology development.

Incentives supporting a greater uptake of energy efficiency - already in place in many member states - are indispensable instruments to reduce the demand for fossil fuels.

Agriculture thriving without subsidies is another vision for Europe in 2030. The continuing support of industrial sectors is not desirable as subsidies usually replace one problem by another. Current agricultural policy is not in line with the goals of sustainable production and healthy food. The authors suggest shifting subsidies from the Common Agricultural Policy (CAP) to support science and research programmes, e.g. on sustainable agriculture and new 'industrial crops'. The heavy dependence on agricultural subsidies as under the current CAP is expected to decline since the integrated production of food, fibre and energy could become profitable in their own right.

Basic research must be strongly supported and budgets for life-science research should be raised. The authors see Europe's bioenergy RD&D programme under-funded by an order of magnitude if desirable rapid progress is to be made to deploy second generation (advanced) biofuels and gasification projects.

The paperwork associated with applications for grants, both EU and national, needs to be simplified.

Costs

Personalised medicine will split up seemingly homogeneous groups of patients into subgroups with different disease patterns. As a consequence, there will be a reduction in the number of patients in clinical trials, e.g. investigating individualised, cell-based therapies. Big pharma companies are currently not encouraged to invest in research on rare diseases. However, despite the low share of patients treated, personalised drugs for chronic diseases could have blockbuster potential.

Biomedical research will eventually amplify the demographic problems related to ageing societies and will have an impact on health insurance and pension schemes. It appears very likely that costs for health care will rise in general and the share of the health sector in the gross national product will increase. However, widely applied personalised medicine will improve the quality of healthcare by earlier diagnosis, more effective prevention, tailored treatment of diseases and lower drug usage associated with reduced drug side-effects. This will eventually lead to more efficient health care services and better control of health care costs.

The economics of the biomaterials/bioenergy sector are not yet well understood on a regional basis given a wide range of variables. Analysis on a project basis is well understood, but in general terms major questions cannot be answered at present as the data of current economic models on such issues as future land use and oil and gas prices have a high degree of uncertainty.[8]

Since both biomass feedstocks and bioenergy conversion technologies are very wide-ranging, assessing their "cost" is complex. Where the feedstock is collected on site as a waste by-product (such as bark, rice husks, coconut shells or animal manures) the cost of disposal can be avoided. Combustion of such waste residues to provide heat and power for use on site can therefore be very competitive with natural gas or coal-fired heat and combined heat and power plants. Conversely, when biomass feedstock is transported 50 to 100 km to the plant where it is converted, the bioenergy cost is comparatively high. Even then the cost range can be vast, as in the case of bioethanol. The production costs of first generation bioethanol at the plant gate, without including any subsidies or grants, can range from US$0.25 per litre of gasoline equivalent (lge) from sugarcane in Brazil to US$0.95/lge from wheat in Europe. The costs of second-generation bioethanol, even when using cereal straw or forest residues as feedstock, are even higher, but they have good potential to become competitive in the future.

Ethanol produced from sugar and starch crops will only be a minor option for Europe. The area of arable land needed to meet Europe's transport fuel demand would be a significant portion of the total area. Even to replace 10% of present European transport fuel consumption would entail using 1/3 of Europe's arable land. With demand outpacing supply Europe would need imports from Brazil and elsewhere that produce ethanol more efficiently from sugar cane. However, once ethanol can be produced commercially from ligno-cellulosic feedstocks, its share of transport fuels could rise significantly due to higher volumes, if produced at a competitive price. There is a considerable amount of waste starch and sugar (for example, incredibly almost 50% of all bread produced in Europe is wasted). This could be processed to ethanol if appropriate collection systems were organised.

More rapid deployment of bioenergy projects would require fossil fuels to become more expensive, whilst the bioenergy alternatives become cheaper as a result of greater learning experience and gaining economies of scale from large commercial plants. For example, without subsidies ethanol produced from corn will only be able to compete with fossil fuels when the price of crude oil has cleared the threshold of around US$120 per barrel.

Legal framework

EU legislation needs to be fully and correctly transposed into national law. In addition, the implementation of EU legislation is not always harmonised across the member states, which leads to inconsistencies, such as diverging national requirements and guidelines. Administrative burdens need to be actively reduced by member states and regulatory procedures should be harmonised through cooperation between member state authorities.[9] Regulatory improvements should aim at simplified, transparent, science-based procedures, while at the same time maintaining a high level of safety. In general, approval procedures should be harmonised and centralised on a European level, avoiding additional obstacles from bureaucracy.

Because of their early stage of development, SMEs face hurdles that are more difficult to overcome than is the case with larger companies. SMEs need help in particular to reduce the cost of IP protection. Ultimately, a single European Community Patent will provide the answer, but in the meantime a specific SME application process, similar to the SME initiative at the EMEA, is needed at the EPO. The single European Community Patent (one language, one agency), in particular, is regarded as helpful in reducing the cost of IP protection.

Regulations pertaining to novel foods should be revised, based on the level of scientific understanding. The experts recommend a "fast track" regulatory process for biomaterials products.

Common European standards for biotechnological research, i.e. stem cell research and field trials with GM plants, and for the protection of inventions should be implemented. The present high European standards of safety and approval regulations for GMO must not be extended with regard to putative health and environmental risks to the detriment of R&D. Testing and registration procedures for GM crops should be made equivalent to the process in the US, regarding both the rules and implementation, in order to support the emerging European plant and forest biotechnology sector.

The removal of import barriers is equally important: European industry must have access to raw materials at world market prices.

European legislators are encouraged to establish a certification system for sustainable production and use of biomass and biofuels in order to make sure that biomass production always complies with good agricultural practice, does not impact on native forests and ecosystems, and ensures a good balance between food and non-food use in adherence to existing international standards and agreements.

Carbon credit schemes for biobased processes, imposing 'carbon charges' on fossil fuels could help to reduce the demand for fossil fuels. Moreover, the producers of biopower (as well as some big producers of bioheat, and biofuels including biogas) need access to the large energy networks under fair and equitable conditions.

Technologies are always prone to misuse. Advanced technologies with controversially discussed ethical and legal implications, like interventions with brain functions (brain doping) or genetic testing, the latter being regarded as indispensable to personalised medicine, will need transparent, balanced and feasible regulation.

Co-ordination

Ideally, politics should stimulate, not react. The actions of the European Commission **(10)** are geared towards ambitious goals. However, the translation into practical steps is often unsatisfactory; more coherent and consistent policies related to KBBE, **(11)** allowing for a high degree of flexibility, are needed.

The European Commission and member states should together improve the co-ordination of policies concerning KBBE. Although competing national activities will certainly stimulate the development of a KBBE, the authors suggest harmonising them by improved ERA-Net-type instruments, ensuring that European R&D efforts are as effective as possible. For example, ERA-Net-like schemes for national bioenergy programmes could help, as do the co-ordinated global research efforts by the IEA through its Bioenergy Implementing Agreement. This would include funding schemes for 'multiple company consortia' to build small-scale plants (biorefineries).

The full implementation of the KBBE-related strategic research agendas (Health Care, Industrial Biotechnology, Plants for the Future, Forestry, Biofuels, etc.) at European and Member State level is essential to the development of a competitive industrial biotechnology sector, the integration of the different technology platforms being a priority.

A clear, enduring commitment by politicians to biotechnology, long-term policies and a reliable regulatory framework are indispensable. A high level representative of the Commission ("KBBE Co-ordinator") should be in charge of implementing KBBE (Research and Development, Healthcare, Agriculture, Environment, Energy, etc.) guided by a "roadmap to KBBE". A more coherent research strategy improving the interaction of the relevant DGs of the European Commission is desirable.

Generally, funding programmes should entail less red tape, which means maximum transparent procedures, less paperwork and bureaucracy, and grant approvals based on scientific quality. Reporting requirements should take into account the limited resources of SMEs.

Resources and sustainability

The vision of a successful KBBE translates into sustainability at all levels: secure income for farmers, reliable sources of raw materials and substantial reduction of greenhouse gas emissions.

Land-use and water supply will be central problems worldwide as the total acreage for food and industrial crops is limited and is likely to decrease over time due to desertification and degradation. Reserving high quality arable land for food production and cultivating high-yield industrial crops on land of lower quality, including 'set-aside' areas in Europe and poorly managed land elsewhere, could be an option. However, the competition for arable land between food and biomaterials/energy production may require political regulation, especially in developing countries which suffer from insufficient food supplies and cannot afford to aggravate any existing food shortage. The import of biomass/ biofuels from developing countries at the expense of food security and the environment must be avoided, the conservation of rainforest being mandatory. Water is likely to become the global limiting factor of agriculture, therefore the production of industrial crops on irrigated land should be discouraged in favour of food crops.

Land-use management for food and fibre production will be an increasingly important issue for agriculture in the future. The increase in global population will be accompanied by a corresponding increase in demand for the current 1.5 bn hectares of arable land (around 10% of total land mass), water and fertilisers. Additional pressure is expected to arise from the cultivation of industrial crops for biomaterials and bioenergy. Progressive desertification and degradation is aggravating the problem. Despite the overproduction of food within its borders, Europe already depends on the import of feed and fertilisers from outside the EU. The efficiency of agriculture needs to be improved without compromising sustainability, e.g. by recovering nutrients from waste (waste management). One efficient way of producing food is aquaculture where the ratio of mass of feed to mass of fish raised is lowest. Efficient use of agricultural waste and raw materials from forests and set-aside land to produce energy should help to save high-quality soils for food production - keeping food prices low. Waste and biomass utilisation technologies will enhance sustainability and increase farmers' income. Biotechnology is expected to contribute to the solution to all these problems by engineering robust, high-yield, self-sustaining plants to survive on poor, arid land.

A 'food vs. raw materials' conflict seems unlikely as long as the productivity of European agriculture can be increased and large areas of set-aside land - a by-product of the current system of subsidies for food production - will come under the plough again.

A secure and affordable supply of biomass feedstock should be achieved through supportive innovation programmes, agricultural policies, and price incentives.

Studies to optimise land use for mixed food and non-food use should be undertaken as in the future it is likely that farmers will demand the flexibility to swap between them as economics and other conditions require.

Competition for limited biomass resources is expected to heat up rivalry between stationary and mobile energy process applications. Biomass for heat or power generation is only one among several renewable alternatives. Biomass for immediate transport fuel substitution is a unique low carbon alternative that negates the need for engine technology alterations or infrastructure investment side-effects.

Work is needed to identify the priority areas for the limited biomass resources and their competing uses (biofuel, bioheat, biopower, biomaterials, biochemicals). Growing concerns about the origin of biomass feedstock and its sustainable production, particularly when imported as vegetable oils, pellets, wood chips, etc., are being addressed by the Global Bioenergy Partnership **(12)** and the International Energy Agency's Bioenergy Implementing Agreement, Task 40 on Trade. **(13)** Major issues relate to producing an international standard for the certification of biomass as being from a sustainable source, and the implications for developing countries of imposing trade barriers.

There are numerous co-benefits from biomass production and bioenergy use. The agricultural sector will be transformed as the need for more plant-derived products increases, especially once the lignocellulose technology bottleneck is removed. Waste land could possibly be cultivated again given a selection of suitable energy crops. Farmers' income is expected to rise; local, decentralised production facilities could help to keep employment in the countryside and to improve social life in rural communities; health benefits from cleaner air emissions are also apparent.

In developing countries the production of biomass, possibly with export potential, could go hand in hand with higher income and local independence, resulting in greater political stability. In turn this would help meet the challenge of fulfilling the United Nations' Millennium Sustainable Development Goals which can only be achieved by improved access to energy supply by the millions currently without.

Participants of the workshops

Name		Institution			Workshop
Aguilar Romanillos	Alfredo	European Commission	Brussels	Belgium	Framework
Baro	Jose	Repsol YPF	Madrid	Spain	Bioenergy
Bausells	Joan	Centro Nacional de Microelectrónica (CNM), CSIC	Barcelona	Spain	New Concepts & Emerging Technologies
Berger	Francois	Centre Hospitalier Universitaire, Grenoble	Grenoble	France	Biomedicine
Bielecki	Stanislav	Technical University of Lodz Institute of Technical Biochemistry	Lodz	Poland	Biomaterials & Bioprocessing
Birkegaard-Staer	Kirsten	Novozymes	Bagsvaerds	Denmark	Framework
Blades	Tom	Choren Industries	Freiberg	Germany	Bioenergy
Bürger	Joachim	Munich Re Group	Munich	Germany	Framework
Carrez	Dirk	EuropaBio	Brussels	Belgium	Framework
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Zabeau	Marc	University of Ghent	Zwijnaarde	Belgium	Bioenergy

Glossary

antagonist drug which inhibits the physiological effects activated by another signalling molecule (agonist)
antibody protein produced by cells of the immune system which bind foreign matter with high specificity
biocatalytic process, biocatalysis processes which employ proteins (enzymes) which specifically catalyse chemical reactions
bioinformatics field involving the use of methods from computing, statistics and mathematics to answer questions in molecular biology
biomarker specific DNA sequence, specific DNA methylation pattern, specific composition of peptides or proteins which are characteristic of physiological states
biomimetics, biomimetic system technical systems imitating biological solutions and inventions
biopharmaceutical pharmaceuticals derived from biological molecules, e.g. therapeutic antibodies, growth factors
bioplastics biodegradable polymers with the characteristic properties of plastics produced by organisms
biorefinery industrial plant or cluster of plants which serve to produce raw materials and fuels from biomass
biosensor device comprising a biological probe (e.g. an enzyme, an antibody or a microorganism) linked to a display via a transducer (electrode, transistor)
blood-brain-barrier protects the brain from harmful substances in the blood stream, while supplying the brain with the required nutrients for proper function.
brain plasticity ability of the brain to adapt to changes: e.g. brain areas may take over some of the function of damaged and non-functional areas
BTL biomass-to-liquid
CAP Common Agricultural Policy, a EU system of agricultural subsidies and programmes
cDNA copy DNA or complementary DNA: DNA obtained from transcription of messenger RNA into DNA (reverse transcription), often used in gene cloning, as gene probes or for the generation of cDNA libraries
cellulosic ethanol ethanol produced by the fermentation of sugars which were obtained from cleavage of cellulosic fibres
CERN Centre Européen de Recherche Nucléaire, the world's leading laboratory for particle physics. It has its headquarters in Geneva.
conventional breeding breeding which does not use genetic engineering of plants
differentiated cell cell which has matured into a specific cell type able to perform characteristic physiological functions
enzymatic hydrolysis enzymatic cleavage of molecules consuming water molecules
enzyme protein which is able to catalyse a chemical reaction (biocatalysis)
epigenetics literally „on" genes, refers to all modifications to genes other than changes in the DNA sequence itself, e.g. chemical modifications like the addition of methyl groups to the DNA backbone.
ERA-Net instrument of the European research policy: the objective of the ERA-NET scheme is to step up the cooperation and co-ordination of research activities carried out at national or regional level in the Member States and Associated States
ERC European Research Council
functional food foods or dietary components that provide a health benefit beyond basic nutrition.
genotype internally coded, inheritable information carried by an individual organism
GM, GMO genetically modified, genetically modified organism
glycosylation chemical coupling of sugars to a (bio)molecule
green biotech biotechnology applied to agricultural processes, including genetic engineering
Human Genome Project global research initiative to sequence the human genome, started in the early 1990s, the first draft (approx. 90%) was published in 2000; a nearly complete version (>99%) is available since 2004.
hydroxylation chemical addition of a hydroxyl (OH) group to a molecule
in silico in the computer
KBBE Knowledge-Based Bio-Economy
lignocellulose main component of wood, consists of cellulose fibres cross-linked by lignin. Lignin makes up about one-quarter to one-third of the dry mass of wood
lipids fats and oils
M&A merger and acquisition
magnetic resonance spectrometer machine measuring signals from atomic nuclei switching between energy levels in strong magnetic fields
microarray piece of glass or silicon onto which molecular probes, e.g. DNA molecules, antibodies, have been attached in an ordered array, used to identify and quantify DNA, RNA or protein molecules present in mixtures
molecular target molecular structure of proteins, DNAs, RNAs or sugars which can specifically bind a drug molecule
mycotoxins toxic substances produced by fungi
nanotechnology a discipline of science seeking to control matter on a scale smaller than 1 micrometer, normally between 1-100 nanometers, as well as the fabrication of devices on this length scale.
nerve growth factor, NGF naturally occurring molecule in the body which stimulates the growth and differentiation of nerves
neurodegenerative diseases e.g. Alzheimer's disease, Parkinson's disease, TSE
NGO non-governmental organisation
odt oven dry tonne, The term "oven dry tonne" derives from the laboratory method used to measure the moisture content of a sample of wood. The method requires that the sample be dried to zero moisture content in an oven.
phenotype the „outward, physical manifestation" of an organism, the phenotype of an individual organism is either its total physical appearance and constitution or a specific manifestation of a trait, such as size, eye colour, or behaviour that varies between individuals
pluripotent cells stem cells which can differentiate to form (almost) any type of cell

porphyrins organic compounds containing four pyrrole rings functioning as a metal-binding cofactor in hemoglobin, chlorophyl and certain enzymes.
post-translational modification chemical modification of a protein after its synthesis
proteins large organic compounds made of amino acids arranged in a linear chain and possessing a defined spatial structure, the sequence of amino acids in a protein is defined by a gene and encoded in the genetic code.
proteome a set of all proteins present in a cell, organelle, tissue, body fluid or an organism under given conditions
psychophysics subdiscipline of psychology dealing with the relationship between physical stimuli and their subjective correlates, or percepts
quadriplegic a symptom in which a human experiences paralysis of all four limbs, although not necessarily total paralysis
R&D Research and Development
RD&D Research, Development and Demonstration
RNA, ribonucleic acid polymer consisting of ribonucleotide monomers, that acts as a messenger between DNA and ribosomes, the sites of protein biosynthesis
single nucleotide polymorphism, SNP DNA sequence variations that occur when a single nucleotide in the genome sequence is altered
siRNA small interfering RNA, a class of 20-25 nucleotide-long double-stranded RNA molecules, siRNA is involved in the RNA interference (RNAi) pathway where the siRNA interferes with the expression of a specific gene
stem cells undifferentiated cells, stem cells can be grown and transformed into specialised cells with characteristics consistent with cells of various tissues such as muscles or nerves
synaptic plasticity is the ability of the connection, or synapse, between two neurons to change in strength
synthetic biology research that combines science and engineering in order to design and build novel biological functions and systems
systems biology study of the interactions between the components of a biological system, and how these interactions give rise to the function and behaviour of that system, the objective is a model of all the interactions in a system (virtual cell)
tissue engineering combination of cells, engineering and materials methods, and suitable biochemical and physio-chemical factors to improve or replace biological functions
virtual cell see systems biology
white biotechnology, white biotech industrial biotechnology, biotechnology applied for the production of chemicals, polymers, fuels

References

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[2] see also Strategic Research Agenda of the SusChem TP (industrial biotechnology section)
[3] calculation based on figures from McKinsey, 2003
[4] see Stern Review, and IEA World Energy Outlook, 2006
[5] see Eurobarometer 64.3 released in May 2006
[6] Bio4EU study April 2007
[7] http://etp.ciaa.be/documents/ETP_ffl_SSRA_240406.pdf
[8] The IPCC – Mitigation 4th Assessment Report, which includes details of biomass and bioenergy costs and potentials will be released in May 2007.
[9] E.g. Directive 98/44/EC on the legal protection of biotechnological inventions, and Directive 2001/20/EC on clinical trials
[10] e.g. Lisbon Strategy, Biomass Action Plan, the EU Biofuels Strategy, the Framework programmes, the Environmental Technologies Action Plan, the European Strategy for Life Sciences and Biotechnology, etc.
[11] biofuels, biomass action plan, climate change and energy policy, GM food/feed regulation, healthcare, sustainable development, eco-innovation and ETAP, etc.
[12] www.globalbioenergy.org established by the G8 at the Gleneagles meeting 2005
[13] www.bioenergytrade.org