The **last frontier**

Laboratory photo of one of the newly discovered bone-eating worms, Osedax frankpressi, which has been removed from a whale bone. Normally only the red and white plumes and the pinkish trunk would be visible. The greenish roots and whitish ovary would be hidden inside the bone. *See also page 21*

The world's ocean is amazingly rich in life and perhaps nowhere more so than in the deep sea. Here, over millions of years, species have developed unique properties to enable them to cope with extreme living conditions, such as high pressure levels[18]. It is the very uniqueness of these properties which offer exciting potential for the development of new drugs to treat all sorts of human ailments. Products based on marine organisms have already found their way onto the market and are now being prescribed to sufferers of asthma, tuberculosis, cancer, Alzheimer's disease, cystic fibrosis and male sexual impotence, among others. Other industries, such as those for oil or paper, are also bioprospecting the deep sea with promising results.

Today, there are no legal restrictions on exploring the deep sea for the purposes of research or financial gain when it comes to its living resources. In principle, it suffices to have the financial means and the sophisticated technology needed to explore a world that in parts lies as far as 11 km beneath the ocean surface. In practice, deep-sea bioprospecting[19] remains the prerogative of the "lucky few". This raises a number of questions. Firstly, as this newly discovered "blue gold" is mostly located in international waters, making it extra-territorial in international law, it can be argued that the genetic resources[20] living in the deep sea belong to humanity as a whole and therefore ought to be exploited equitably. Secondly, if we are to protect these precious resources and the ecosystems in which these are found, we shall have to exploit them in a sustainable manner.

The need to regulate the use of deep-sea genetic resources was one of the themes dealt with by a global conference last January devoted to Moving the Oceans Agenda Forward (see page 8). It was also the subject of a report published in 2005, upon which the current article is based.

Why bioprospect in the oceans?

The marine habitat is unique for the diversity of its living organisms. Of the main taxonomic groups (phyla), almost all are found in the oceans and half are exclusively marine. If bioprospecting will be crucial to improving human well-being, it is in the oceans that bioprospecting's greatest potential lies.

Examples of compounds derived from marine species or materials

Biological source	*Compound and area of application*
Cyanobacteria	Cryptophycins: anti-cancer; treatment of viral diseases
Sponges and ascidians	Bryostatin-1, ecteinascidin 743, dolastatin-10, halichondrin and spongistatin (anti-tumor); sponge derivate for treating leukemia; sponge steroid contignasterol (asthma drug)
Eleutherobia sp.	Derivatives to treat breast and ovarian cancer
Other marine organisms	Several compounds with properties that are: antioxidant, anti-fungal, anti-HIV, antibiotic, anti-cancer, anti-tuberculosis, immunosuppressant and antimalarial; compounds for the treatment of Alzheimer's disease, cystic fibrosis and impotence

Marine biodiversity is amazingly dense in certain parts of the world. In the Indo-Pacific Ocean, for example, there are as many as 1000 species per square metre. In this highly competitive and sometimes harsh environment, marine species have had to develop strategies for survival, such as resistance to the toxicity, extreme temperature, hyper-salinity and pressure that characterize the deep seabed.

We know from experience that there is a higher probability of selecting active compounds of potential interest to the health and other industries from marine organisms (or parts thereof) than from terrestrial organisms. This means that, statistically, marine organisms are of greater commercial interest than terrestrial ones.

Potentially big business

It is hardly surprising then that many pharmaceutical firms have marine departments. One could cite the examples of Merck, Lilly, Pfizer, Hoffman–Laroche and Bristol–Myers Squibb. Biotechnology companies are also interested in marine products, as the related licenses can be sold not only to pharmaceutical companies but also to industry. Nowadays, it is biotechnology companies, which tend to be small, flexible and adaptive structures, which are responsible for most of the discoveries, whereas 'big pharmaceuticals' tend mostly to license the latter.

Examples of commercial products derived from deep-sea species and materials

Company name	*Product and related properties*
Sederma	Enzymes isolated from deep-sea bacteria used in skin protection products (UV-resistant)
California Tan	*T. thermophilus enzymes* (same type of products as above)
Roche	*T. thermophilus*, *Thermotoga maritime* and other deep-seabed species which thrive at high temperatures Several DNA polymerases (a polymerase is an enzyme that builds new strands of DNA)
Diversa Corporation	Pyrolase™ 160 enzyme, used in industry to reduce viscosity; ThermalAceTM DNA Polymerase
New England BioLabs Inc.	Deep Vent® DNA Polymerase, Therminator[a] DNA Polymerase
Aquaartis	BactoScreen™, a library of extracts of some 1000 marine bacteria isolated from marine organisms and sediments with several potential applications
HyTest Ltd	*Thermus aquaticus* DNA polymerase Taq Red
Promega	Thermostable Tth DNA Polymerase[a]

Marine bioprospecting of the deep seabed is developing rapidly. An analysis of Patent Office databases reveals that several organisms have been used for commercial purposes. These inventions relate to the genomic features of deep seabed species but also encompass techniques developed to determine these features or to isolate active compounds. These techniques are not inventions, *sensu stricto*, but are nevertheless considered as such under the current international property rights regime.

Other patents deal with the isolation of enzymes important for industrial processes, the isolation of cellular compounds that guarantee unique properties (such as resistance to extreme pressure and salinity) and the discovery of mechanisms ensuring resistance to extreme temperatures and toxicity, these extreme properties being of interest for both biomedical and industrial applications.

There is no consensus on the financial benefits derived from worldwide sales of biotechnology-related products taken from all types of marine environments but these are estimated to represent a multibillion dollar market. A marine sponge compound used to treat herpes, for example, generates earnings of US$50–100 million a year; and the value of anti-cancer agents taken from marine organisms is estimated at close to US$1 billion a year.

The oddity of the deep-sea environment

What sources of energy are available to communities living in dark zones? Biochemists have long demonstrated that different forms of energy can sustain life. Light is probably the first to spring to mind, as this serves as the basis for photosynthesis (from *photo* meaning light), but methane, sulphides[21], oil, etc. are also forms of energy. Where there is no light, as in the deep sea, creatures rely on chemical energy (or chemosynthesis). The hydrothermal vents, cold seeps and methane vents we shall shortly discover are all ecosystems which depend on chemical energy.

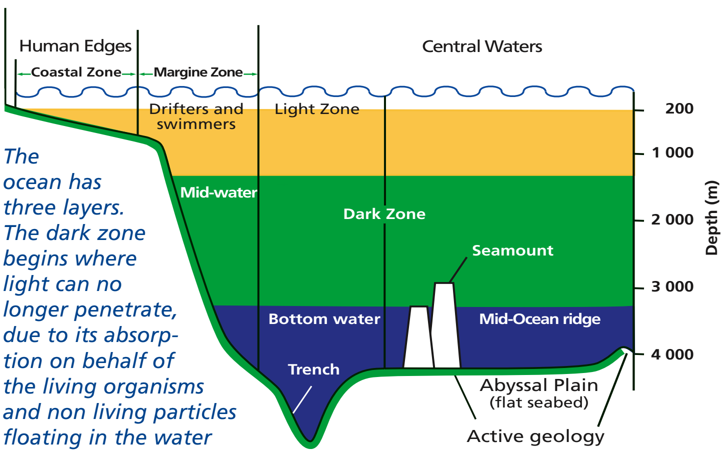
In the absence of light, life in dark waters can also depend on organic substances – dead or alive – reaching the depths of the ocean. Thus, the composition of benthic communities (the term indicates a dependency on the bottom) will rely partly on the availability of organic substances falling all the way down to the seabed. Whale bones for example are known to constitute an excellent surface on which benthic communities deprived of local sources of energy can settle and develop (see photos).

Hot vents and black smokers

Hydrothermal vents develop next to seawater which has penetrated the Earth's crust at the bottom of the ocean and been heated by magma. The seawater then flows back into the ocean through a hot vent, bringing with it mineral substances. Hydrothermal vents are thus home to communities capable of withstanding extremely high temperatures; at their source, these temperatures can be nearly as hot as 400°C, in immediately adjacent waters, they can be as hot as 120°C or more. The hottest of these vents are normally referred to as 'black smokers' but vents can also be characterized by lower temperatures (40–75°C).

Vents are ubiquitous. They have been spotted along the Southwest Indian ridge, in the Mid-Atlantic Ridge, the East Pacific Ridge, in the Arctic Ocean, etc.

Vents are typically inhabited by a well-developed microbial community. Deep clams, worms, crabs and other macro-



The ocean has three layers. The dark zone begins where light can no longer penetrate, due to its absorption on behalf of the living organisms and non living particles floating in the water column. The light zone normally extends for a few hundred metres, depending on how 'rich' that particular part of the ocean is in 'nutrients' (mainly phosphorus and nitrogen), which form the basis for photosynthesis by marine plants, algae, dinoflagellates, etc. Thus, for example, the Sargasso Sea located off the costs of the southeastern part of North America and the Bahamas – a sea very poor in nutrients – is characterized by a deeper light zone than costal areas adjacent to large urban settings or river deltas, where organic particles and sediments hamper the diffusion of the light beyond shallower waters. Given the average thinness of the light zone in comparison with the dark zone, the ocean is essentially a dark environment

Source: Adapted from Baseline Report of the Census of Marine Life

Photomontage of the whale fall in Monterey Canyon, as it appeared in February 2002, soon after its discovery. Note the large numbers of red worms carpeting its body. The small pink animals in the foreground are scavenging sea cucumbers

organisms feed on this community, which comes at the bottom of the food chain. Both micro- and macro-organisms at vent locations can withstand extreme toxicity and pressure.

Cold seeps

Along the continental margins, other equally remarkable ecosystems can be observed. In deep soft-bottom areas, oil or gases seep out of the sediments, or water combined with lipids (fats) and other organic compounds. These complex chemical substances serve as a source of energy for the local community of micro- and macro-organisms that feed on them.

Seamounts

The deep ocean also inhabits areas that tend to be currently geologically inactive but biologically very active, namely seamounts. These impressive formations, which are millions of years old, create dynamic water circulation phenomena, as they break deep ocean currents and participate in the development of water upwelling. Seamounts form the basis of a typical community of organisms made up of cold corals, sponges and the like. They also provide a habitat for fish and other species of ecological and commercial interest, such as orange roughy, swordfish, tuna, sharks, turtles and whales. Seamounts are home to a particularly high number of endemic species.

If exploitation has only just begun of life forms found in hydrothermal vents, cold seeps and similar deep-sea formations like mud volcanoes and brine pools, the same cannot be said for seamounts. Destructive fishing methods have been used on the rich fauna of seamounts for several years now, including bottom trawling.

Marine scientific research in the deep sea

Submersibles are manned or remote-operated vehicles that can rove the deep seas for long periods. In 1977, hydrothermal vents were discovered by the submersible Alvin during an expedition along the Galapagos Rift in the eastern Pacific Ocean at depths of more than 1000 m (see photo overleaf).

Nowadays, many scientific programmes focusing on the deep seabed, its processes and the life therein are being implemented. One of these is the very ambitious Census of Marine Life Programme, whose mission is to assess and

Close-up view of a whale bone covered with O. frankpressi *worms at the whale fall in Monterey Canyon, showing their red and white plumes, which are believed to function as gills*

explain the diversity, distribution and abundance of marine life and whose efforts are in a large part devoted to studying the deep-sea environment.

A host of research-driven expeditions are taking place in the deepest parts of the world's oceans on a regular basis. Scientists have set up facilities for managing information related to deep-sea research and for exchanging this information. One example is InterRidge, a voluntary scientific initiative which seeks to facilitate cooperation among deep-sea scientists through knowledge networking, the identification of problem issues and research questions, representation of the scientific community in policy discussions and the promotion of education on deep-sea research.

In the early days of deep-sea exploration, the main motivation for marine scientific research was probably the quest for knowledge, with scientists reasoning that, on a human-dominated planet, those areas out of visual reach must hold the promise of new discoveries. Although marine scientists are not bioprospectors, it is difficult – and often impossible – to distinguish 'pure' from 'applied' marine scientific research in the deep sea.

It is probably fair to say that deep-sea research today is equally important to both pure and applied research, since the discovery of new species not only nurtures basic knowledge but is also likely to lead to the identification of new chemicals, which in turn tend to lead to new applications and new economic markets.

The blurring of the borders between pure and applied research – and public and private interests – would normally

Deep-sea scientific cruises

Many scientific monitoring programmes with at least a deep-sea component have seen the light in the last few years. Examples are:

- the European Science Foundation-sponsored EUROMARGINS Programme to improve understanding of deep-sea ecosystems like cold seeps in European seas;
- the US National Oceanic and Atmospheric Administration (NOAA) Vents Programme;
- the activities of the Japan Agency for Marine–Earth Science and Technology's (JAMSTEC) Extremobiosphere Research Center;
- the educational Black Smokers Expedition organized by the American Museum of Natural History; and
- the REVEL expedition, a teacher development programme sponsored by the US National Science Foundation and the University of Washington; this enabled scientists and teachers to conduct joint observations in the Juan de Fuca Ridge deep sea in the northeast Pacific.

Since 1992, more than 400 scientific deep-sea cruises have been undertaken by the USA, France, Japan, Germany, Canada, Russia and Portugal. From interviews with scientists active in deep-sea exploration, it would seem that scientists from other countries have participated in these expeditions.

Plans for the future include:

- an international programme on Monitoring the Mid-Atlantic Ridge (MOMAR), sponsored by the European Commission;
- the North-East Pacific Time-series Undersea Networked Experiments (NEPTUNE), which foresees the establishment of a permanent system of deep seabed multidisciplinary observations on the entire Juan de Fuca plate;
- the European Sea Floor Observatory Network (ESONET), which will undertake repeated observations in the seabed on the Atlantic and Mediterranean coasts;
- Japan's Advanced Real-time Earth Monitoring Network in the Area (ARENA) in the Japan Trench; and
- the New Millennium Observatory (NEMO), which will monitor the impact of volcanic activity on hydrothermal vents.

A remotely operated NOAA vehicle is seen here in position for hot fluid sampling at this black smoker vent. Known as ROPOS, this vehicle descends to the seafloor on a fibre optic cable from a ship. ROPOS is equipped with two manipulator arms, video cameras and lights

not be an issue, if the technology used to explore the deep sea were accessible to the majority or if the legal and policy framework regulating access to deep seabed genetic resources, and the use of these, were clear and equitable. But this is not the case.

Deep-sea technology: the prerogative of the lucky few?

Specialized research institutions in a handful of developed countries have come up with unique technologies and techniques based in part on post-war efforts from the 1950s onwards to find peaceful applications for military-based technology.

One example is JAMSTEC, located in the Tokyo Bay area in Japan. JAMSTEC has developed impressive capabilities for descending to extreme depths and operating there on a regular basis. Its fleet is composed of both manned and remotely operated vehicles that allow many deep-sea features to be assessed from a physical, chemical and biological viewpoint. JAMSTEC has developed a device known as the Deep Bath[22] for sampling deep-sea sediments and micro-organisms and maintaining them at the same levels of pressure and temperature as in their original environment, so that they can be subsequently cultivated. This is important, as creatures from the deep tend to lose their shape and functions once brought to the surface, causing them to die.

The US-based Woods Hole Oceanographic Institution has embarked on ambitious plans to develop the first unmanned vehicle to be deployed without cables. The vehicle is being designed to attain the deepest oceanic point on Earth and should be operational within the next few years.

The French Research Institute for Exploitation of the Sea (Ifremer) is studying the features of deep seabed ecosystems to understand better how to use them in oil-drilling operations. It is also studying the specific functions of deep-sea organisms.

Deep-sea research is a costly business. From interviews with deep-sea scientists and administrators, it would seem that the cost of sampling operations by a manned deep-sea vehicle down to a depth of a few thousand metres and back to the surface can be as high as US$1 million per day, excluding maintenance costs.

Although costs are steadily decreasing due to greater efficiency, reliability and simplicity in operating deep-sea equipment, they remain relatively high. If it is true that scientific collaboration has involved a non-trivial number of scientists from developing countries, these are normally visiting scientists. Moreover, developing countries lack the necessary capabilities, including in terms of knowledge and skills, to handle land-based deep-sea research, with the notable exception of molecular biology techniques, which have become increasingly available worldwide. Deep-sea research therefore remains an 'extravagance' only a handful of countries and companies can afford.

No-man's land

For the time being, living resources found in the deep seabed in international waters are in a kind of 'no man's land'.

This is because the current legal and policy regimes under relevant international legal instruments, and especially the United Nations Convention on the Law of the Sea (UNCLOS) and the Convention on Biological Diversity, do not specifically deal with the conservation and sustainable and equitable use of the biodiversity of the deep seabed.

Non-living resources – commonly known as polymetallic nodules – were thought to represent an important economic stake for the international community at the time UNCLOS was adopted in 1982 and up until recently. The International Seabed Authority was set up in 1994 to regulate these resources in the deep seabed in areas beyond national jurisdiction, a portion of the ocean bottom otherwise known as 'the Area.' The utilization of non-living resources, including in intellectual proprietary terms, adheres to the principle of 'common heritage', according to which these resources belong to all and must be regulated as such.

The same cannot be said for living resources in the deep seabed in areas beyond national jurisdiction, for which there is a clear legal and policy gap. Neither UNCLOS nor the Convention on Biological Diversity regulates the use of living resources found beyond continental shelves or Exclusive Economic Zones. (Within these Zones, the related provisions of UNCLOS, which favour essentially national interests, would apply.) Living resources in the deep seabed were unknown when UNCLOS was being negotiated. Today, the living resources present in the international water column are regulated under UNCLOS' high seas regime, which is quite liberal and permissive overall, with the exception of the adverse impact of activities carried out under State flags[23], for which countries are deemed responsible.

Alvin (pictured) has made over 4000 dives since it was built in 1964. The US Navy-owned submersible is operated by the Woods Hole Oceanographic Institution. A typical eight-hour dive takes two scientists and a pilot as deep as 4500 m. When working at maximum depth, it takes about two hours for the submersible to reach the seabed and another two to return to the surface. Alvin can hover, manoeuvre in rugged topography or rest on the bottom. Alvin's most famous exploits include locating a hydrogen bomb accidentally dropped into the Mediterranean Sea in 1966, exploring deep-sea hydrothermal vents discovered two decades ago and surveying the sunken ocean liner Titanic

The Convention on Biological Diversity adopted in 1992 applies solely to territories falling under national legislation, although the Convention does have the power to regulate activities taking place in territories beyond national jurisdiction whenever these have an adverse impact on biodiversity.

The way forward

The time has come to fill in the important legal and policy gaps described above. Some would argue that this is premature, as long as our scientific knowledge remains incomplete. That is not a valid argument. Once a serious risk of harm to the environment has been identified on the basis of the best scientific evidence available, we must act, even if this evidence is not yet exhaustive. This is known as the precautionary approach.

The United Nations General Assembly offers hope in this regard. The General Assembly has taken the responsible step of setting up an Open-Ended Informal Working Group on Marine Biodiversity in Areas beyond National Jurisdiction. The Group met for the first time last February. Let us hope that the process set up by the General Assembly will be effective and its deliberations wise, for the sake of these resources, humanity and the planet as a whole.

Salvatore Arico[24]

This article is based on a report co-authored by Salvatore Arico and Charlotte Salpin and published in 2005 by the Institute of Advanced Study of the United Nations University, entitled Bioprospecting of Genetic Resources in the Deep Seabed.
Read the report: www.ias.unu.edu/binaries2/DeepSeabed.pdf

---

18. *Atmospheric pressure is caused by the force of gravity. Normal atmospheric pressure is defined as 1 atmosphere (atm) at the level of the sea. In the sea, the pressure caused by the weight of the water column overhead is known as hydrostatic. This pressure increases by 1 atm with each 10 m of depth. The highest pressure is found in the Challenger Deep of the Mariana Trench in the western Pacific. It is about 11 000 m deep with almost 1100 atm of pressure*
19. *Bioprospecting is loosely defined as the search for compounds contained in living organisms that hold potential or actual commercial value for applications based on such compounds*
20. *Marine genetic resources can be defined as marine plants, animals and micro-organisms, and parts thereof, containing functional units of heredity that are of actual or potential value*
21. *Compounds containing sulphur but no oxygen*
22. *For Deep sea Baro/Thermophiles Collecting and Cultivating System (thermophiles are creatures which thrive at high temperatures)*
23. *Often, States use flags of convenience to register their ships in other countries and thereby benefit from the latter's fishing quotas, etc. This problem is at the heart of the issue of illegal unreported and unregulated fishing (see page 8 for details)*
24. *UNESCO Programme Specialist in the ecological sciences. The author wishes to thank Ms Salpin and the IAS-UNU for their indirect contribution to this article, the responsibility for which remains solely with the author*