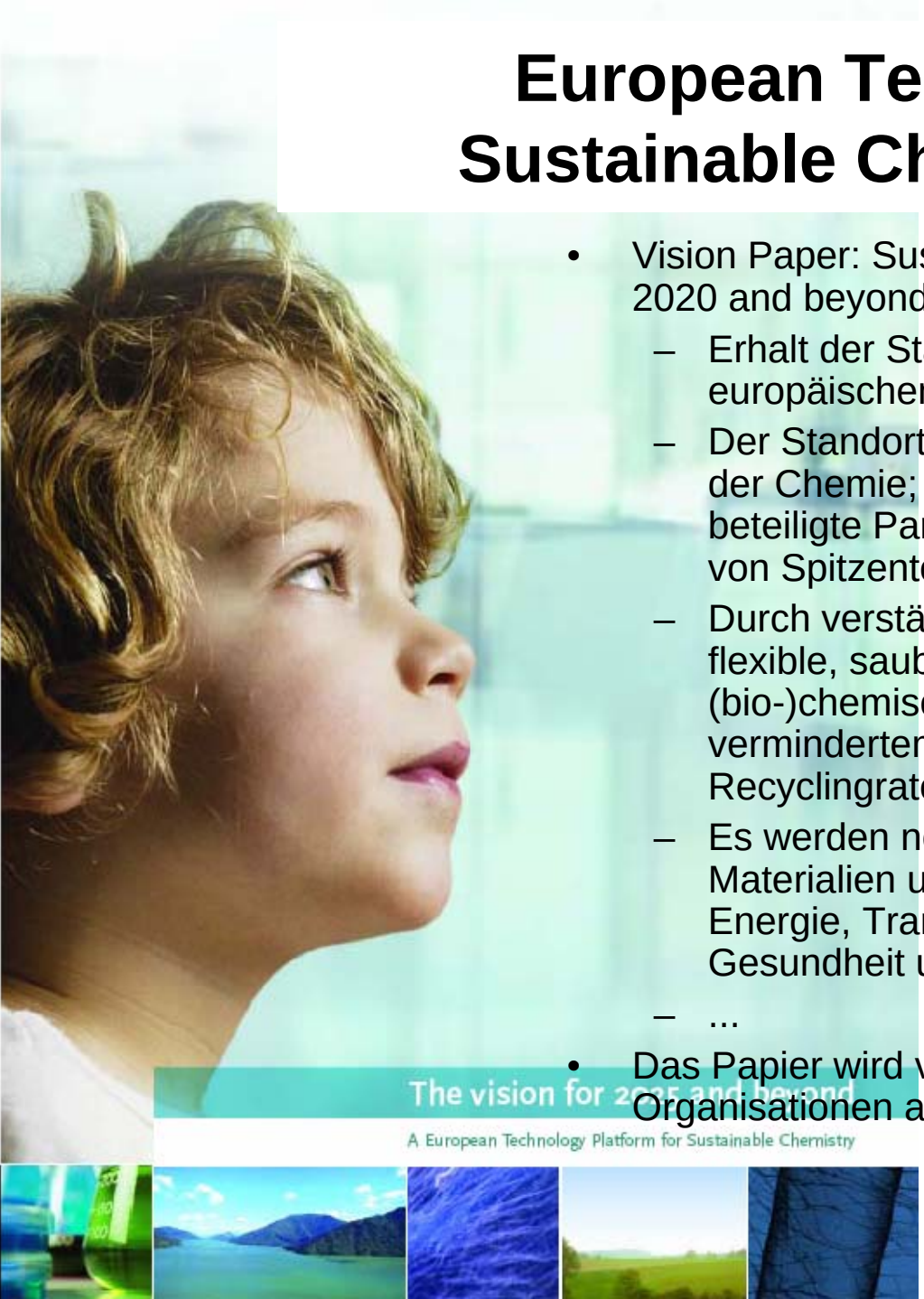
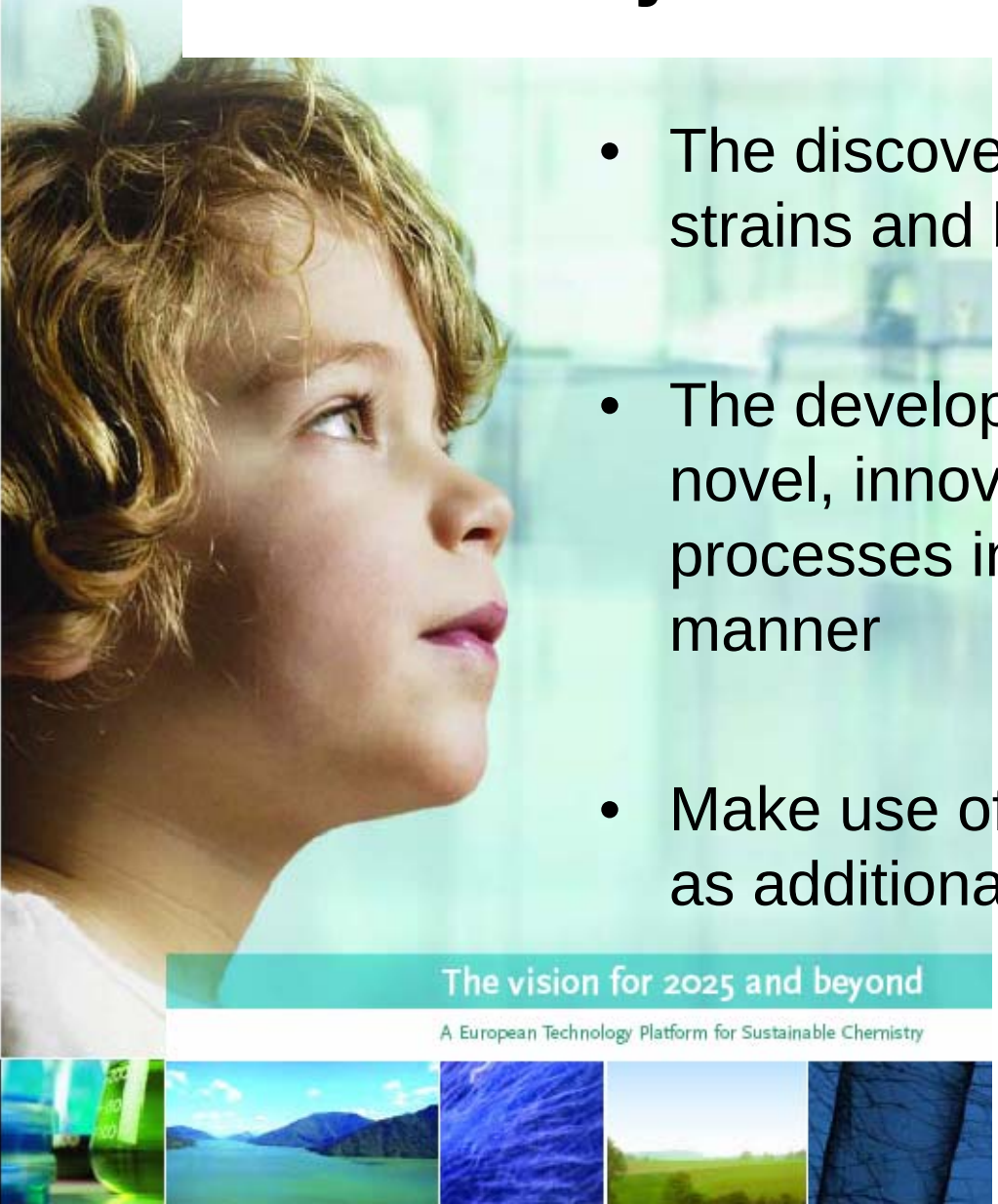
European Technology Platform Sustainable Chemistry – SusChem



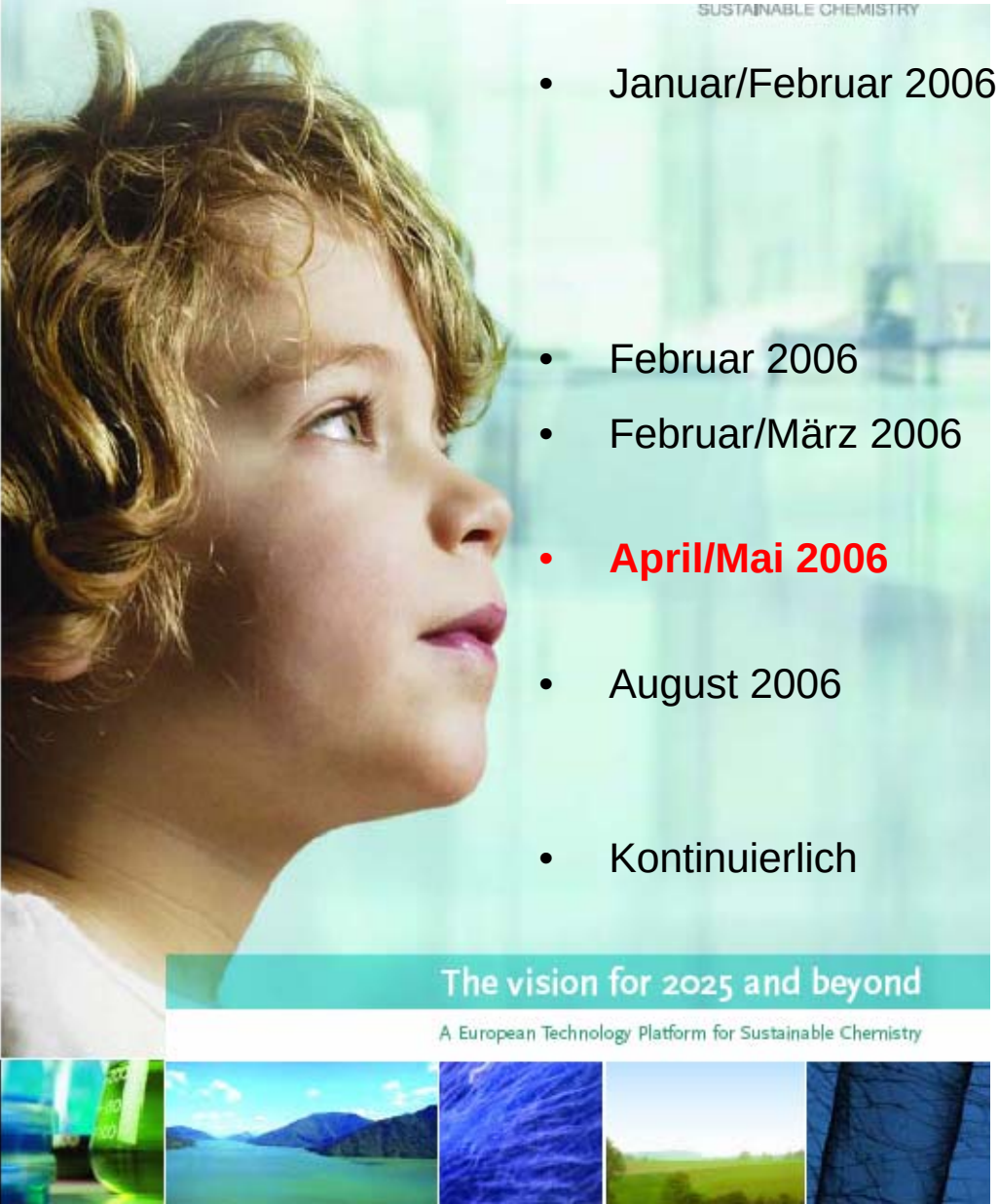
- Vision Paper: Sustainable Chemistry . The vision für 2020 and beyond:
  - Erhalt der Stärkung der Konkurrenzfähigkeit der europäischen Industrie durch Spitzentechnologie
  - Der Standort Europa ist führend für Innovation in der Chemie; alle an der Wertschöpfungskette beteiligte Partner arbeiten an der Entwicklung von Spitzentechnologien zusammen
  - Durch verstärkte F&E werden kosteneffiziente, flexible, sauberere und energieeffiziente (bio-)chemische Prozesse mit hohen Ausbeuten, vermindertem Abfallaufkommen und maximaler Recyclingrate entwickelt
  - Es werden neue funktionale und intelligente Materialien und Komposite für Anwendungen in Energie, Transport, Kommunikation, Elektronik, Gesundheit und Sicherheit entwickelt
  - ...
- Das Papier wird von mehr als 150 Firmen und Organisationen aus Europa unterstützt

Main objectives for R&D in IB



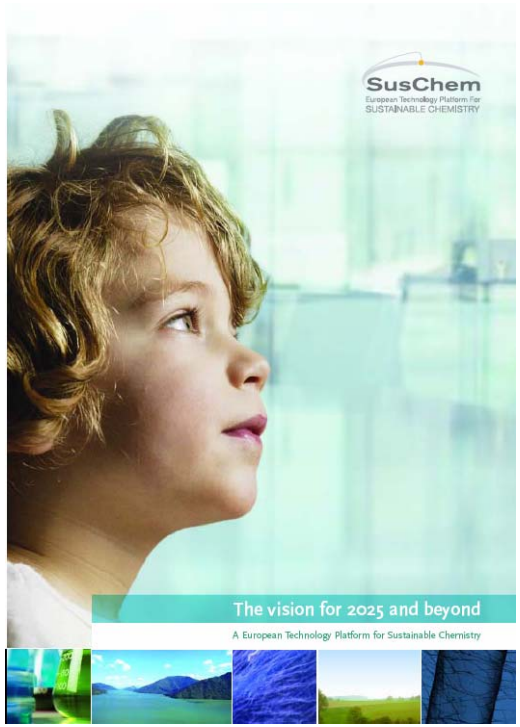
- The discovery and optimization of strains and biocatalysts
- The development and production of novel, innovative products and processes in a cost- and eco-efficient manner
- Make use of renewable raw materials as additional feedstock

Zeitplan



• Januar/Februar 2006	Workshop der drei Technologie-sektionen und der Horizontal Issues Group zur Definition der Fachthemen für den Implementation Action Plan (IAP)
• Februar 2006	Erster Entwurf des IAP
• Februar/März 2006	Diskussion mit anderen Technologieplattformen
• **April/Mai 2006**	**Workshops zur Erstellung des endgültigen Inhalts des IAP**
• August 2006	Vorstellung des IAP im Rahmen des 4. Stakeholder Meetings, 27. August 2006, Budapest
• Kontinuierlich	Diskussion und Interaktion mit der Europäischen Kommission

Industrial Biotechnology



Fermentation science and engineering

Scope

Fermentation engineering is at the heart of industrial biotechnology. Products and active ingredients are obtained by means of the cultivation of microorganisms. The discipline, therefore, is extremely important and has to benefit from novel developments in molecular biology, genome research, microbiology, biochemical engineering, process analyses, computer science and automatic control. Since the modern tools of bioinformatics and genome research will lead to more and more optimised high-performance strains of microorganisms fermentation engineering has to keep pace with this development.

Fermentation science and engineering constitute the workhorse of most bioprocess industries as well as of those industrial sectors making use of one or more bioprocessing steps in their flow sheets. This discipline is at the cross-section of life sciences, chemistry and chemical engineering and has as its focus the implementation of a cellular (prokaryotic or eukaryotic) culture within bioreactor systems on a production scale.

Research priorities

Microbial physiology

The application of specific stresses may sometimes be beneficial. Particular attention should be paid studying the physiology of microorganisms under conditions of extremely slow growth, because the normal fermentation process should yield a maximum of product and not of microbial biomass. Further improvements may result from developing processes working at extreme conditions of temperature and pH, or high substrates and product concentrations, as is crucial for efficient and economical fermentation.

Micro bioreactors for screening

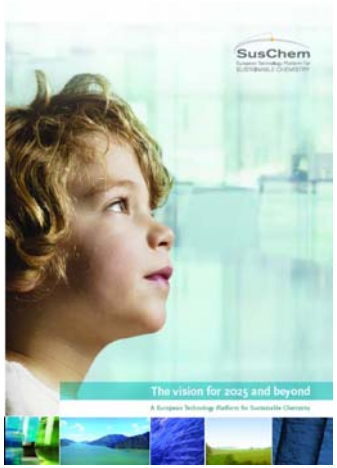
Shortening of process development time is required. This includes, besides a knowledge-based approach, the development of highly parallel cultivation systems in order to be able to converge the development process rapidly into an optimised solution. This is why engineering of microreactors is entering biotechnology. This also means that highly parallel cultivation systems on small scale would have to be run under conditions met in industrial fermenters.

Measurement and control

A better automation of processes goes in parallel with better means of online measurement. Steam sterilisation still restricts the arsenal of analytical tools applied to fermentation processes. However, there are still a lot of interesting approaches, which have to be brought to the level of routine applications. Thus, fluorescence based techniques together with optical fibres are still very promising. Optical analyses combined with numerical image treatment may yield important analytical information.

Combination of systems biology and engineering

The highly parallel techniques of analysis known to end in "-omics" will rapidly increase in importance. Access to, for example, the transcriptome, proteome, fluxome, and metabolome, together with advances in systems biology, will have a dramatic influence on process development for processes of primary importance, although most of these techniques are still far from being applicable as routine methods. However, massive advances may only be obtained when interdisciplinary teams are formed and working together and are receiving feedback of knowledge from each step of process development. Such a strategy would help to avoid carrying out experiments under conditions far from those being expected under process conditions.



Metabolic engineering and modelling

Scope

Metabolic engineering is the improvement of cellular activities by manipulation of enzymatic transports and regulatory functions of the cell, typically using recombinant DNA technology.

This can for example be achieved via:

- Introduction of novel, non-native enzymes (e.g. from extremophiles) in an "optimal" microorganism, which has desirable properties with respect to its specific growth rate, genome, stability, process efficiency, growth requirements, etc., but which is a non-native producer of a certain metabolite. The product range of a popular production strain can thus be enlarged.
- Optimisation of microbial metabolism via manipulation of enzyme levels. Enzyme levels can be altered to redirect the metabolic flux towards a particular metabolite. This entails more than the use of knock-out or over-expression mutants. Nowadays the focus is shifting from massive over-expression and/or respectively inactivation of genes, towards fine tuning.

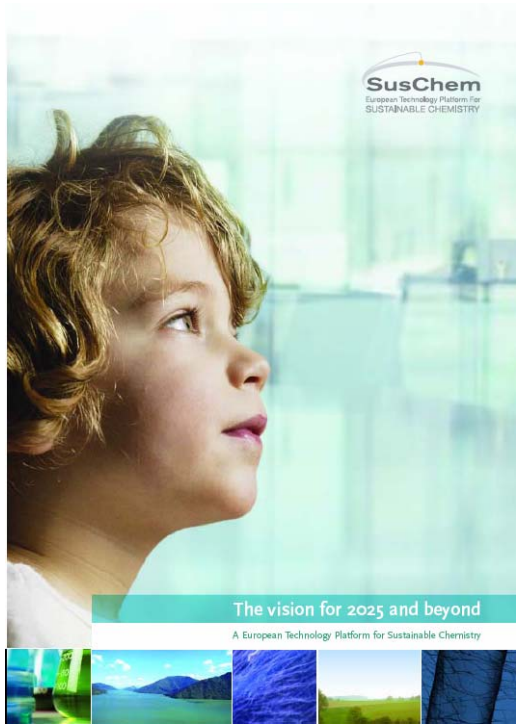
Research priorities

Molecular aspects under industrial conditions - systems biotechnology
The combination of genomics techniques with evolutionary engineering (selection of mutants equipped with new, better and more enzymes) must be exploited. High throughput screening of mutants is required to shorten the development phase of a new process or product. Gaps in the knowledge on the regulatory network of cells via protein-protein interactions, protein-DNA interactions etc. must be filled. This also holds for product export from cells and metabolic compartimentation in eukaryotic cell factories. These and other aspects of cellular regulation should be put into mathematical models. Crucial in this respect is that the information about cellular function should be obtained for conditions prevailing in industrial processes which involve stress, slow growth, fluctuations in nutrient concentrations, mixed substrate utilisation (such as mixtures of D-glucose, D-xylose and L-arabinose, originating from biomass hydrolysis), product formation under "zero growth conditions", kinetics of membrane transport at the extreme conditions in industrial bioreactors, product inhabitation in relation to product recovery, etc.

Industrially relevant products by metabolic engineering
Advanced metabolic engineering research for the efficient production of bioethanol, biomaterials and bulk chemicals, and also of specialties including enantiopure molecules, is required as well as research on the design and invention of new pathways and/or networks with a focus on new non-natural products, and on the extension of the range of industrial microbial production hosts.

Modelling of microbial metabolism
Mathematical modelling of microbial metabolism, directed towards both steady state and dynamic models, including the development of methodological tools, particularly for flux analysis and measurement of intracellular metabolites has to be developed. Special emphasis has to be given to relevant operating conditions.

Reaction & Process Design



Biotechnological processing

Scope

In the past few years conditions for the application of biotechnological processes in industrial production have improved. New tools, such as screening methods and metabolic engineering, and also global analysis methods, such as genomics, proteomics, metabolomics, and bioinformatics tools, are gradually becoming more widely available. These new instruments make it possible to reduce the time needed to develop and establish new industrial biotechnological products and processes; to develop biocatalysts (enzymes) and microorganisms which render manufacturing processes more economical and facilitate new manufacturing processes and, for the first time since the beginning of the oil age in the early fifties, to apply processes with economic potential in the production of basic chemicals and biopolymers. It is time to intensify, extend and implement this new potential of biotechnological methods in industry so that it can hold its own both independently and in synergy with chemical processes. From the very outset biotechnology should be included in decision making as an alternative to chemical processes. It has the potential to replace several chemical process steps by one enzymatic or fermentative production step that is both cost-effective and environmentally benign.

This chapter on biotechnological processing focuses on process technology aspects of industrial biotechnology. It is complementary to Chapter 5 *Industrial Biotechnology* and in several cases describes research priorities, which are also mentioned there. It is the aim of this chapter to emphasize, that the approaches of chemical reaction & process design and biotechnological reaction & process design comprise many parallel elements and synergies. Both approaches will increasingly supplement each other and become intertwined technologies. Further differentiation between biotechnological processing and industrial biotechnology will be subject to the implementation action plan.

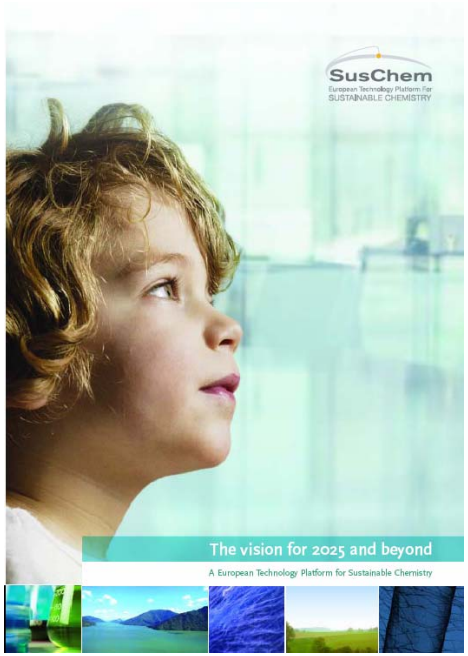
Research priorities

- **Biocatalyst improvement by strain optimisation.** Biotechnological process development must be founded on a broader genomic basis, tapping into the huge number of unknown biocatalysts based on the millions of naturally occurring microorganisms as opposed to the only 100 microorganism strains currently used in approximately 130 industrial processes.

- **New technologies as the basis for novel optimised biocatalysts.** Exploitation of new emerging techniques for quantitative metabolome analysis (metabolic fingerprinting, metabolic profiling), supplemented by technological developments such as pre-calculation of 3D enzyme-structures, development of protein-protein interaction cards based on measurement techniques, and in vivo imaging techniques with reporter molecules to determine complex effects quantitatively and holistically. There is every reason to expect that systems biology is a good basis for new process strategies.

- **More rapid development and industrial application of biocatalysts – shorter time-to-market.** In addition to high throughput screening and selection processes apply thermodynamic principles to the assessment of biotechnological processes (metabolism modelling, downstream processing). This goes hand-in-hand with the need for a high degree of miniaturisation and parallelisation of plant engineering in the framework of micro bioprocess engineering. This explicitly includes downstream processing, which is frequently the main cost factor, although in typical process developments it is often neglected. It is imperative to develop novel downstream processes for low- and high-molecular products and to promote techniques which facilitate the effective identification of suitable purification strategies approaches, e.g., by improved mechanistic understanding.

Materials Technology



Analytical chemistry provides an understanding of the nature of a material through the characterisation of its structure, the measurement of its physical parameters, and the observations of its interaction with other materials and/or environments. The information gleaned in this manner cannot only be used in the development of further new materials, but also in developing new-targeted analytical methodologies. Therefore those charged with the task of promoting advancement in analytical techniques should not only include academics specialising in analytical methods and small-medium-enterprises (SME) who provide analytical services and instruments, but also those researchers working at the frontier of new material technology research and agencies that are responsible for establishing norms and standards. Conceivably these parties could combine their input and expertise into the creation of analytical technique competence centres.

Europe has a strong position within these fields, as it hosts excellent academic research groups within the field, a strong chemical and microelectronic industry providing analytical tasks as well as novel transducer technologies and a range of SMEs that are actually willing and capable of bring chemical sensor systems to the market.

Research priorities

For the development of analytical techniques:

- Development of new single molecule/entity characterisation techniques.
- Development of new high-volume throughput, fast analysis techniques.
- Development of new instrumental methods for the analysis of emerging material technologies.
- Development of the ability to monitor at an atomic level the nucleation and growth of nanostructured materials, this is necessary to validate the models of synthesis, to predict structure and composition of the nanomaterials, including catalytic mechanisms.
- Provision of a framework for the promotion of the development of norms and standards.
- Development of reference materials.