1. Introduction to Marine Biotechnology

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Marine biotechnology is an innovative field of research in science and technology concerning the support of living organisms with marine products and tools. To understand the *omics* of the living species: it is a novel way to produce genetically modified food, drugs, and energy to overcome global demand. The exploitation of biotechnology for drug discovery, including enzymes, antibiotics, and biopolymers, chemical compounds from marine sources are deliberated in this book. The concepts of marine microbiology and molecular biology are explored extensively in the present book. Biomedical applications of marine biomaterials such as tissue engineering, drug delivery, gene delivery, and biosensor areas are thoroughly discussed. Bioenergy from marine sources is a groundbreaking achievement in the field of marine biotechnology and is also covered in this book. Finally, industrial uses of marine-derived products are explored for mankind.

1.1 Marine Biotechnology – Definition

More than 80% of living organisms on earth are found in the aquatic ecosystem. The largest ecosystem on the planet is the ocean; it can be divided into photic, pelagic, benthic, epipelagic, and aphotic zones. More than 40 000 different kinds of species are present in the marine environment, and they are classified as microorganisms, seagrasses, algae, corals, and animals [1.1]. The marine world is considered as a huge reservoir of various biological active compounds. Marine organisms have the capacity to produce unique compounds due to exposure to exceptionally different oceanic environments, such as temperature, chlorophyll content, salinity, and water quality [1.2, 3]. The oldest known fossils are marine stromatolites, which have been evolving for 3.5 billion years; land fossils are about 450 million years old [1.4, 5]. Although the marine world represents nearly $\frac{3}{4}$ of the earth's surface, it is one of most underutilized biological resources.

Biotechnology is the most powerful tool to discover the many secrets of marine organisms and their compounds. There are numerous definitions and explanations that have been given to marine biotechnology since the day its term was coined [1.6, 7]. According to *Food and Agricultural Organization* (FAO, #8), biotechnology can be defined as [1.8]:

> *any technological application that uses biological systems, living organisms, or derivatives thereof, to make or modify products or processes for specific use.*

J. Grant Burgess suggested that marine biotechnology is [1.4]:

> *biotechnology carried out using biological resources which have come from the marine environment rather than from the terrestrial environment.*

Alternatively, marine biotechnology is also defined as *the industrial use of living organisms or biological techniques developed through basic research*. In another words, The Organization for Economic Cooperation and Development (OECD) defines biotechnology as

> *the application of science and technology to living organisms, as well as parts, products and models thereof, to alter living or non-living materials for the production of knowledge, goods and services.*

Thakur et al. defined the Marine biotechnology as [1.9, 10]

> *the application of scientific and engineering principles to the processing of materials by marine biological agents provide good and services.*

Another possibility to define the marine biotechnology is that it might be derived from marine bio (techno) logy.

1.2 Marine Biotechnology – Tools

In recent years, advances in instrumentation and a combination of proteomic and bioinformatics are accelerating our ability to harness biology for commercial improvement [1.4]. The marine biotechnological process has significant capacity to improve human life. Several biotechnological tools have been developed for cost-effective products that can be used for medical, industrial, and environmental applications. A variety of biotechnological methods have been adopted from marine sources such as transgenic methods, genomics, fermentation, gene therapy, bioprocess techniques, bioreactor methods, etc. Marine biotechnology is more often considered in terms of molecular or genomic biological application to generate desirable products. It encompasses the production and application of living organisms and is expected to have numerous impacts on our economy. Marine biotechnology promises breakthroughs in areas such as aquaculture, microbiology, metagenomics, nutraceuticals, pharmaceutical, cosmeceuticals, biomaterials, biomineraliza-

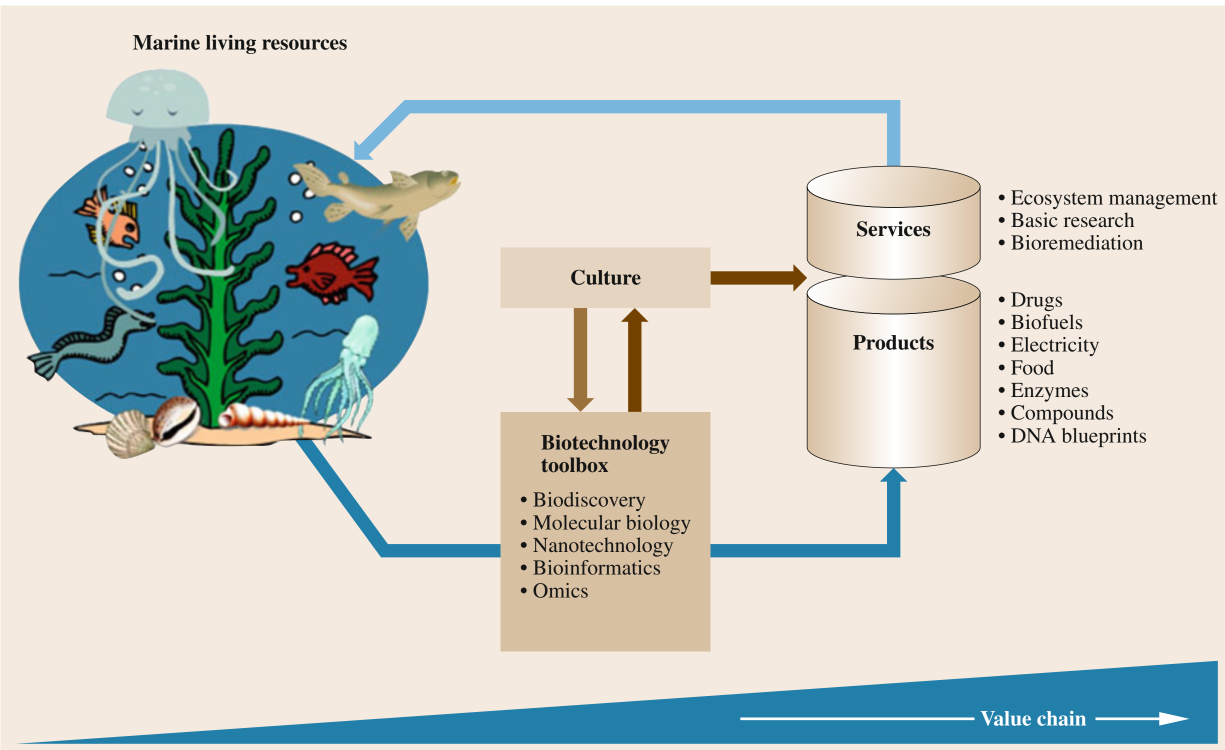

Fig. 1.1 Examples of products and services developed by technological applications using marine bioresources. After [1.11]

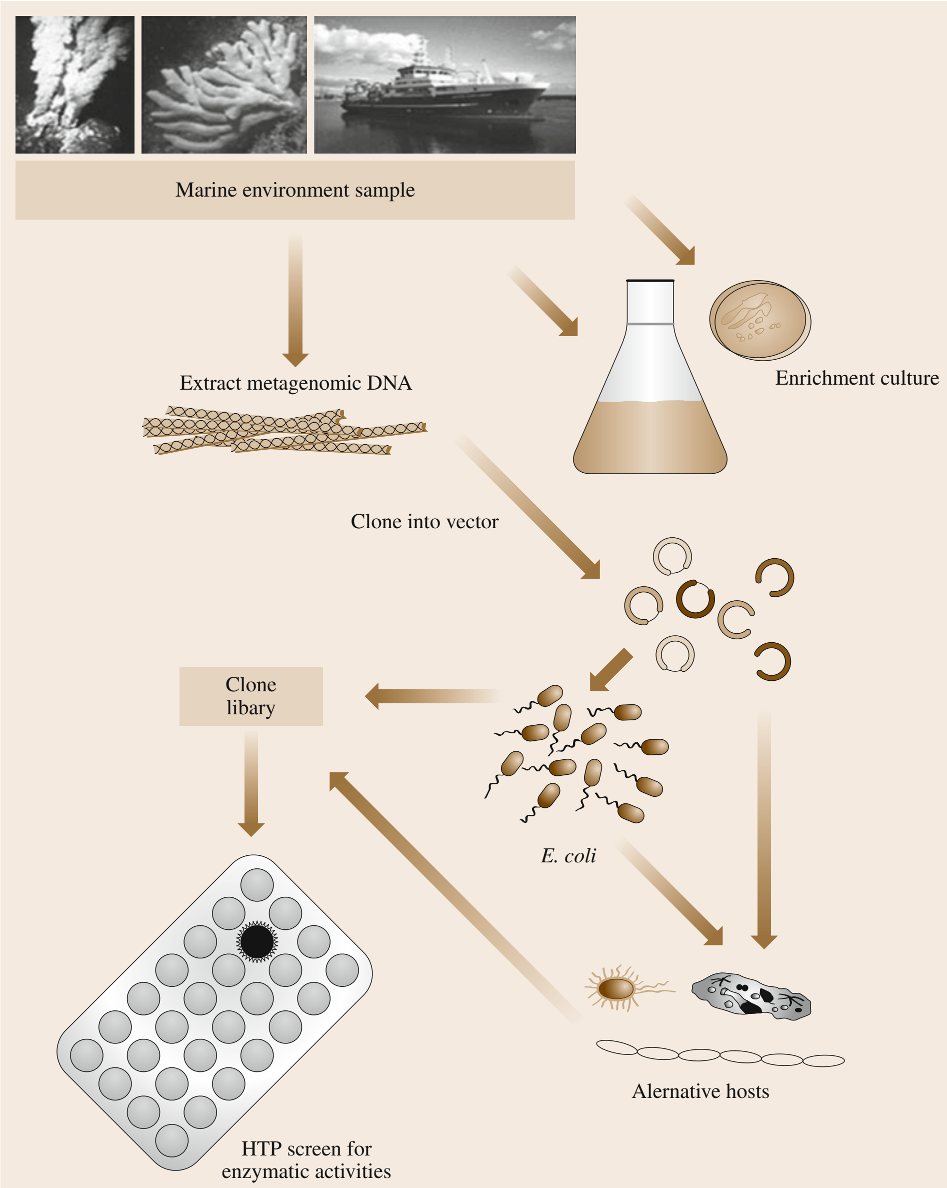

Fig. 1.2 Schematic depiction of functional metagenomic approaches for identification of novel biocatalysts

tion, biofouling, and bioenergy. Products derived by biotechnological methods are commonly more cost efficient with regards to production and also in pure form (Fig. 1.1).

An important consideration in transgenic research is the choice of promoter for regulating the expression of a foreign gene. The discovery of novel processes and techniques in marine biotechnology will create fresh opportunities for the development of innovative materials. The science of biotechnology has given us new tools and tremendous power to create genes and genotypes of plants, animals, and fish. *Lakra* and *Ayyappan* explored the use of synthetic hormones in fish breeding, the production of monosex, uniparental, and polyploid individuals, molecular biology and transgenesis, biotechnology in aquaculture nutrition and health management, gene banking, and marine natural products [1.12].

The biosynthesis and regulation route of many secondary metabolites in marine organisms should be addressed. It is possible, with the recent development of a novel transcriptome profiling methodology that allows for rapid and high-throughput screening of changes in messenger ribonucleic acid (mRNA) sequence pools. The application of genomics-based techniques and the integration of both biochemical and molecular data sets in marine organisms complement ongoing drug discovery efforts [1.13].

Metagenomic-based strategies are powerful tools to isolate and identify enzymes with novel biocatalytic activities from the uncultivable component of microbial communities [1.14]. The recent advances in biotechnological tools such as bioreactors, fermentations, and bioprocessing are useful in the production of functional ingredients, including enzymes that can be used in the food industry [1.15]. Molecular biology is playing a major role in marine biotechnology for an understanding of the genome level. Genomic analysis of marine organisms should be identified to utilize novel genes, proteins, enzymes, and small molecules. The knowledge of metabolic pathways and their genomics is the novel way to understand the mechanism behind the production of the compounds. Metabolic engineering is defined as the optimization of genetic and regulatory pathways to increase the production of compounds by cells (Fig. 1.2).

1.3 Marine Sources and Research Areas

Science and technology continues to move forward in making different technological tools to develop new products from the marine source. Important marine sources in the research are microorganisms, algae, and sponges. Various biotechnological products have been commercialized, ranging from novel drugs, chemicals, and enzymes to bioenergy [1.16–22]. Marine biotechnology plays an important role in the development of various biomaterials, biosensors, seafood safety, aquaculture, bioremediation, and biofouling (Table 1.1). Several drugs are obtained from natural sources, and researchers are still searching for potential organisms from marine sources.

1.4 Applications of Marine Biotechnology

1.4.1 Marine Aquaculture

Marine aquaculture is one of the best examples of marine biotechnology. Fish is one of the most important marine sources for protein supplement in human food. Overfishing and changes in the global environment are contributing to the slow disappearance of this important food resource. By applying marine biotechnological tools, we may be able to provide or improve aquaculture procedures through recombinant technology to develop genetically modified organisms [1.23–26], which could be useful to overcome the global food demand.

1.4.2 Marine Natural Products for Medicine

Marine bioresources are huge reservoirs for various potential biological molecules, which have tremendous potential as human medicines. Natural products are both a fundamental source of a new chemical diversity and an integral component of today's pharmaceutical collection [1.27–33]. Numerous marine compounds are isolated from marine animals, algae, fungi, and bacteria with antibacterial, anticoagulant, antifungal, antimalarial, antiprotozoal, antituberculosis, and antiviral activities. There are now 4 approved products, 13

Table 1.1 Important marine sources and research areas

Research area	Marine source	Aims
Food	Algae, invertebrates, fish	Development of innovative methods, to increase aquaculture production and zero waste recirculation systems
Energy	Algae	Biofuel production, biorefineries
Health	Algae, sponges, microorganisms	To find novel bioactives
Environment	Marine microorganisms	Biosensing technologies for marine environment monitors and non-toxic antifouling technology
Industrial products	Algae	Production of marine biopolymers for food, cosmetics, health

Table 1.2 Examples of market level marine-derived products

Products	Source	Application
Ara-A	Marine sponge	Antiviral
Ara-C	Marine sponge	Anticancer
Okadaic acid	Dinoflagellate	Molecular probe
Manoalide	Marine sponge	Molecular probe
Vent TMA polymerase	Deep-sea hydrothermal vent bacterium	PCR enzyme
Aequorin	Bioluminescent jelly fish	Bioluminescent calcium indicator
Green fluorescent protein	Bioluminescent jelly fish	Reporter gene
Phycoerythrin	Red algae	Conjugated antibodies used in ELISAs and flow cytometry
Cephalosporins	*Cephalosporium* sp., marine fungi	Antibiotic

in clinical trials, and large number of pre-clinical investigations, coming from a wide range of marine sources from many different parts around the world. Prialt ziconotide, a painkiller originally isolated from a Pacific (Philippines) cone snail, Yondelis trabectidin, an anticancer molecule from the Caribbean tunicate *Ecteinascidia turbinata*, and 3-(2,4-dimethoxybenzylidene)-anabaseine (DMXBA) from the ribbon worm *Paranemertes peregrina*, from the Pacific Rim, are a few examples [1.10] (Table 1.2). 59 marine compounds have been reported to affect the cardiovascular, immune, and nervous systems, as well as to possess anti- inflammatory effects. 65 marine metabolites have been shown to bind to a variety of receptors and miscellaneous molecular targets, and thus upon further completion of the mechanism of action studies, will contribute to several pharmacological classes [1.34]. The route to market involves isolation and chemical characterization, followed by synthesis or semi-synthesis of the molecule or an active analog.

Natural product lead compounds from sponges have often been found to be promising pharmaceutical agents. Most of these drugs are used in the treatment of the human immunodeficiency virus (HIV) and the herpes simplex virus (HSV). The most important antiviral lead of marine origin reported thus far is a nucleoside Ara-A (vidarabine), isolated from the sponge *Tethya crypta*. Marine compounds that act on the six hallmarks of cancer presented self-sufficiency in growth signals, insensitivity to antigrowth signals, evasion of apoptosis, limitless replication, sustained angiogenesis and tissue invasion, and metastasis [1.35–39].

Marine microbes have a huge biochemical diversity and are likely to become a rich source of novel drugs. Marine microbial compounds are an important source for drug development [1.22]. Marine bacteria are one of the important sources for many bioactive compounds, antibiotics, and pharmaceuticals. They are usually found in marine sediments and are also found to be associated with marine organisms [1.40]. Marine fungi are also reported to be a potential source for bioactive compounds. Polyketide synthases are a class of enzymes that are involved in the biosynthesis of secondary metabolites (erythromycin, rapamycin, tetracycline, lovastatin, and resveratrol).

Actinomycetes are one of the most efficient groups of secondary metabolite producers; they exhibit a wide range of biological activities, including antibacterial, antifungal, anticancer, and insecticidal, and enzyme inhibition. Several species have been isolated and screened from the soil in the past decades. Among its various genera, *Streptomyces, Saccharopolyspora, Amycolatopsis, Micromonospora*, and *Actinoplanes* are the major producers of commercially important biomolecules [1.41]. Actinomycetes are virtually unlimited sources of new compounds with many therapeutic applications and hold a prominent position due to their diversity and proven ability to produce novel bioactive compounds; 70% of which are produced by actinomycetes, 20% from fungi, 7% from *Bacillus* sp. and 1–2% by other bacteria [1.42]. Antimicrobial peptides are promising candidates, because their initial interaction with microbes is through binding to lipids [1.43].

Dinoflagellate toxins and bioactives are of increasing interest because of their commercial impact [1.44]. Functional screens to isolate novel cellulases, lipases and esterases, proteases, laccases, oxidoreductases, and biosurfactants have been described [1.45]. Enzyme inhibitors have received increasing attention as useful tools for the study of enzyme structures and their mechanisms. Marine organisms have been documented as a productive source for the enzyme inhibitors. Several commercialized products are shown in Table 1.2. Arebinosyl cytosine (Ara-C) is currently sold by the Pharmacia and Upjohn company under the brand name Cytosar-R [1.10].

1.4.3 Marine Nutraceuticals

Marine nutraceuticals can be derived from a vast array of sources, including marine plants, microorganisms, and sponges. Marine nutraceutical products currently promoted to various countries include fish oil, chitin, chitosan, marine enzymes, chondroitin from shark cartilage, sea cucumbers, and mussels. As mentioned earlier, the marine world represents a largely unexploited reservoir of bioactive substances that can be used for food processing, storage, and protection. Enzymes extracted from fish and marine organisms can provide numerous advantages over traditional enzymes. Fish protein such as collagens and their gelatin derivatives operate at relatively low temperatures and can be used in heat sensitive processes such as gelling and clarifying. Polysaccharides derived from alga, including alginate, carrageenan, and agar types are widely used as thickeners and stabilizers in a variety of food ingredients. In addition, Omega-PUFA (polyunsaturated fatty acid) is an important ingredient in the nutraceutical industry [1.46]. It has been proven that Omega-PUFA, especially eicosapentaenoic acid (EPA) and docosahexenoic acid (DHA) play a significant role in number of aspects of human health [1.47]. The application potential of chitin and chitosan are multidimensional, for example, in food and nutrition, biotechnology, material science, drugs and pharmaceuticals, agriculture and environmental protection, and gene therapy [1.48–52]. Fucoidan is a complex-sulfated polysaccharide, which can be derived from brown algae. Fucoidan has been used in several biological activities and is important for its high bioactive properties, for example, antibacterial, anticoagulant, antiviral, antitumor, etc., and many more yet to be explored [1.53].

1.4.4 Marine Biomaterials

In the recent years, much attention has been paid to marine-derived biomaterials for various biological, biomedical, and environmental applications. A recent report estimates that the global markets for marine biotechnological products might exceed US$ 4.1 billion by 2015, to which the following product segments, marine biomaterials (including food hydrocolloids) could contribute over 40%; marine bioactive substances for healthcare would be the most important and fastest-growing sector. Non-toxic, biocompatible, natural chitin and chitosan from crustaceans have potential use in cosmetics, food, and pharmaceuticals [1.54]. Seaweeds are the abundant source for polysaccharides, which are commercial products (alginate, agar, agarose, and carrageenan) [1.55–61].

1.4.5 Marine Bioenergy

Bioenergy from marine algae is a groundbreaking achievement in the field of marine biotechnology [1.62–67]. Biofuels derived from marine algae are a potential source of sustainable energy that can contribute to future global demands. The realization of this potential will require manipulation of the fundamental biology of algal physiology to increase the efficiency with which solar energy is ultimately converted into usable biomass [1.68]. Anaerobic digestion of microalgae is a necessary step to make microalgae biodiesel and biogas sustainable [1.69, 70]. The potential biomass sources for bioenergy are photosynthetic microalgae and cyanobacteria. There are versatile marine organisms that can be used in the production of biogas, biodiesel, bioethanol, and biohydrogen [1.71–76].

1.4.6 Marine Bioremediation

Bioremediation is also an important area of marine environmental biotechnology. Marine microorganisms have the capacity to degrade the variety of organic pollutants. *Pseudomonas chlororaphis* produces pyoverdin, which catalyzes the degradation of organotin compounds in seawater. Biopolymers and biosurfactants are also applied to environmental waste management and treatment [1.77–81].

1.5 Research Scope

Marine biotechnology plays a vital role in the exploration and study of various marine resources. Marine biotechnology comprises a broad range of subjects: marine bioactive substances, genetics, marine culture, fermentation engineering, and enzyme engineering. The marine biotechnology market is still in the promising stages; during the years 2008 and 2009, the global marine biotechnology market witnessed a slowdown owing to the global economic meltdown. The market gained drive in 2010 with the recovery of the economic situation and is expected to post substantial growth in ensuing years.

Table 1.3 Countries and their marine biotechnology research priorities

Countries		Research priorities
Africa	Mozambique, Nigeria, South Africa, Tunisia and Kenya	Biofuels and bioactives
Central and South America	Brazil, Chile, Argentina, Mexico, Costa Rica	Biodiscovery, bioenergy, bioremediation and biofouling
North America	USA, Canada	Biodiscovery, aquaculture and biofuels
Asia	China, India, South Korea, Japan, Taiwan	Biofuels, biodiscovery for human pharmaceuticals, food, feed, cosmetics
Middle East	Israel	Sponge biotechnology, marine bioactives and biofuels
South East Asia, Indian Islands	Thailand, Vietnam, Indonesia, Malaysia, Singapore, Sri Lanka, the Philippines	Biodiversity for novel bioactives and aquaculture,
Australia Pacific	Australia and New Zealand	Aquaculture and marine bioactives

The research drive on marine biotechnology is high in countries like USA, Brazil, Canada, China, Japan, the Republic of Korea, and Australia, as well as in other countries where activities are grow from a smaller base (Thailand, India, Chile, Argentina, Mexico, and South Africa), and where there are signs that marine biotechnology is increasing in importance as a research priority. It is notable that the major international effort, the Census of Marine Life (CoML), involved 2700 researchers, about 31% from Europe, 44% from USA and Canada, and 25% from the rest of the world, notably Australia, New Zealand, Japan, China, South Africa, India, Indonesia, and Brazil (Table 1.3) [1.82].

The United States is the world leader and represents the single largest region for marine biotechnology worldwide. The marine bioactive substances market is forecasted to register the fastest growth rate of more than 4.0% during the period 2009–2015. Healthcare/biotechnology constitutes the largest, as well as fastest growing, end use for marine biotechnology. Very few countries have initiated national R&D programs to exploit the benefits of biotechnology in the marine sector. However, advances in aquaculture, drug discovery and fisheries are expected to encourage applications of marine biotechnology. The research report titled as *Marine Biotechnology: A Global Strategy Business Report* provides a comprehensive review of the marine biotechnology market, recession on the markets, current market trends, key growth deliverers, introductions of recent products, recent activity in the industry (Aker Bio Marine ASA, CP Kelco US Inc., Cyanotech Corp., Elan Corporation plc, FMC Corp., FMC Biopolymers AS, GlycoMar Ltd., Integrin Advanced Biosystems, International Specialty Products Inc., Lonza Group Ltd., MariCal, Marinova, Martek Biosciences Corp., Mera Pharmaceuticals Inc., New England Biolabs Inc., PharmaMar S.A, PML Applications Ltd., Primex Ltd., Prolume Ltd., Sea Run Holdings Inc., and Tequesta Marine Biosciences), and the profile of major global as well regional market participants. The harnessing of marine resources through biotechnology and development of products and services should be a serious target for any country with significant aquatic biodiversity.

A major task of marine biotechnology is to develop an efficient process for the discovery of novel molecules from the marine environment. The high level of marine biodiversity of marine organisms makes them a prime target for bioprospecting; these are enzymes, bioactive molecules, and biopolymers with varied industrial applications. Biochemical studies of marine organisms are an important task for the discovery of new drug molecules and biological tools and management of biodiversity.

1.6 Organization of the Handbook

This handbook combines the knowledge of sea flora and fauna, biotechnological methods, product development and industrial applications. It is divided into 10 parts. The introduction of the book comprises the definition, history and research scope of marine biotechnology. The first part introduces marine flora and fauna in detail, such as fungi, phototrophs, viruses, microalgae, seaweed, coral, and sponges. In this part, a detailed explanation is given on the production, cultivation, and processing of flora and fauna. The second part of the book introduces the tools and method of marine biotechnology; it covers, bioprocess engineering, bioinformatics techniques, bioreactors, transgenic technology, quorum sensing, and molecular methods for the detection of invasive species. The third part of the book provides details about marine metagenomics, proteomics, marine metagenomics and supporting technology, microfluidic systems, and genomic mining. The fourth part of the book deals with algal biotechnology, starting with the structure and biological activities of marine algal polysaccharides, two centuries of research on iodine in seaweeds, marine macrophytes, and heavy metal removal by marine algae. The fifth part of the book covers marine microbiology, marine microbial biotechnology, and marine actinomycetes.

The sixth part of the book provides details about marine-derived metabolites, starting with marine natural products, biocatalysts, antimicrobial peptides, marine-derived fungal metabolites, dinoflagellates, carotenoids, Cnidarians, fatty acids, biotoxins, microbial enzymes, and polysaccharides. The seventh part of the book focuses on applications of marine biotechnology, starting with pharmaceuticals, functional food, nutraceuticals and cosmeceuticals. The eighth part of the book covers bioenergy and biofuels; here, the lead authors discuss marine bioenergy, marine algal biotechnology for bioenergy, and biofuels. Biomedical applications are extensively discussed in the ninth part of this book; the topics are marine biomaterials, gene delivery, biosensors, and biomineralization. Finally, the last part of this book focuses on industrial applications of marine biotechnology.

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