ESF Marine Board Position Paper 4

# Marine Biotechnology

## A European Strategy for Marine Biotechnology

Marine Board

ESF Marine Board
Feasibility Study
Group Report

*December 2001*

The European Science Foundation (ESF) acts as a catalyst for the development of science by bringing together leading scientists and funding agencies to debate, plan and implement pan-European scientific and science policy initiatives.

ESF is the European association of 67 major national funding agencies devoted to scientific research in 24 countries. It represents all scientific disciplines: physical and engineering sciences, life and environmental sciences, medical sciences, humanities and social sciences. The Foundation assists its Member Organisations in two main ways: by bringing scientists together in its scientific programmes, EUROCORES, forward looks, networks, exploratory workshops and European research conferences, to work on topics of common concern; and through the joint study of issues of strategic importance in European science policy.

It maintains close relations with other scientific institutions within and outside Europe. By its activities, the ESF adds value by cooperation and coordination across national frontiers and endeavours, offers expert scientific advice on strategic issues, and provides the European forum for science.

**ESF Marine Board**

The Marine Board operating within ESF is a non-governmental body created in October 1995. Its institutional membership is composed of organisations which are major national marine scientific institutes and funding organisations within their country in Europe. The ESF Marine Board was formed in order to improve co-ordination between European marine science organisation and to develop strategies for marine science in Europe.

Presently, with its membership of 24 marine research organisations from 16 European countries, the Marine Board has the appropriate representation to be a unique forum for marine science in Europe and world-wide.

In developing its activities, the Marine Board is addressing four main objectives: creating a forum for its member organisations; identifying scientific strategic issues; being the voice of European marine science; and promoting synergy among national programmes and research facilities.

# Marine Biotechnology

## A European Strategy for Marine Biotechnology

***ESF Marine Board Feasibility Study Group Report***

## Contents

# Foreword

One of the core activities of the ESF Marine Board is to identify, review, and publish Feasibility Study Group (FSG) reports on emergent and exciting R&D themes in European marine science and technology. Recent reports have covered marine biodiversity, deep-sea drilling and strategy for marine science.

Marine biotechnology is a scientifically fascinating and economically expanding enterprise which harnesses the enormous but uncharted gene pool and functional diversity of marine life towards finding new genes, organisms, biosensors, natural products, and unusual biochemical processes of importance to industry, nutrition, medicine and the environment.

Marine aquaculture is now a mature and highly successful example of marine biotechnological activity in Europe. Its R&D focus is increasingly shifting from engineering/ husbandry/nutrition to environmental sustainability of prolific aquaculture.

Microbial extremophiles abundant in deep hydrothermal vents, sub-seafloor sediments, hypersaline lagoons, methane seeps, and endosymbiotically within marine animals, are ideal targets for bioprospecting unusual and efficient enzymes and drugs.

This report outlines R&D priorities in marine biotechnology which could strategically refocus Europe's extensive but dispersed infrastructure into concerted action. This initiative could benefit from catalytic and directed funding from EU's Sixth Framework Programme.

This report goes beyond the normal Science review to suggest European and National actions and policies to accelerate implementation of a European Vision for Marine Biotechnology.

I would like to thank the chairman, Professor Harlyn Halvorson and the members of the Feasibility Study Group, who willingly gave of their time and expertise in preparing this excellent and timely report on marine biotechnology. And finally, I would like to acknowledge the support of the International Marine Centre (Sardinia) and the Marine Institute (Ireland) for hosting Working Group meetings at Torregrande (November 2000) and Galway (July 2001) respectively.

**Fauzi Mantoura**
***Chairman, ESF Marine Board***

# Executive Summary



For the last two decades the common conclusions of international fora considering strategic challenges in science have uniformly identified the marine biotope as a large and untapped area for exploration. The rich diversity of marine form and function, and its unique physiological adaptations to the harsh marine environment coupled with new developments in biotechnology, has opened up a new and exciting vista for the extraction of bioactive products of use in medicine, novel industrial processes and environmental monitoring. Yet to this day no concerted and focused initiative to realise this vision has materialised in Europe. Current events and needs suggest that now is the time for such action.

A European initiative in marine biotechnology will mobilise the current human capital currently dispersed throughout different countries and addressing issues in a stoichastic and disjointed manner. A common European endeavour in marine biotechnology will encourage a new generation of young scientists to contribute their talents and energy to the field and thus further its success. The urgency of the problems in terms of human health and nutrition, environmental impact, and also a new ability to understand and further biodiversity and balanced reproduction, add to the attraction and potential of this initiative. The combined expertise of many fields from biology to chemical and physical oceanography will be needed in order to understand how life and its propagation is shaped by the parameters of the marine biotope. A European initiative will integrate these activities with clear synergies and enthusiasm stemming from a new focus, and with broad appeal to industry, to biomedicine and to society at large.

## Key objectives

- To promote the development of marine biotechnology in Europe in order to extend and enhance existing marine and biotechnology industries.
- To identify the opportunities and R&D requirements to establish Europe and European expertise in the evolving area of developing novel marine bioactive products and marine bioscreening.
- To improve contacts and collaboration between molecular biologists and traditional marine biologists and between marine biotechnologists and industry.
- To support the inclusion of marine biotechnological R&D in future European Union Framework Programmes.

## Implementation

Some means of implementation follow directly from the objectives, but some can be further expanded:

1. Include biotechnological aspects and techniques in surveys of organisms sampled by inexpensive devices with research vessels.
2. Investigate marine organisms for their capability to produce novel bioactive substances. Establish networks between laboratories with special competence to screen for selected effects.
3. Optimise culture conditions for bioactive substance production by the organisms, and study how this production is regulated on a molecular level.
4. Improve primary culture conditions and the large-scale culture of marine microorganisms and of cells from marine multicellular organisms with potentially interesting properties.

5. Organise and establish a European bioscience marine network, including Web-based services where participants are invited to join and to interact with other European laboratories. Particularly important will be the encouragement of cooperation opportunities between traditional marine biologists and biotechnologists, and between basic scientists working on potentially commercially exploitable findings and industry. Other related European or international organisations should be invited to give information about their activities to the network.

This strategy is suggested by the European Science Foundation Marine Board Feasibility Study Group on Marine Biotechnology as a blueprint for the implementation of a Marine Biotechnology Plan applicable at European, regional, and member state level.

If implemented, the Feasibility Study Group believes that the benefits to be derived across a diverse range of sectors, including quality of life, novel industrial processes, increased food supply, environmental protection and sustainable development of natural resources, are considerable.

## Vision

Life originated in the sea and has sustained itself to the present day. The world's oceans comprise the largest part of the biosphere and contain the most ancient and diverse forms of life. The marine biotopes contain an unmatched metabolic and organismal diversity. Over billions of years marine microorganisms have moulded the global climate and structured the atmosphere. The quantum leap of our understanding of life during the last five years through the advent of genomics and bioinformatics at an organismal, cellular, or genetic level, has opened new perspectives.

*Our vision for the 21st century is that marine biotechnology will apply advanced tools from molecular biology and information technology to a carefully selected suite of marine habitats and organisms represening the total diversity of marine systems, in order to obtain novel genes and processes that can be turned into new products and approaches for the benefit of industry, biomedicine, and the sustainable use and management of the world's oceans.*

**Marine biotechnology could provide entirely new products from the sea and new ways of exploiting marine resources while providing improved technologies for the existing aquaculture and fishing industry, and help us to monitor and harvest the diverse marine resources in a more predictable way.**

**Marine model systems could provide new insight into basic biological principles that will benefit further development of medicine and industry.**

### European infrastructure and marine networks

Research activities in marine biotechnology can draw upon an already extensive infrastructure as well as accumulated knowledge concerning marine ecosystems, populations and organisms regarding where to find them as well as how to cultivate them.

For well over a century, a network of European marine stations, and marine/oceanic institutes, assisted by well-equipped research vessels, has been collecting information about the marine biota, its populations and their biology. This was driven by the need to acquire accurate assessments of fish stocks for sustainable fisheries, and for the study of biological features of marine organisms of commercial or scientific interest. With the growing importance of marine science and the emergence of the rapidly expanding aquaculture industry, the number of modern and well-equipped marine research stations has increased. These stations and their infrastructure (including research vessels) will also be important instruments in the cultivation of and study of marine organisms for biotechnological purposes.

New methodology emerging from rapid advances within molecular biology make it possible to study and utilise new aspects of marine life at a molecular or genetic level. This has resulted internationally in the establishment of a number of research centres focused on marine biotechnology, successfully merging methods of molecular biology with the experience from marine biology. Particularly during the past decade, governments and industry have recognised the importance of establishing interdisciplinary research centres focusing on marine biotechnology. This development has been an important factor in the growth of marine biotechnology, since new scientists will have easy access to already existing model systems. Moreover, scientists can draw on already established regional or international cooperation and initiatives and thus will have access to previously unavailable model systems. A number of organisations and meetings have been instrumental in facilitating and accelerating such endeavours (see Appendix 1).

Europe is well equipped with research stations and vessels, and thus the scientists have relatively easy access to a rich variety of marine life from the Mediterranean to the Arctic. Through regional and international cooperation European scientists will also have access to biota and experimental models of all the world's marine resources.

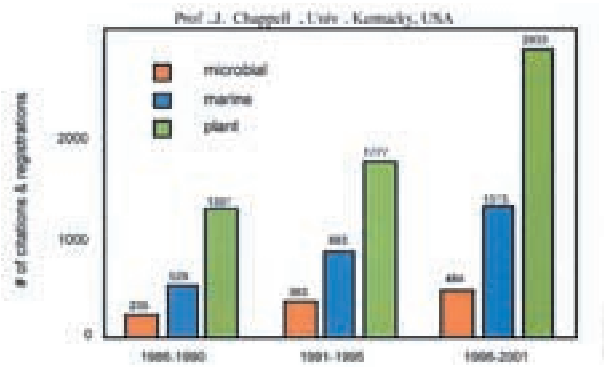
Italian CNR research vessel Urania.
© CNR

## Benefits from Marine Biotechnology

For millennia, the oceans have been a source of food, minerals and natural products. However, as populations and human needs continue to increase so too do the pressures on resources. If we are to meet these growing needs by taking advantage of the oceans' bounty, while protecting our marine environment, and maintaining biodiversity, we must commit ourselves to a programme that will build on our current scientific achievements and develop European expertise for the future. Europe has the resources and the means to develop these resources, but they cannot be exploited in a balanced manner until we "see them better" through the magnifying-glass called science!

The sea contains a wide and largely unexplored diversity of life and environments (see *A European science plan on marine biodiversity,* EMaPS Position Paper 2, 1998). Marine organisms represent a dramatically different environment

**The publication and registration rates of natural products is increasing**



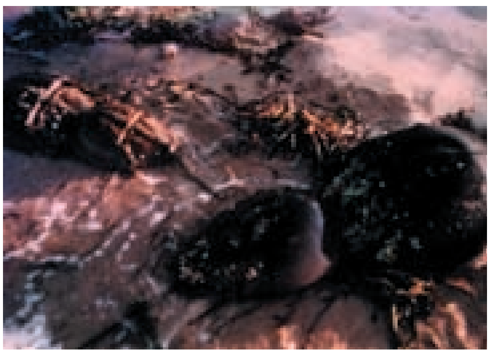

for biosynthesis than do terrestrial organisms and therefore represent a vast untapped resource with potential benefits in many different areas such as medicine, aquaculture and fisheries, industry, research tools and environmental applications. In order to expand and compete, the biotechnology industry constantly seeks new or improved sources of products. The infrastructure and expertise are available for large-scale bioprospecting in order to identify and collect a variety of organisms or genes of potential use. Bioscreening then selects out those with the most desirable characteristics. Sources include microorganisms, plants or animals which may be harvested or cultured.

A commitment to research and to development in marine biotechnology will respond to the critical needs of society by:

1. developing novel drugs for treating disease;
2. producing diagnostic devices for monitoring health;
3. providing new techniques to monitor and assess, restore, protect and manage marine environments;
4. ensuring sustainable and safe aquaculture and fisheries;
5. discovering new types of composite materials, biopolymers and enzymes for industry.

## Developing novel drugs for treating disease

The potential applications offered by the screening of marine substances extend to pharmacology, agrochemistry and the environment. Moreover, the use of combined approaches enhances these possibilities because marine molecules often belong to new classes without terrestrial counterparts; for example, halogenated compounds. High-throughput screening techniques are particularly suitable for such combined approaches. In addition, marine microorganisms are a source of new genes, the exploitation of which is likely to lead to the discovery of new drugs and targets. Secondary metabolites produced by marine bacteria and invertebrates have yielded pharmaceutical products such as novel anti-inflammatory agents (e.g. pseudopterosins, topsentins, scytonemin, manoalide) anti-cancer agents (e.g. bryostatins, discodermolide, eleutherobin and sarcodictyin) and antibiotics (e.g. marinone). Melanins have a range of chromophoric properties that can be exploited for sunscreens, dyes and colouring. They also sequester different kinds of organic compounds, inducing fungicides and antibiotics, which may allow them to act as slow-release agents.



The lysate from the horseshoe crab provides the major assay for bacterial endotoxin.
© Associates of CAPE COD Inc.

| Examples of commercialised medicines from marine organisms | | | | |
|---|---|---|---|---|
| **Chemical name** | **Origin** | **Activity** | **Type of molecule** | **Year of commercialisation** |
| Cephalosporins | *Cephalosporium* sp. marine fungi | Antibiotic | β-lactam | 1965 |
| Cytarabine (Ara-C) | *Cryptotethya crypta* Sponge | Antitumoral (cytostatic) | Nucleoside | 1972 |
| Kainic acid | *Digenea simplex* Red alga | Anthelmintic Insecticide | Amino acid | Early 1900s |
| Spongoadenosine (Ara-A) | *Cryptotethya crypta* Sponge | Antiviral Herpes | Nucleoside | ? |
| Ziconotide | *Conus magus* Mollusc | Analgesic | Peptide | 1999 |

Antioxidant peptides have been isolated from protease digests of prawn muscle, and the mycosporine amino acid (MAA) precursor, 4-deoxy-gadusol, has been isolated from seaweeds; these have applications as food additives and in cosmetics.

Also, the development of new cell-culture techniques from marine organisms will allow the sustainable production of novel drugs and other marine products. This will be accomplished through an improved understanding of the biology of potentially useful species, an ability to induce production of the desired compound, and the development of immortalisation strategies for cell lines and scale-up procedures.

A “living fossil”, the horseshoe crab, has furnished us with useful biochemicals and insights. Its circulating cells (amoebocytes) contain molecules that react with the lipopolysaccharide of Gram-negative bacteria, and thus has been of use in detecting early infection in humans as well as traces of LPS (pyrogens) in biotechnological products. That this ancient creature has an effective defence against bacteria is no surprise, considering that it thrives in areas where it is exposed to large numbers of them. Yet it has no conventional immunity – as we know it – such as memory and adaptability. Even so, the horseshoe crab contains molecules, lectins, that take part in defence reactions. Lectins are found in all invertebrates, and in some structural and functional properties one class resembles certain proteins (CRPs, pentraxins) that constitute the acute-phase defence against infection in mammals. However, in invertebrates, and in most fish species, these molecules do not partake in any acute-phase reaction. Thus the study of such molecules and mechanisms can yield new insights into the ancient defence systems against bacteria – and to evolution. Moreover, lectins as biochemicals are currently being used to target cancer cells, screen bacteria and immobilise enzymes.

**Examples of products from marine organisms**

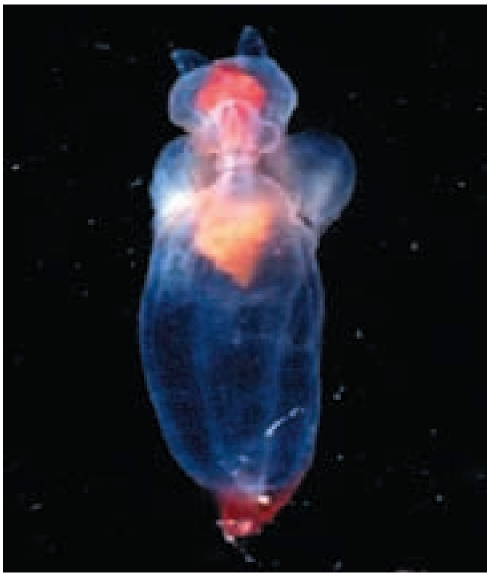
| Products | Specific product | Source | Uses | Enterprise / trade name |
|---|---|---|---|---|
| Algal polysaccharides | Carrageenans<br>Agars<br>Alginates | Red algae | Cosmetics, thickener, pharmacy,<br>Mucoprotector<br>Anti-coagulant, antiviral | Marine colloids USA<br>Danisco Denmark<br>SOBALG France |
| Glycosamino-glycans | Chondroitin sulfate | Fish | Cosmetics<br>Tissue replacement<br>Anticoagulant | CTTP ( France) |
| Collagen | | | Cosmetics<br>Artificial tissue | |
| Chitosan | B (1-4) N-acetyl glucosamine | Crustacean shells<br>Fungi | Cosmetics, colloids<br>Pharmacy, microencapsulation | |
| Lipids | Long chain PUFA (AA, EPA, DHA) | Microalgae, seaweed<br>Fish | Prevention of heart disease, mental development in premature children<br>Antitumoural<br>Lipid metabolism | BIONAGROL 3000<br>AGE OMEGA 3 (Arkopharma)<br>MAXEPA (Pierre Fabre Medicament) |
| Peptides | Hormones, cyclic peptides | Fish hydrolysates | Antioxidant<br>Immunostimulants<br>Nutraceutical products | Promarine |

## Producing diagnostic devices for monitoring health

Microorganisms provide the basis for development of sophisticated biosensors, and diagnostic devices for medicine, aquaculture and environmental biomonitoring. Intact cell preparations and isolated enzyme systems for bioluminescence are used as biosensors. The *lux* genes encoding these enzymes have been cloned from marine bacteria such as *Vibrio fischeri* and have since been transferred successfully to a variety of plants and other bacteria.

The encoded enzymes are expressed only under defined environmental conditions. Other bioluminescent proteins from marine organisms are also currently under study in order to produce gene probes that can be employed to detect human pathogens in food, or fish pathogens in aquaculture systems. Green fluorescent protein, a naturally fluorescent protein first found in the jellyfish *Aequorea victoria* is now widely employed as a sensitive fluorescent molecular “tag” to identify and localise individual proteins within a cell or a sub-set of cells within a tissue and to follow gene expression in various systems. Thermostable polymerases, such as Taq and Vent from aquatic extremophiles, *Thermus aquaticus* and *Pyrococcus furiosus*, are commercially available enzymes used in molecular biology.

Understanding of genome properties and function is a fundamental task in modern bioscience and will have a major role to play in



Bioluminescence. © Steven Haddock, The Bioluminescence Web Page Image

many aspects of marine biotechnology. Genome studies of model freshwater fish species, e.g. fugu, medaka, zebrafish and tilapia as well as important fish in Europe e.g. carp and catfish, are related to marine biotechnology. Genome analysis of marine bacteria, e.g. Vibrio, will facilitate the use of genes for cell factories and bioindicator strains as well as identification of new drug targets. It is hoped that new useful genes and regulatory mechanisms will be discovered. Mechanisms of molecular evolution with possible implications for genetic engineering will thus be better understood.

## Providing new techniques to monitor, assess, restore, protect and manage marine ecosystems

One of the first tasks in documenting naturally occurring microbial diversity is to assess accurately both the variety and the variability of organisms present in any specific habitat. It is estimated that less than 0.1% of marine microorganisms can be readily recovered by standard cultivation techniques. However, this problem may now be approached by the application of molecular phylogenetic analyses. Phylogenetically informative genes can be isolated from nucleic acids extracted from mixed microbial populations. These genes can be clonally isolated, sorted and sequenced using standard molecular biological tools.

Marine microorganisms, either as independent strains or as members of microbial consortia, express novel biodegradation pathways for breaking down a wide variety of organic pollutants. Several such consortia have been described but many others should be explored. This will lead in turn to the extensive development and subsequent control of such bioremediation processes in shaping new applications in environmental biotechnology. Moreover, in addition to biodegradation, marine microorganisms frequently produce environmentally friendly chemicals such as biopolymers and non-toxic biosurfactants that can also be applied in environmental waste management and treatment. Recent findings into the basis of cell-cell communication have shown that this process is involved in biofilm formation leading to environmental corrosion and plugging. This has generated a search for new bioactive molecules that prevent such communication and control subsequent fouling. In addition, further understanding of the interaction of marine microbes with toxic heavy metals or radionuclides has suggested their use in various biosorption, bioprecipitation and biocrystallisation applications for treatment of contaminated water systems.

Marine microorganisms are frequently adapted to survive at very different substrate concentrations. Thus they may change between dormant, starving cells floating free in the oceans and more bulky adherent forms on marine biological surfaces. The majority of marine bacteria adhere well to surfaces, and may colonise some hosts with high specificity. Yet we know very little about host-adhesion properties of marine bacteria. Such knowledge may also have implications for understanding pathogen interactions and epidemics in the marine environment. Bacteria that are pathogenic to humans (e.g. *Vibrio cholerae*) or to fish (e.g. *Vibrio anguillarum*) may be specifically bound to shellfish as part of the resident, normal microflora of these organisms and in this way may help us to understand why shellfish can act as vectors for fish and human pathogens.

Overuse of broad-spectrum antibiotics, particularly in hospitals, has resulted in the emergence of antibiotic-resistant pathogens, and also in dramatic (and dangerous) changes in the normal, protective microflora of some patients. A similar threat, of course, applies to aquaculture that has also used great amounts of antibiotics. There is a constant need to find new, effective antibiotics. But there one must also start to employ different strategies such as antiadhesion therapy, antimicrobials targeted at selected pathogens (microflora management) or the use of competition, antagonism and probiotics in the constant struggle against pathogens. This will particularly apply to aquaculture – animal husbandry in an aqueous medium. However, as regards host interactions, the marine environment may also furnish models applicable to human medicine.

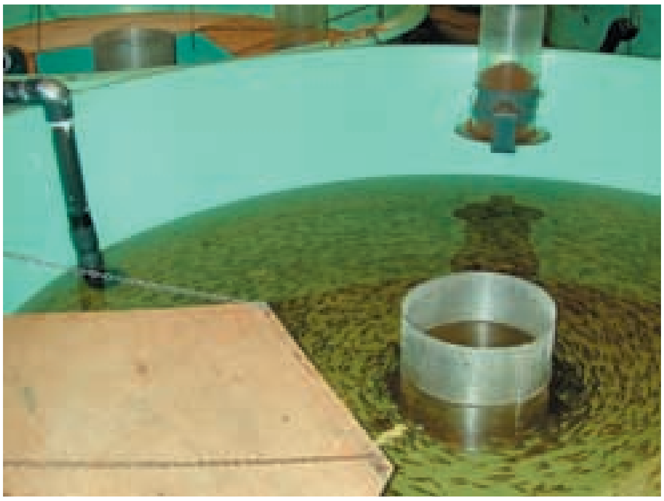
An increased understanding of marine ecological systems will allow the specification of the “normal” baseline level of their biological function, the monitoring and prediction of potential changes or biological impacts on the systems. Marine ecology research will benefit fisheries management. Biotechnological tools can now be used to determine the effect of natural and anthropogenic perturbations on commercial stocks, to propose management tools, to determine predator-prey relationships and to restore habitats. The development of predictive models for analysing potential global climate changes depends on the acquisition of fundamental information on molecular regulatory mechanisms of plankton growth in the oceans.

## Ensuring safe and sustainable aquaculture and fisheries

Exploitation of fisheries’ resources has increased at a rapid pace and needs to be controlled. Overfishing interferes with marine ecosystems and has resulted in landing quotas. Rational enhancement of populations by stocking and mariculture may be used to overcome limitations in marine food production. Supportive breeding and hatchery production of alevins for release into the natural environment accompanied by tagging and supported by molecular tools has been tried. Populations of anadromous and marine species such as salmon, sea trout, turbot and many others including shellfish (e.g. mussels) have been increasingly enhanced with dramatic benefits to the fishery and recreational industries. This biotechnology is also used for restitution of endangered populations and species. However, artificial enhancement of natural populations can also inflict negative consequences. To avoid this, molecular techniques should be more commonly used and research into better understanding of reproductive systems and conservation of genetic resources is essential.

The exploitation of fish resources needs to be controlled to avoid overfishing and crude and inadequate implementation of landing quotas.

The improvement of cooperative daily contacts between molecular biologists, geneticists and traditional biologists and ecologists allows the use of molecular markers to discriminate individuals, populations, stocks and sister species of commercially important or endangered species. Among molecular probes, species-specific or highly polymorph genetic markers such as mitochondrial DNA fragments (16S rDNA, D-loop) or nuclear probes could be easily isolated and amplified, then characterised by electrophoresis and sequencing to provide useful tools to identify the individuals, to survey populations and to assess accurately both variety and variability of living organisms.



Salmon hatchery. © Marine Institute, Ireland

Aquaculture can supply high-quality food in a sustainable way. The main issues of concern for improving aquaculture production are species diversification, optimal feeds and feeding, health of cultured populations and resistance to diseases, as well as minimal environmental impact. Promising new techniques include development of molecular-marker-assisted selection, family and mass selection programmes, finding new molecular markers to be used in parent and pedigree analyses, and the use of triploids in hatcheries. Investigations into the use of marine microorganisms as probiotics in aquaculture are resulting in improved fish health and production.

Molecular biology techniques can be used to monitor genetic improvements using traditional breeding methods. Under controlled conditions genetically modified organisms (GMOs) with particularly useful features such as fast growth, resistance to pathogens or low-temperature tolerance can be made available for basic research proposals by recombinant technology. Comparable gains can be achieved by classic or molecular-marker-assisted selection programmes performed under hatchery conditions. Transgenic technology, while providing a tool for stock improvement for aquaculture purposes, is not widely used because of customer concerns regarding GMOs.

Polyculture, an integrated system of culture of different species in which the waste of one species provides food for another, achieving water filtration, removal of organic matter and increased production, is used in some instances for overcoming environmental problems and aiding in parallel production of other useful products such as bivalves, seaweeds, and high-protein phytoplankton biomasses.

The continuous expansion of the human population generates an increasing demand, not only for high-quality protein but also a need for the upgrading of fish species or fish remains (skins, viscera, heads etc.) or shellfish (e.g.wastes of squid viscera, oyster, mussel) or of undesirable molluscs (e.g. the slipper limpet). At a global level, directly accessible marine biomass represents up to 100 million tonnes per year of fish, crustacean and molluscs from fisheries and aquaculture. This represents about 10% of the animal protein consumed by humans. From this huge quantity of potential food and biological molecules it is estimated that more than 50% is waste or underutilised.

Currently, some non-edible fish, fish-filleting residues and various discards (unsold stocks) are treated industrially for the production of fishmeal. However, this biomass is also an important source of biologically active molecules possessing unusual properties. Specific commercial successes have been achieved and there are promises of further applications in various areas.

Extracts, hydrolysates and enzymes from seawater fish species and marine invertebrates have revealed interesting characteristics. In particular, many marine enzymes have characteristics deviating significantly from their mammalian counterparts. Most important is the activity-temperature relationship; high activities are obtained at 5-12°C for enzymes of marine origin, instead of 30-35°C for classical mesophilic systems. Hence, these enzymes are suitable for optimal processing at low temperatures.

Enzymatic hydrolysates of fish, molluscs or shellfish are known to display antioxidant properties. Free radicals play a major role in various diseases, for example, ischemia, cancer, and Aids. Nutritional studies show that some compounds (peptides, amino acids, and fatty acids) may act to prevent the oxidative damage due to free radicals. Recent developments in the use of marine products to prevent free radical pathologies in humans are promising.

Fish oils are sources of polyunsaturated fatty acids (PUFA) e.g, arachidonic acid (AA), eicosapentaenoic acid (EPA) and docosohexaenoic acid (DHA). They are also of interest due to their physiological effects: e.g. prevention of atherosclerosis, their role in anti-ageing and in brain development in premature infants. These PUFA may now be produced from metabolically controlled microalgae and possibly from Arctic bacteria.

## Examples of the application of molecular genetics methodology to fisheries

- Identification of populations as management units; Pacific and Atlantic salmon, brown trout in Europe, red fish in the North Atlantic.
- Mixed stock analysis; cod in the gulf of St Laurence, and Baltic salmon.
- Interactions between hatchery and wild populations; Atlantic salmon.
- Consequences of enhancement of natural populations; brown trout and salmon, turbot.
- Estimation of the efficiency of stocking by parental/pedigree analysis.

## Discovering new types of composite materials, biopolymers and enzymes for industry

Macroalgae (seaweeds) have been used in Asia, for more then two thousand years as a subsidiary food and have also been used extensively in medicine. These benthic marine algae grow from the high intertidal down to the subtidal to 250 m and are grouped into 12 divisions and 30 classes. Macroalgae make use of different photosynthesising pigments that divide them roughly into three groups: the brown, green, and red algae, in contrast to the terrestrial environment which has only the green plants. One can add to this series the so-called “blue-green algae”, which are generally considered photosynthetic bacteria but in

The brown seaweed, *Fucus serratus*, used in thalassotherapy in Europe. © Marine Institute, Ireland

reality, they bridge the gap between algae and bacteria. Their pigments, storage products, cell-wall components, ultrastructure, reproduction mode and morphology, amongst others things, identify the different classes. From a biotechnological point of view, the biochemical diversity in seaweeds provides a potentially enormous variety of products, some of them of current biotechnological use. For example, polysaccharides from certain red algae (carrageenans and agars) or brown algae (alginates) are still largely used as jellifying or thickening agents in the food industry, in cosmetics or even in building materials. Other examples are shown below.

More recently, seaweeds have been used in aquaculture diets for urchin, abalone and fish as an alternative food source, due to the scarcity of fish meal and fish oil and the rise in costs in the feed industry. These seaweeds used in the feed contain all the essential amino acids, PUFAs, vitamins and minerals, and include a small portion of the protein as well. Seaweeds, in general, are high in essential minerals and vitamins and have been used for centuries in the human diet as a health food or for therapeutic uses. Only in the last decade has it been known that compounds such as laminarin and fucoidans are known to have an antitumoral action, provide protection against radiation damage, lower cholesterol levels, help in wound repair, have an anti-inflammatory action, have strong immonomodulatory effects, increase resistance to bacterial, viral and parasitic infections (e.g. they prevent infection after surgery), prevention of opportunistic infections in immunocompromised individuals (HIV sufferers; geriatric patients etc). Secondary metabolites, such as halogenated compounds, extracted from macroalgae are of great promise as antibacterial and antiviral agents or as antifouling agents. Extracts from certain red algae are used in bone-replacement therapy and in reducing “cellulite”.

## Biotechnological applications of seaweeds

- ⇒ **Food industry, nutraceutics**
- ⇒ **Biomedicine/health care**
- ⇒ **Bio-pharmaceutics**
- ⇒ **Dental health care**
- ⇒ **Novel excipients/Delivery systems**
- ⇒ **Enzyme biotechnology**
- ⇒ **Biosensors**
- ⇒ **Bio-energy**
- ⇒ **Bioremediation**

*Lophelia pertusa* – cold water corals "bioherms" found at depths of 200 - 1 000 m along the full extent of the European Atlantic margin.


Deep-sea hydrothermal vents now offer a new source of a variety of fascinating microorganisms well adapted to these extreme environments. This new bacterial diversity includes strains able to produce new molecules such as enzymes, polymers and other bioactive molecules. Screenings of isolates recovered from oceanographic cruises led to the discovery of a number of unusual microbial exopolysaccharides with interesting chemical and rheological properties. Among these polymers, poly-ß-hydroxyalkanoates (PHA) are of special interest.

In the same range of high molecular weight biological polymers, chitin, a co-polymer of N-acetylglucosamine and glucosamine, and chitosan, its N-deacetylated form, are found associated with proteins in the exoskeleton of many invertebrate species; annelids, shellfish, insects and also in the envelope of many fungi, moulds and yeasts. Chitin polymers are natural, non-toxic and biodegradable and they have many applications in food and pharmaceuticals as well as cosmetics.

New molecular tools will be applied to gain insight into the basic molecular processes by which marine organisms adapt to their environments, including extreme environments. Examples of basic research leading to commercial applications are "antifreeze glyco-proteins" inhibiting ice crystal growth found in the tissues of fish in the Artic and Antartic (e.g. Arctic char) and in psychrophilic microorganisms. These may prove useful in industrial and medical cryopreservation processes.

# Science and Technology Plan Objectives

## Rationale

The major goal of this proposal is to set out the intellectual framework and establish guidelines for implementation of a new European science and technology initiative in marine biotechnology. Like all such coordinated initiatives that anticipate the development of new and innovative technologies for industrial applications, marine biotechnology will involve coupling the results of high-quality research in all areas of marine biology with applications-oriented activities both in and outside the laboratory. The proposed advanced research will use state-of-the-art tools to investigate fundamental processes associated with marine organisms. Simultaneously, applied research will exploit new knowledge of unique properties of marine biota for industrial purposes.

A critically important element of this initiative is that the creativity of the individual scientist must be respected and supported since, ultimately, this will be the source of new ideas. Modes of technology transfer and subsequent larger scale development will also be considered. Accordingly, the most effective projects should contain a multidisciplinary component involving participation of marine and other biologists, biochemists, chemists, biochemical, chemical and process engineers all coming from the academic and from the industrial sectors. In addition, participants with commercial R&D, economic, business and marketing expertise should also be involved at some stage in the programme. Recognising the large variety of approaches by which developments in biotechnology have been and are being commercialised (spin-off, start-ups, joint ventures, strategic alliances, limited partnerships, acquisitions etc.), the initiative will not focus on a specific mode of commercialisation. Nevertheless, there should be a concerted effort to protect the intellectual property rights of both the individual scientists involved as well as those of the participating institutions (many of which will already have such provisions in their institutional guidelines). This is of particular importance for marine-based biotechnological discoveries since complications may arise from territorial issues and the problems of exclusion zones in coastal regions.

Recent technical advances have made life in the oceans more accessible to researchers and the general public alike. It should be emphasised that any coordinated effort in marine biotechnology has to consider the fact that the field suffers from a serious lack of fundamental understanding. This deficiency is mainly a consequence of the oceans containing most of the organismal biodiversity, with many organisms uniquely different from evolutionarily younger terrestrial organisms. Hence, it is to be anticipated that the development of the programme will almost certainly lead to an in-depth contribution to an understanding of basic science and that this new knowledge will have a very positive effect on the subsequent applications-oriented research. Thus, rather than being mutually exclusive, the two approaches are expected to actually nurture each other and to contribute synergistically to a more productive effort in marine biotechnology.

## Objectives

In accordance with the principles outlined above, the science plan outlined for the prospective European initiative in marine biotechnology aims to identify innovative, multidisciplinary, cooperative research programmes to be initiated in European universities, research institutes and industrial groups. It will be of particular importance:

- to develop a coordinated effort which successfully incorporates the activities of scientists, engineers, industrial and business people in order to facilitate the development of new knowledge and technology and its subsequent transfer to potential users;
- to direct primary efforts towards those areas of research in which marine systems offer distinct advantages as sources of novel compounds in bioprospecting efforts;
- to focus research on areas confronted by specific problems (i.e. ecological) which threaten the environment (such as major forms of pollution in coastal regions);
- to incorporate mechanisms and frameworks whereby technology can be successfully transferred to appropriate industries for subsequent R&D activities, scale-up and subsequent commercial development. Concepts such as proof of principle, ease of scale-up, protection of

intellectual property rights and environmental impact should be taken into consideration in developing such programmes;

- to evaluate the current status of European marine bioprospecting/bioscreening (in comparison with developments in the USA, Japan and elsewhere), to identify key European marine ecosystems for bioprospecting (e.g. deep water *Lophelia* coral banks, cold water vents, etc.), and to promote the opportunities and R&D requirements for establishing Europe and European expertise in the evolving area of developing novel marine bioactive products and marine bioscreening;
- to establish a mechanism whereby the new knowledge gained from the research phase of the various projects funded within the initiative can be publicised within the professional literature, among the relevant industries and to the public at large;
- to establish guidelines whereby progress in the execution of these programmes can be realistically evaluated both in terms of their scientific merit and in terms of their potential for subsequent commercial application;
- to develop a framework whereby students, post-doctoral researchers and other scientists can gain high level training in specialised areas of the marine sciences and in marine biotechnology.

### Some potential areas for research and development

The rapid developments and dramatic shifts in focus and public response in all aspects of biotechnology preclude the possibility of preparing a complete and exhaustive list of all research areas which can be expanded to fit the needs of a programme in marine biotechnology as outlined above. The areas presented in the following table are intended to convey some directions that appear to be important and promising areas for identification and development.

## A European Strategy for Marine Biotechnology

Biotechnology is an area of key national and international importance particularly in R&D as a foundation for the growth of industry, technology and medicine. Unfortunately, Europe has remained uncoordinated in its approach to reaping the benefits of marine biotechnology. This, however, can be reversed through the development and execution of an integrated strategy involving the following elements:

- Funding, in a coordinated manner, creative, well-planned multi- and interdisciplinary research programmes.
- Upgrading and maintaining the expertise, infrastructure and networking of European marine centres. This will allow for the improved coordination and integration of larger scale projects and provide for a more accessible, realistic monitoring of such projects.
- Establishing a global network for dissemination of relevant discoveries in marine biotechnology accessible to all relevant academic, industrial, business and public sectors.
- Providing incentives and guidance for establishing new modes of technology transfer; an important – and frequently the key element – in R&D efforts and subsequent industrial development.

| Target Areas for research in marine biotechnology | |
|---|---|
| **Research Area** | **Objectives** |
| **Genomics & Proteomics** | Organismal and product databases and networks<br>Novel genes and gene products<br>Profiling genes and metabolic pathways<br>Identification of model organisms |
| **Bioinformatics** | New algorithms for specific predictions of drug actions based on models of biological processes |
| **Nanotechnology** | New materials<br>Feasibility of carrying out biological and chemical processes at the molecular and atomic level |
| **Bioprospecting** | Bioactive molecules<br>Pharmaceuticals<br>Added value products from fish waste<br>Novel drug targets |
| **Environmental biotechnology** | New processes<br>Biosensors and biomonitoring<br>Bioremediation<br>Detection and control of biofouling and corrosion |
| **Aquaculture** | Environmentally friendly production systems<br>Health improvement<br>Improved vaccines and microbial control<br>Models of host-pathogen interactions<br>Improvements in quality and productivity of marine organisms<br>Mariculture of novel species<br>Production of novel biomolecules<br>Production of germ-free marine animals |
| **Cell culture** | Basic insights into fundamental cellular processes in marine model organisms<br>Reliable biopharmaceutical production |
| **Education & Training** | Training and mobility grants for young scientists<br>Training and mobility grants for experienced marine scientists in molecular biology |

## A vision for marine biotechnology in the 21st century

Implementation of a strategy for marine science and technology in Europe and in particular in marine biotechnology is built upon a vision, which has been defined and recognised by the major economic countries of the world. That vision itself arises from a number of significant facts that have major implications for the future of the human race.

**1.** The seas are essential to life on this planet and are widely regarded as the ecosystem where life began, and are therefore of enormous scientific interest. This system is also unique in that signalling, communication, feeding and defence mechanisms all take place in an aqueous medium,which in itself constitutes a unique environment.

2. The variety and complexity of marine organisms is greater than for any other environment, and they represent a unique source of genetic information and chemical complexity.
3. Marine microorganisms play a major role in control of the Earth's climate, and in mineralising many man-made pollutants.
4. Marine life provides vast quantities of food.
5. Marine organisms are unexplored and relatively understudied in comparison to terrestrial organisms.

**Europe must invest in expanding the knowledge base on marine life so that its intelligent management and application can be achieved.**

This can be carried out through a coordinated European Strategy for Marine Biotechnology, which must have the following components:

- *Increase knowledge in key areas of marine biotechnology through funding scientific research and its biotechnological application;*
- *Collaboration on a European scale in which Europe's marine stations are networked efficiently;*
- *The promotion of industrial involvement in the application of scientific research;*
- *The promotion of public understanding of the responsible and sustainable use of marine organisms.*

# Key Areas for Development in Europe

## Bioprospecting/bioscreening for novel compounds

European marine ecosystems with specific biological characteristics should be studied as possible sources of novel compounds. Sampling should concentrate on specific groups of marine organisms, such as microorganisms (including marine algae) and invertebrates, which indicate a potential for novel compound development.

Rocky bottom locality (ca. 20 m depth) at Kongsfjordnesset in Kongsfjorden, Svalbard with the sea urchin *Strongylocentrotus droebachiensis* and the cnidarians *Gersemia rubiformis* and *Urticina eques*. © Bjoern Gulliksen

Modern approaches in screening for biologically active compounds comprise highly automated systems with high-throughput screens and sophisticated molecular assays. The provision of diverse but standardised samples is currently regarded as the major bottleneck in screening for bioactive compounds. Therefore, intelligent screening projects are needed that combine knowledge of marine habitats and organisms with appropriate high-throughput screens and molecular targets.

The best combination of partners for such projects might be between biotechnological industries and academics.

## Genomics and proteomics of marine organisms

Sequencing of the total genomes of many organisms is rapidly advancing. With respect to marine organisms, the total genome of two microorganisms, common to marine waters of the archaebacter, *Methanoccus jannaschii* and of *Vibrio cholerae*, has now been completed. The genome sequence of the round-spotted pufferfish is nearing completion and that of the zebrafish is virtually 50% complete. Genetic screening will become a lot more important in the near future when the full relevance of bioinformatics and data mining are realised in the development of gene probes for antibiotics and other molecular targets. This means that the more we learn about gene sequences from genomics projects the better we can design specific gene probes to search for variations of gene products in these gene libraries. The molecular screening of genes and communities is complemented by a functional analysis of the obtained clone libraries after appropriate expression in industrial high-throughput units to detect novel biomolecules such as enzymes and antibiotics. Overall, this molecular approach shows great promise in making the genetic resources of most marine microorganisms accessible and should be supported.

## Biosensors for the assessment of environmental quality and management of marine environments

Biosensors are emerging from the combination of molecular biological tools, such as nucleic acid probes, with information technologies such as silicon chips and nanotools. They are in demand for the assessment of environmental quality parameters of biological relevance such as inorganic and organic nutrients, toxic products of marine organisms and trace amounts of pollutants. Ideally, these biosensors have the capacity to operate unattended in automated systems accessible by remote sensing to provide data for large-scale surveillance of marine environments to enable forecasts of major threats to fisheries, aquaculture or public health. Biosensors are needed for major threats to human or animal welfare, for example, algal toxins and pathogenic organisms. The development of biosensors would need specific information from the genome of marine organisms and would assist bioscreening for toxic or valuable compounds.

## Study of fundamental biological processes in lower invertebrates

Research is required to determine what seasonal factors and life cycles or reproductive states are linked with the natural production of desired substances by lower invertebrates such as shellfish and crustaceans. Diet, physical and chemical conditions, distribution by phylogenetic affiliation, geographic location, water depth or association with symbiotic microorganisms might be some of the factors influencing production. Understanding their influence will be important in developing and/or optimising methods for the production of selected metabolites. To achieve this we need to improve our understanding of physiology, genetics, bio-chemistry and the ecology of marine organisms.

## Development of new methods for the production of marine organisms

A reliable supply of marine organisms in large quantities is a major prerequisite for marine biotechnology. The problem, however, arises with sustainable development of these resources to ensure that the environmental impact is acceptable and that a uniform supply can be guaranteed. The most obvious route to ensure supply and quality of products that are found only in rare marine species is to develop effective production methods for these organisms. Development of culture methods provides one way of controllable and clean production with little negative environmental impact since harvesting from natural habitats would not be necessary. Alternative methods of production include culture of specific cell lines of marine invertebrates and molecular approaches to cell and tissue culture.

## Safe and sustainable aquaculture

The major research issues in aquaculture are similar to those of other agricultural sectors, but the knowledge base for aquaculture is comparatively meagre. Development of this knowledge is a particular challenge due to the diversity of cultured aquatic species and the systems for their production. Despite the progress made in the cultivation of certain organisms, not all of them are adequately studied to allow optimum production, and the requirement for species diversification increases the need for research in this area. Further research is required on reproduction, larval and juvenile nutrition, optimal feeds and feeding, health of cultured populations, and to improve the quality of the final product.

Marine fish farm. © Marine Institute, Ireland

Improved understanding of environmental, hormonal, nutritional and genetic control of reproduction as well as genetic selection of broodstock is required to optimise production and produce fish and shellfish of required growth, health and quality characteristics. Larval nutrition, diversification of marine organisms used for their first feeding, and development of efficient artificial diets for early larval stages together with feed-dispersing techniques would add to the quality of larvae and reduction of production costs. Exclusion of traditional raw materials from aquaculture feeds and possible limitation in the use of those remaining impose a great risk to aquaculture sustainability. New raw materials should be explored and/or developed for inclusion in fish feeds. Further understanding of the fish immune system and the relation of its condition to nutrition and stress would help in improvements in growth and disease resistance. The tools of molecular biology can furnish information about life cycles and mechanisms of pathogenesis, antibiotic resistance and disease transmission. Improved technologies must be developed for detecting and diagnosing pathogens and for enhancing the genetic basis of disease resistance. Improvements of the quality of the final product can be achieved through genetic selection and/or understanding of biochemical and hormonal control of tissue growth and nutrient deposition.

Polyculture of marine species should be further explored as an environmentally friendly system of production of various marine organisms such as fish, bivalves, seaweeds and high protein phytoplankton biomasses. Culture of ornamental fish and captive breeding of species now rare in their native environments is of importance for the market and for the conservation of natural populations, and research efforts are required in this direction.

# Appendix 1

## International Marine Biotechnology Initiatives

### Marine biotechnology centres

For well over a century a network of marine stations and, more recently, oceanographic institutes have been collecting information about the marine biota, marine animal husbandry and physiology. Led by interest in natural products from marine organisms, especially during the past decade, governments and industry recognised the importance of establishing interdisciplinary research centres focusing on marine biotechnology.

The initial leadership occurred in Japan. In the late 1980s, a cooperative initiative between industry and government (MITI) led to the establishment of two marine biotechnology institutes, one in Kamaishi and the second in Shizuoka. In 1990 the Japan Marine Sciences and Technology Center (JAMSTEC) was established in Yokoska to investigate the deep-sea environment (DEEP-STAR). Modifying the submersible vehicle (*Alvin*), designed initially at the Woods Hole Oceanographic Institute (USA), JAMSTEC built *Shinkai 2000* and *Shinkai 6500* capable of retrieving biological specimens at greater depths in the ocean.

The creation of a Sea Grant program in the USA through NOAA led to a funding mechanism for marine biotechnology in the USA. Shortly thereafter the University of Maryland, with federal support, established the Center of Marine Biotechnology in the University of Maryland Biotechnology Institute, and Canada developed the Institute for Marine Biosciences in Halifax for the study of basic marine science with the aim of promoting marine biotechnology through a study of genomics and proteomics.

In Italy, the Stazione Zoologica in Naples has strong initiatives in molecular evolution and developmental biology.

Norway has four universities pursuing marine science including marine biotechnology: in Oslo, Bergen, Trondheim and in the Arctic at Tromsø. There are also several marine research institutes, such as the Institute of Marine Research in Bergen and the Norwegian Institute of Fisheries and Aquaculture in Tromsø, and large-scale aquaculture stations are located near Bergen, at Sunndalsøra and in Tromsø. There is also a research station at Ny Ålesund on Spitsbergen at 79°N. The creation of a Research Council for fisheries and the establishment of two national institutions in Tromsø (The Norwegian College of Fishery Science, part of the University of Tromso, and the applied Norwegian Institute of Fisheries and Aquaculture Research) in the early 1970s resulted in the establishment of a national centre of marine biotechnology involving these institutions. In the mid 1990s an international marine molecular biology centre (The SARS Centre) was established in Bergen, and is devoted mainly to marine developmental biology.

In Germany a centre for marine natural products is being planned/formed in the Bremerhaven/ Wilhemshaven area, and an Institute for Marine Biotechnology has been established within the University of Greifswald. The state programme of Lower Saxony on marine biotechnology is in its fourth year and will terminate in December 2002. The first phase was completed in December 2000 with over 20 research groups that include projects studying areas such as marine actinomycetes. Several new bioactive substances have been found and are in analysis. The Federal programme for marine natural products research is in its third year. There are about 25 universities or research institutes; in addition about 15 companies from Germany are involved. The results are currently restricted, but promising results have been obtained with marine fungi.

A Department for Marine Biotechnology was established in Heriot-Watt University, Edinburgh that offers courses in marine biotechnology, including marine microbiology, aquaculture related subjects e.g. nutrition, disease) as well as marine lipids.

In France, research in marine biotechnology is carried out at several locations, and in funded universities, IFREMER and CNRS. There are concentrations of such activities in the Brest-Nantes region, and in the south (Montpellier-Marseille). Activities are mainly centred on biomass upgrading, hyperthermophilic polymers and enzymes and marine natural substances. IFREMER has also a strong research activity in aquaculture and aquaculture-related pathogenesis. The French marine stations have also developed programmes in molecular developmental biology.

Australia concentrated its activity at the Australian Tropical Sciences and Technology Park, James Cook University in Townsville and at the Australian Institute of Marine Science (AIMS) for researching the animals and plants of the Barrier Reef for biologically active compounds.

In 1997 the Centre de Investigacion Cientifica y de Educacion Superior de Ensenada (CICESE), Mexico, set up graduate programmes in acquaculture and marine biotechnology. In Chejo City, Korea, a Department of Marine Biotechnology is being formed at Chejo National University. An international (BET/BATCHEN) Centre of Marine Biotechnology has been established at the Ocean University of Qingdao.

The critical factor in the establishment of these centres was the willingness of the respective governments to recognise the importance of marine biotechnology and commit major funds to support them.

## Professional marine biotechnology activities

Since 1989 there have been five International Marine Biotechnology Conferences (IMBC) (Tokyo 1989; Baltimore 1991; Tromso 1994; Sorrento 1997; and Townsville 2000). The Japanese Society for Marine Biotechnology, the Foundation for Advancement of International Science, the International Scientific Committee for Biotechnology and the International Council of Scientific Unions organised the first IMBC. An International Organising Committee and an International Scientific Advisory Board was formed which has planned the subsequent IMBC meetings. The first European meeting took place in 1992 in Montpellier. In 1998 and 1999, Marine Biotechnology meetings involving European participants took place respectively in Willemshaven (Germany) and Noordwijkerhout (Netherlands). In August 1998, the first UK Marine Biotechnology Conference was held in Edinburgh, Scotland. Two new marine journals were established: *Journal of Marine Biotechnology* (Japan) and *Molecular Marine Biology and Biotechnology* (USA). These have recently merged to form *Marine Biotechnology*, an international journal on the molecular and cellular biology of marine life and its technology applications.

The Japanese Society for Marine Biotechnology was organised in 1989. Since then the American Society for Molecular Marine Biology and Biotechnology, the Asian-Pacific Society of Marine Biotechnology and the Pan-American Marine Biotechnology Association were formed. In the USA the National Association of Marine Laboratories and, in Europe, the European Network of Marine Laboratories were formed, with strong interests in marine biotechnology. Marine biotechnology institutes have been created in Japan, USA. and Europe. In the past few years in the USA the Committee on Life Sciences and Health of the Federal Co-ordinating Council for Science, Engineering, and Technology has pointed out the opportunities in marine biotechnology. In 2000 Canada initiated a 27 million Canadian dollar interdisciplinary programme (Aquanet) to support aquaculture in that country.

## Marine Biotechnology Conferences and Organisations

| **Conferences** | |
|---|---|
| • *International Marine Biotechnology Conference (IMBC).*<br>1989, Japan; 1991, Baltimore, US; 1994, Tromsø, Norway<br>1997, Naples, Italy; 2000, Townsville, Queensland | |
| • *10th International Symposium on Marine Natural Products*<br>Okinawa, Japan, 24-29 June 2001 | |
| • *Natural Products from Marine Microorganisms. International Conference (2002)*<br>Greifswald, Germany. | |
| • *Ist European Conference on Marine Biotechnology*<br>1992. Montpellier, France. | |
| • *Marine Microorganisms for Industry' Symposium*<br>1997. Brest, France. | |
| • *Marine Bioprocess Engineering' Symposium*<br>1998. Noordwijkerhout. The Netherlands | |
| • *Asia- Pacific Marine Biotechnology Conference (APMBCI)*<br>1995, Shimuzi, Japan;<br>1997, Phuket, Thailand;<br>1999, Marine Science Inst., Univ. Philippines | |
| • *Asia Pacific Conference on Algal Biotechnology*<br>1997, Phoket, Thailand | |
| • *1st UK Conference on Marine Biotechnology, (UKMBC)*<br>1996 Edinburgh | |
| • *Marine Lipids*<br>Brest, France, 19-20 November 1998 | |
| • *EU/US Task Force on Marine Biotechnology: research Issues in Biotechnology*<br>Brussels, 8-9 August 1996 | |
| • *International Symposium on Marine Biotechnology*<br>Wilhelmshaven, Germany, 19-22 July 1998 | |
| • *International Symposium on Progress and Prospect of Marine Biotechnology (ISPPMB '98)*<br>Qingdao, China, 6-9 October 1998 | |
| • *EU-China Aquaculture Biotechnology Workshop*<br>Huangzhou, China, 16-19 January 2000 | |
| • *International Symposium on Marine Biotechnology*<br>Qingdao, China, 6-9 December 2000 | |
| **Organisations** | |
| • *European Society for Marine Biotechnology (ESMB)* | Founded in 1995 |
| • *Japanese Society for Marine Biotechnology* | Founded in 1989 |
| • *Pan American Marine Biotechnology Association* | Founded in 1999 |
| • *Asian-Pacific Marine Biotechnology Society* | Founded in 1995 |

## Marine biotechnology initiatives in Europe

A comprehensive programme for Marine Biotechnology at the European level has not been formulated. However, the EU's Marine Science and Technology (MAST III) programme (part of the Fourth Framework Programme, 1994-1998) did include a technology section that supported marine biotechnology projects. Nine such projects were supported under MAST-III (see Table below).

The current Fifth Framework Programme (1998–2002) while not containing a specific programme on marine science and technology, supports marine research under the Key Action "Sustainable Marine Ecosystems". This Key Action in turn supports biotechnology applications under area 3.2.3 *"Technologies for safe, sustainable and economic exploration and exploitation of marine resources"*. To date, four marine biotechnology projects have been supported under this Key Action (see Table below) and as the programme is not yet closed, additional marine biotechnology projects may be supported in the future.

| **Marine Biotechnology Projects supported under the EU's Fourth and Fifth Framework Programmes**<br>***Collaborative marine biotechnology projects supported under MAST-III Programme (1994-1998)*** |
|---|
| ● Bioactive marine natural products in the field of antitumoral, antiviral and immunomodulant activity. Project Co-ordinator: Université de Nantes, France. |
| ● Microorganisms in deep sea vents and marine hot springs as sources of potentially valuable chemicals (MICROPHI). Project Co-ordinator: Centre National de la Recherche Scientifique (France) |
| ● Application of marine biotechnology for the development of antifouling coatings. Project Co-ordinator: X-GNAT Laboratories Ltd.(UK). |
| ● Biomarkers in marine sponges: molecular approaches to assess pollution risks and ecosystem health in the ocean in order to support management for its sustainable use (BIOMARK). Project Co-ordinator: Johannes Gutenberg Universität. (Germany). |
| ● Marine bacterial genes and isolates as sources for novel biotechnological products (MARGENES). Project Co-ordinator: Gesellschaft für Biotechnologische Forschung GmbH. (Germany). |
| ● Methods to improve the supply of marine organisms for pharmaceutical-related natural products chemistry (FAIRE). Project Co-ordinator: Instituto Biomar S.A. (Spain). |
| ● Electroacoustic prototype for controlling the behaviour of marine mammals. Project Co-ordinator: S. Vito Pesca Arl. (Italy). |
| ● Biology of sponge natural products (SYMBIOSPONGE). Project Co-ordinator: Universiteit van Amsterdam. (The Netherlands) |
| ● Marine cyanobacteria as a source for bioactive (apoptosis modifying) compounds with potential as cell biology reagents and drugs. Project Co-ordinator: University of Bergen (Norway) |
| ***Collaborative marine biotechnology projects supported under Key Action 3 " Sustainable Marine Ecosystems " (1998-2002)*** |
| ● Lead potential of marine microorganisms from coastal, shelf and deep sea sediments, a comparative assessment for optimised search strategies (MICROMAR). Project Co-ordinator: Technical University Berlin (Germany) |
| ● Development of non-degrading, Novel Marine TECnologies (NOMATEC) for the sustainable exploitation and protection of Mediterranean marine resources. Project Co-ordinator: Universität Gesamthochschule Essen (Germany) |
| ● BIODEEP - Biotechnologies from the deep. Project Co-ordinator: British Museum - Natural History Museum (UK) |
| ● Deep Bacteria Under Ground (deepBUG). Project Co-ordinator: The University of Bristol (UK) |

National initiatives of single countries within the European Union rarely focus directly on marine biotechnology. They often focus on single topics within marine biotechnology that are of specific interest to the scientific community in the respective country. For example, within its marine research programme, Germany has a section on marine natural products where projects with a 50% industrial support that lead to products for pharmaceutical and chemical industries will be funded. France has a special programme on the study of high value-added molecules from hydrothermal microorganisms and algae. The United Kingdom has initiatives on marine biofouling and marine microbial biodiversity which seek biotechnological exploitation. Norway has a biotechnology programme, which also for a period launched a sub-programme in marine biotechnology. Apart from that, Norway also has had several programmes related to disease prevention in aquaculture. These nationwide programmes are often complemented by regional programmes that are substantially smaller in size and geared towards specific interest of coastal regions in profiting from the exploitation of local marine resources.

## Programmes to study European marine ecosystems

Marine ecosystem research has been well supported by the EU Framework Programmes and summaries of many of these projects can be found in the Proceedings of the various MAST days and EurOCEAN Conferences (Brussels, 1993; Sorrento, 1995; Lisbon, 1998; Hamburg, 2000). Large Regional Ecosystems projects have also been supported and include BASYS (Baltic Systems Study), MATER (Mediterranean Mass Transfer and Ecosystem Response1996-1999) and more recently a cluster of projects focusing on the Lophelia corals of the European Atlantic Margin.

Information on EU-funded projects, including marine projects, can be accessed from the CORDIS Website (http://www.cordis.lu/eesd/src/proj_env.htm).

National programmes of single EU countries for the study of European marine ecosystems are normally limited to "backyard" studies, i.e. the country's own shoreline and the adjacent seas. In addition to these research programmes, the individual countries maintain large monitoring and survey programmes to control obligations stemming from international treaties for the protection of the sea such as HELCOM for the Baltic and OSPARCOM for the northeast Atlantic. A very comprehensive review of the state of marine ecosystems on the European Atlantic Margin is contained in the OSPAR Quality Status Report 2000 (http://www.ospar.org/eng/html/welcome.html) and in the supporting Regional and Sub-Regional Reports. These national monitoring programmes, together with the European Marine Research Stations network (MARS) could provide a very economical means of obtaining material from the European seas for biotechnological research projects.

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# Appendix 2

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