

Grand Challenges in Biology and Biotechnology

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Grand Challenges in Marine Biotechnology

 Springer

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Foreword

Marine biotechnology (MBT) gives different associations and meanings depending on where you are in a value chain and what your aims are. To approach this area in a coherent manner, MBT should be understood by the enabling role biotechnology has in making it possible to realize value creation from marine, biological resources. For defining MBT, the OECD has recommended to use their generic definition of biotechnology by introducing “marine” in the text, and this has been the ERA-NET Marine Biotechnology project’s (2013–2017) common ground for the development of this area. Then it applies to and involves all stakeholders from basic science to developers of industrial products and services. However, to a limited degree, MBT is a separate business sector in its own right. This concept is illustrated in Fig. 1, showing that the application of biotechnology early in the value chain enables innovations for industries within diverse sectors like pharma, food, nutraceuticals, cosmeceuticals and process industries to develop products and services. The book chapters illustrate this principle well, highlighting the importance of basic applications of the biotechnology toolbox and infrastructure to enable different industrial sectors to develop products and values from marine bioresources. This also applies to the farming of fish and shellfish where MBT has a significant role in breeding, health, feeding and environmental matters.

The book describes how the marine environment has delivered, and is expected to deliver, biological molecules and principles that can only be discovered from this unique biosphere. Economic estimates have been made on how MBT will contribute to societal matters, and it is evident that utilization of the marine biological resources and principles through the application of biotechnology will contribute substantially to the development of the emerging circular bioeconomy.

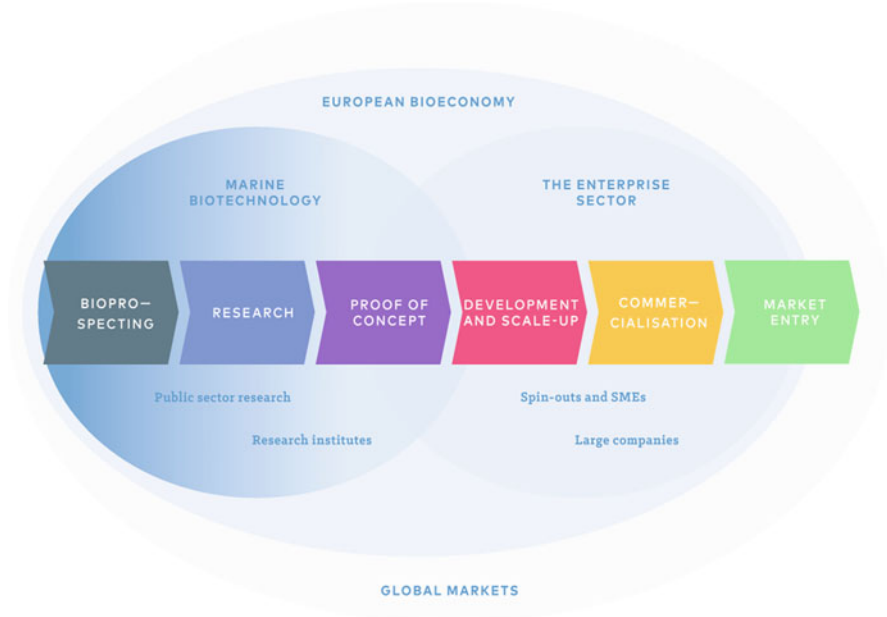


Fig. 1 The contribution of marine biotechnology to business areas along the value chain (Hurst et al. 2016)

The *Marine Biotechnology Strategic Research and Innovation Roadmap*, published by the ERA-NET MBT project in September 2016¹, emphasized the need to continuously develop the biotechnology toolbox and infrastructure in a broad sense to be able to work efficiently and sustainably with exploration of marine bioresources. In addition to the technology development, there is a need to sustainably produce and process marine biomass within a frame of political support, as well as product innovations and differentiations as illustrated in Fig. 2.

Taken together, the book pulls these aspects well together in a coherent way, emphasizing the need to continue to develop MBT as an enabler for the discovery of valuable and innovative marine products and services to be refined in their respective value chains. The legacy from the ERA-NET MBT project is taken further in a new European ERA-NET project developing the Blue Bioeconomy. It is a pleasure to observe that regional involvement, industrial engagement as well as open science

¹Hurst D, Børresen T, Almesjö L, De Raedemaeker F, Bergseth S (2016) Marine biotechnology strategic research and innovation roadmap: insights to the future direction of European marine biotechnology. Marine Biotechnology ERA-NET, Oostende

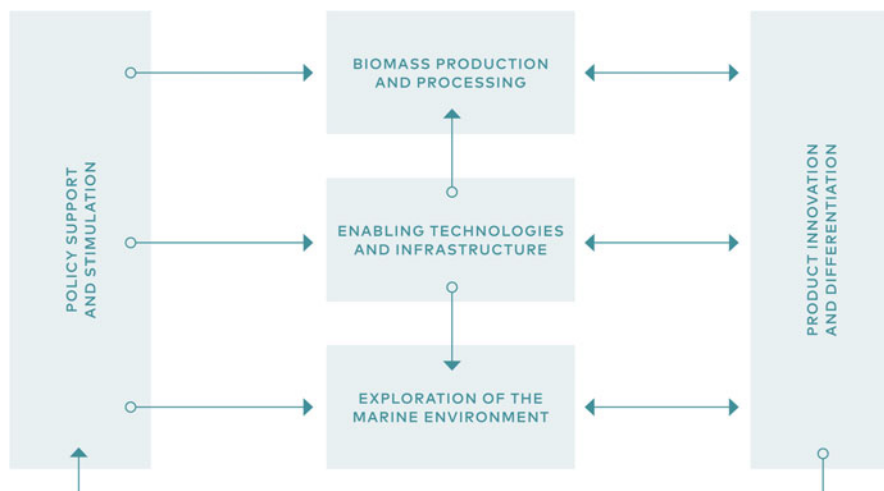


Fig. 2 The five thematic areas of the MBT roadmap and their interconnections (Hurst et al. 2016)

and data management incorporating all stakeholders through workshops and conferences will secure increased literacy and developments based on marine biological resources with value for our societies.

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Preface

The idea of this book is primarily a fruit of our nice cooperation in the last years. We both have been involved as editors and guest editors in several editorial projects highlighting the potential of marine biotechnology. As a natural consequence, by late 2015, we found ourselves discussing the interesting possibility of joining our efforts towards a landmark project in the field, i.e. a book within the Grand Challenges in Biology and Biotechnology series. As part of this series, the book would have a unique perspective on the subject by exploring how marine biotech can contribute to the achievement of major national and international policy goals, such as economic growth and job creation, public health, environmental protection and sustainable development. In general, it is expected that the knowledge made available through this reliable reference will be used by leading authorities in their efforts towards the development of a blue bioeconomy.

The 15 chapters that compose the book are organized in three sections. The first one discusses how marine may provide new solutions to some of the grand challenges of the twenty-first century. The second section explores the economic potential of marine biotechnology, while the third and last section focuses on how to unleash this enormous potential by presenting major national and international strategies, policies and programmes designed to support the development of marine biotechnology.

In developing this book, we recognize that advances in marine biotechnology may foster the much-needed source of innovation and economic growth, closely aligned with the sustainable use of marine bioresources in ways that establish new markets, generates revenue and increases employment. It is our hope that this fine collection of chapters will be a valuable resource for scientist and decision-makers and will stimulate further research and development (R&D) into the vibrant area of marine biotechnology.

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Introduction

The marine environment is considered Earth's last frontier of exploration. In fact, a common belief is that just less than 5% of the vast and rich marine environment has been explored. Our seas and oceans represent a very unknown resource for the discovery of novel organisms, (bio)products, (bio)processes, and for the development of bioinspired synthetic drugs.

Recent advances in genetics and other (bio)molecular techniques are providing all necessary tools to access these still-untapped marine resources on a larger scale and, consequently, enabling exploitation of the true promise of the blue biotechnology.

Acknowledgment of the potential of marine biotechnology is in due course by many governments in the world to provide solutions to some of global Grand Challenges of the twenty first Century such as sustainable supply of food and energy, development of new drugs and health treatments, and providing new industrial materials and processes. For this reason, the advances in marine biotechnology may foster the much-needed source of innovation and economic growth in many countries and pave the way towards the development of a global blue economy, i.e., a new economic model based on the sustainable exploration of our ocean ecosystems. They can create jobs and wealth by contributing to the development of greener and smarter economies.

The Promise of the Blue Biotechnology

Marine biotechnology can play an important role towards meeting challenges of the new century and can greatly contribute to economic recovery and growth worldwide by delivering new knowledge (scientific knowledge of marine life and ecosystems) and facilitating access to products and services by cutting-edge technologies.

In 2011, it was estimated that 20,000 marine natural products were discovered in the previous five decades, and preclinical and clinical pipelines for new pharmaceuticals contained almost 1500 molecules, specially related to anticancer research. However, in

marine biotechnology field, significant contributions for new antibiotics, anticancer, and immune system modulator can be accounted. Due to widespread use of known molecules (i.e., antimicrobial resistance), new antibiotics are necessary, and this is one of the point of worldwide interest in applied marine pharmacology. In this context, more than in others, marine microbes are still seen as untapped resource.

Other metabolites from marine organisms with nutraceutical applications are considered within food lines of research, as well; this field requires relatively less economical efforts compared to the pharmaceuticals above indicated. Nutrients, enzymes, and other metabolites (essential fatty acids) are the key molecules considered within this aspect.

Another great challenge relates to the application of marine biotechnology for algal biofuels since algae biomass is used to generate biodiesel, bioethanol, biogasoline, biomethanol, biobutanol, and other biofuels. Absence of lignin, present in cellulosic biomass, and cultivation that hardly impacts on food production are the two major positive points for marine biofuel revolution. In this context, cultivation of microalgae may have a smaller footprint in comparison to land biomass. This energy sector is positively marked by microalgae, macroalgae, and bacteria showing their utility in microbial fuel cells, i.e., systems that harvest the electricity generated by microbial metabolism. However, an overall opinion is that marine biorefining is in his infancy compared to biorefineries for terrestrial biomass.

The first part of this book discusses how marine biotechnology can realize these increasing contributions, highlighting the most important topics at the current state of the art in these scientific sectors. Seven chapters, compiled by worldwide leader groups, identify cutting-edge areas that may benefit from a greater attention by governments supporting policies to general field of marine biotechnology. The pharmaceutical sector is very present embracing marine originating antibiotics, seaweeds with health promoting activities, sustainable food supply of their bioactive materials, and an overview of the literature with a special focus on structural features and mechanisms of action of many lead compounds. The present decline in the development of antibiotics over the past few decades and the decrease in the development of new antimicrobial agents, with increasing number of bacteria showing multiresistance to the existing antibiotics, have raised an important problem in this respect as above mentioned. A need to find new molecules is clear. Marine nature environment is an enormous source of biodiversity and may provide us with new molecules from plants, fungi, and other macro- and microorganisms. Seaweed bioactives possess a wide spectrum of biological actions, including antioxidant, anti-inflammatory, antiviral, anticancer, antihypertensive, fat-lowering, and neuroprotective activities and have gained much importance in pharmaceutical sector, in particular with their polysaccharides, pigments, phlorotannins, peptides, minerals, and vitamins. Current research is focused on intensive efforts for isolation and identification of these new ingredients. This section of the book includes other three key topics such as marine fungi, marine eubacteria with the highest hydrogen production yield, and the use of gasification and anaerobic digestion of seaweed for the production of biofuels. As for fungal organisms, not only obligate marine fungi but also a multitude of terrestrial fungi (whose occurrence at sea has been considered incidental) are increasingly regarded as an

evidence of marine ecological flexibility. Thus, special physiological adaptations of these organisms are considered in view of their possible biotechnological exploitation. There are many examples of the production of bioenergy from marine organisms; however, the potential of algal biomass as a source of liquid and gaseous biofuels is still a highly topical theme. The last two chapters in this section focused on energy theme: a summary of the fermentative pathways related to hydrogen production in the thermophilic microorganisms of the genera *Thermotoga* and *Pseudothermotoga* (marine species with the highest hydrogen yields among eubacteria), and a detailed report on major projects in the UK on gasification and anaerobic digestion of seaweed, suggesting promises of these technologies for exploiting bioenergy.

The Economic Potential of Marine Biotechnology

Understanding socioeconomic contributions of marine biotechnology is important for a number of reasons and is necessary to drive correctly the future developments. Bioeconomy has a political priority because of its potential for economic growth and social benefits and in almost every continent, the planning of related strategies started as governmental actions. Marine biotechnology can make important contributions to bioeconomy through the construction or the greening of a number of industries with flourishing of innovative products and processes, and the consequential creation of new jobs. It is within the concepts under the term bioeconomy that this point can be discussed, marine biotechnology being fully framed within those economic sectors that are founded on bioscience and biotechnology innovation.

Market value of marine biotechnology products and services is difficult to estimate; important elements are the tracking of the range of products and services across different sectors and precise identification of the roles and contributions of marine biotechnology, separating them out from other factors. In recent reports evaluating statistically its value, the market of marine biotechnology is traditionally separated in different sectors such as pharmaceutical products for the marine-derived drugs, biotechnology itself, including all other related bioproducts, fish and shellfish for aquaculture industry, and the biomass-related markets, for other specialized compounds including those derived from agar, alginates, and carrageenan. All these sectors were estimated at 2.8 billion EUR in 2010 with an annual growth of 4–5%.

The second part of this book explores the economic potential of marine biotechnology. In the first chapter of this section, a thorough description of the firms and of organizations belonging to the marine industries is reported, with geographical distribution, dimension, main markets served, and production activities. Through the construction of an original database as the result of a multiple phases methodology, based on the use of a wide number of sources, a first investigation of the organizations that belong to the marine industrial sectors is reported. Some case studies of marine firms are also presented. It is evidenced that the absence of a shared definition of the blue industries translates into a lack of thorough analysis of the global sector. The survey offers a general idea on the characteristics that are shaping this young sector. A

focus is given, in the second contribution, on compounds that successfully reached the market; particularly, the approaches employed by the nutraceutical, pharmaceutical, and cosmeceutical companies in marketing their products are described as found in novel and/or ongoing marine natural products development programs. As for highly promising marine bioactives, in order to improve their market entry success rates, suggestions are provided highlighting what can be done in novel and/or ongoing development programs. This section of the book is concluded by a report on the activity of the European Marine Biological Research Infrastructure Cluster, with a reflection about major issues such as lack of connectivity, practical and cultural difficulties in connecting science with industry, and different regional developments throughout Europe. Managing these multi-country and multi-stakeholder collaborations characterizing international partnerships is extremely important to better address benefits of marine biotechnology. A common opinion is that there is a need to look for synergies among supported projects to reduce the likelihood of duplication. Conclusions drawn outlined lack of connectivity between research services, some practical and cultural difficulties in connecting science with industry, including uneven regional development and innovation policies throughout Europe.

Supporting the Development of Marine Biotechnology

Despite significant progress, marine biotechnology is yet far from fulfilling its potential. How to unleash this enormous capability is the grand challenge that this field is facing. Moreover, marine biotechnology brings up a number of ethical, legal, and social issues connected to the harvesting of marine bioresources, thus raising questions of trans-boundary approach for benefit sharing and intellectual property rights. This very aspect cannot be neglected. Moreover, due to the global presence of marine bioresources, R&D infrastructures are the most important keys to drive innovation.

This last section is devoted to investigating on real supports that marine biotechnology field have had, discussing national and international strategies, policies, and programs. Four chapters in this section give a great overview with the last one about legal landscape regulating the access to and utilization of marine genetic resources. SeaBiotech, BluePharmTrain, and ChiBio are specifically covered in single contributions while many other research programs such as BAMMBO, Bluegenics, GIAVAP, LIPOYEASTS, MaCuMBA, MAMBA, MAREX, MARINEBIOTECH, PharmaSea, Polymode, SeaBioTech, Sunbiopath, EMBRIC, INMARE, NOMORFILM, and TASC MAR are collectively analyzed in detail. A large number of libraries are mentioned as research activity products: sequences, active species, extracts, active fractions, and compounds composing a massive quantity of data that needs to be deeply studied considering all possible fields. The effort of the EU Marine Biotechnology ERA-NET (ERA-MBT) in preparing a roadmap that identified an optimistic future for marine biotechnology is also reported, summarizing the five thematic areas: (1) exploration of the marine environment, (2) biomass production and processing, (3) product innovation

and differentiation, (4) enabling technologies and infrastructure, and (5) policy support and stimulation. Long-term actions of the marine biotechnology field are identified in building research networks and international collaborations and implementing global agreements on access to resources.

A clear implication for scientists working on marine biotechnological research as well as any user of genetic resources along the biodiscovery pipeline is the legal landscape regulating the access to and the utilization of genetic resources. Recent changes with the entry into force of the Nagoya Protocol in 2014, and the adoption of the related EU Regulation on user compliance in 2014, are discussed in the last chapter of this section. This chapter informs users on their legal obligations regarding access and benefit-sharing with a focus on marine genetic resources.

Conclusions and Perspectives

To realize the potential that the oceans offer in terms of new products and processes requires the concerted effort of many parties. Effective academic–industrial collaboration is essential to bring any novel marine biotechnological outputs to the market. Key to this success is the establishment of formal and informal agreements with stakeholders and institutions to enhance the commercialization of marine biotechnologies through education, market research, and business development activities. That will provide the parties with access to new tools and research capabilities which would otherwise be unavailable to them on an individual basis.

Stimulating the development of research strategies and programmes for marine biotechnology research and aligning these at the national and international level is also of primary interest, as well as the development of local and major networks, which allows productive face-to-face interaction between academic and industrial partners that can help to break down last barriers from applied to commercially exploited science.

As such, this book highlights the relevance of collaborative industry–academia approach and uses the “Grand Challenges” as the basis for a logical analysis of the current and possible future development of marine biotechnology, set against its capacity to deliver products and processes to address high-level societal needs and opportunities in the areas of food, energy, environmental health, human health and well-being, as well as industrial products and processes.

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“When he is not working, Pabulo enjoys spending time walking in the woods, in the mountains, and near the sea. . .thinking, always thinking”. (Lifeboat Foundation, 2016)



Antonio Trincone is author of more than 140 scientific publications (articles, reviews, book contributions) that appeared in international leading scientific journals. He has been a senior researcher working since 1983 in Naples at the Istituto di Chimica Biomolecolare belonging to Consiglio Nazionale delle Ricerche, Italy. He has been professor of organic chemistry in charge for several years at the University of Salerno, Italy. His research activity focused on biomolecular aspects, many regarding stereochemistry and bioorganic

chemistry of enzymes as biocatalysts. Recent achievements are directed to practical interest in the biorefinery pipeline context using thermophilic and/or marine enzymes and to the biocatalyzed synthesis of bioactive compounds. Antonio has been the editor of different scientific books and special issues dedicated to marine biotechnology. He is specialty chief editor of marine biotechnology (*Frontiers in Marine Science*), editing different research topics for this journal, and he is part of Editorial Board of MDPI journals *Marine Drugs* and *Molecules* and guest-edited different special issues for these journals. Most of his recent work is dedicated to the editorial process and review activity for scientific projects, published articles and scientific positions.