The research programme Marine Paint aimed at developing new and effective marine antifouling paints, which are more environmentally friendly than those in use today.
Preface

Making a difference for the marine environment

Mistra – The Foundation for Strategic Environmental Research – has generously financed and actively supported the Marine Paint programme for the last eight years, and is also financing the remaining research during 2011.

Marine Paint is a research programme at the University of Gothenburg and Chalmers University of Technology aimed at making a difference in the way antifouling paints for ships, leisure boats and other under-water surfaces and structures are formulated.

To continue with the present environmental impact of biocides originating from marine paints is not a sustainable solution for any of the stakeholders involved; from the paint producers, the shipping industry and all living organisms in the waters, to all of us who are in need of and depend on healthy seas.

The highly-qualified, enthusiastic and innovative researchers on the Marine Paint programme have developed significant enablers to improve the situation over the years to come. The research has crossed departmental and institutional boundaries, giving the members the excitement and resources of a truly multidisciplinary environment, and creating a network promoting future research for a better marine environment.

The first phase of the programme was dedicated to the development and evaluation of medetomidine, an antifouling agent that has proven highly efficacious against barnacles. I-Tech, the company which owns and manages medetomidine for use as an antifouling agent, is dedicated to the commercialisation of medetomidine (under the trademark Selektope®) and has applied for approval of medetomidine as an active antifouling substance under the EU’s Biocidal Products Directive (BPD). The level of commercial interest is considerable; the company has signed a license contract with Volvo Penta for leisure boat applications and is in the process of finding partners for larger ship applications. So far, the response from the BPD-authority is positive and approval is expected in 2012. The substance is approved for use in South Korea and Japan.

The second phase of the programme has the broader aim of developing marine paints that protect against all fouling organisms in addition to barnacles. The developed concept of optimised mixtures is based on the usage of several different biocides making it possible to formulate marine paints with full fouling protection while at the same time treating the environment with the utmost respect. During the work on optimised mixtures, a new microencapsulation technology was developed enabling the optimised mixtures of biocides to be incorporated into paint systems. Both innovations are looking promising. The members of the programme have funded a start-up company (MBRiG, Marine Biofouling Research Göteborg) with the aim of continued research and making the concepts available for commercial use.

The field of antifouling is complex and, as history has shown, it is easy to create environmental disasters by implementing technologies and biocides without understanding their full impact on the environment and also how different marine organisms react on exposure to biocides. The research on barnacles and medetomidine is also ground-breaking in the sense that the mechanism of the interaction down to the receptors and the DNA of barnacles have been investigated. Such a depth of knowledge helps ensure better-informed decisions are made in the long run.

I have served as Chairman of the Board for the programme for the last four years with great satisfaction. It is inevitable that, during such a long research programme in such a complex field, many ideas and problems arise, some of an internal nature and some external. It is like a long distance sailing trip, you need both stability and the ability to change course as needed. The programme has been very well led by the excellent management team and their leaders, Krister Holmberg for the first year, Björn Dahlbäck for the next six years and Thomas Backhaus since then. The Board members have provided stability with their vast experience and knowledge from research, business, environmental legislation, the shipping industry and programme leadership. I am grateful to the management team, to Björn, Thomas and to all the Board members. It has been a delight to work with such a committed group of people.

It is my sincere belief that the Marine Paint programme will make a significant contribution to reducing the global environmental impact of biocides originating from marine paints. I also believe that, besides the innovations and accumulation of knowledge, the approach to working as a team – including the crucial management of the interface between the researchers and the commercial world – will have lasting effects among the members and hopefully also in their organisations.
Executive Summary

Marine Paint: medetomidine – a novel biocide – and clever mixtures minimise the environmental footprint of tomorrow’s antifouling paints

Marine Paint has conducted intense research on marine antifouling on the Swedish west coast for several years. The programme started in 2003, investigating the possibilities opened up by the unexpected finding that medetomidine – a substance with a long history as a veterinary pharmaceutical – efficiently prevents fouling of ships’ hulls by barnacles. An application for Europe-wide registration as a new antifouling biocide and for inclusion in “Annex I” was filed in 2009. To combat the full range of fouling organisms, Marine Paint then broadened its research activities and developed a system of environmentally optimised, micro-encapsulated biocide mixtures.

Biocide content can be minimised with clever mixtures without sacrificing paint efficacy

Current antifouling paints often contain only one or two “active ingredients” or “biocides”, chemicals that are specifically designed to be toxic to fouling organisms. These need to be applied at rather high doses, in order to inhibit fouling by any of the whole range of different fouling organisms, which encompasses not only barnacles but also various other calciferous organisms (e.g. tube worms, mussels), as well as higher plants (e.g. sea lettuce) and slime (microbial biofilms). Marine Paint uses specifically designed biocide mixtures to prevent settling by any of these organisms. Each biocide in the mixture has a specific activity profile and is efficacious to a known extent against a known sub-set of fouling organisms (Figure 3, page 26). Acting in concert, the compounds in the mixture completely prevent fouling. The ratios and concentrations of the compounds in the mixture are optimally adjusted, in order to provide full antifouling efficacy but avoid overdosing. This not only increases the environmental performance of paints, but can also lead to substantial commercial benefits.

Marine Paint developed the recipes of these optimised (“clever”) mixtures through a conceptual mixture-model system where the efficacy contributions of different biocides are balanced against their expected environmental risks. The result is a vast collection of several thousand recipes, with different concentrations and combinations of biocides, all equally effective in their antifouling properties, but with estimated too-fold differences in environmental risk.

This collection considers major fouling biocides available on the world market as mixture components, including classic compounds such as copper and Irgarol as well as modern organic biocides such as the pyrithiones, DCOIT (Sea-Nine), botocide, tolylfluanid and the aforementioned medetomidine. This provides great flexibility to react to new perspectives on environmental protection, stemming from the recent adoption of the proposal for a new European Biocide Regulation (COM(2009)267). It also provides a basis for swift adjustments when new scientific findings on the environmental risks associated with individual compounds emerge, and it enables the final paint recipe to be adapted to meet various local conditions in different areas of the world’s oceans.

Development of high tech paint systems

A common problem with current paint systems is the fast initial burst during which excessive amounts of biocides leach into the surrounding waters. This means that large amounts of biocides must be added to the initial paint to ensure antifouling performance over its whole service life. This practice not only leads to an unnecessary high environmental burden, it also incurs high costs. Marine Paints chemists have been working with a number of systems for controlling and decreasing this initial burst of biocide release. In the first phase of the project the initial release of medetomidine was successfully slowed down by binding the compound to metallic nanoparticles. However, the situation becomes more challenging when the release rates of several biocides in a mixture need to be controlled simultaneously. Marine Paint approaches this problem by embedding each biocide separately in microcapsules, microscopic bubbles measuring a couple of micrometers in diameter and consisting of an organic polymer. The biocides are solubilised in the core of the microcapsules. The use of microcapsules not only dampens the initial release burst drastically, it also helps avoid chemical interactions between the different biocides, which greatly facilitate paint formulation. Marine Paint has already achieved large-scale production of these microcapsules at low cost, which makes the technology particularly attractive for commercialisation.

Medetomidine is currently being evaluated in respect of the Biocidal Products Directive (Annex I inclusion) Marine Paint focused exclusively on the evaluation of medetomidine during the first four years. Interdisciplinary studies on antifouling performance, environmental properties, mode of action, and technical feasibility were carried out. Marine Paint has examined the ecotoxicology of the compound on a broad range of marine species as part of the environmental risk assessment. Furthermore, Marine Paint investigated the consequences of medetomidine’s unique mode of action on its application as an antifouling biocide.

Medetomidine causes behavioural changes in mussels and shrimps at high concentrations. It also affects respiration in fish and leads to an aggregation of the pigment...
granules in skin melanophores, which gives exposed fish a paler appearance. Thanks to our extensive knowledge of the ecotoxicology of medetomidine, such critically high concentrations can be avoided in the final paint recipes. Ecotoxicological effects are only encountered at concentrations higher than those currently expected from the paint formulations being evaluated, even in worst case scenarios (small marinas with poor water exchange). Final tests on biodegradation and bioaccumulation are currently underway and will complete the environmental risk assessment of medetomidine.

I-Tech, a spin-off from the University of Gothenburg, served as the commercial partner of the Marine Paint programme. The company now commercialises medetomidine as an antifouling agent under the trademark, Selektpe®. In spring 2009 a dossier for the evaluation of medetomidine for an inclusion in the positive list of the Biocidal Products Directive (Annex I) was submitted. In parallel with this, the first real-world tests of medetomidine-containing paints are underway: patches of the hull of a car ferry owned by the Wallenius shipping company were recently painted, and are now continuously monitored during routine shipping operations.

New fundamental knowledge on the biology of barnacles

In the course of this work, Marine Paint also developed fundamentally new knowledge on the biology of barnacles. In particular, in-depth investigations on the molecular events that govern the settling of barnacles were implemented. Five different octopamine receptors – the molecular structures that lend medetomidine its antifouling activity – were cloned, and a complete cDNA library of barnacle larvae is now available.

More details

The remaining chapters of this report describe the various projects involved in the Marine Paint programme. Scientific details will be compiled in a special issue of “Integrated Environmental Assessment and Management”, which is scheduled for publication in late 2012. Please contact us for further details, and let us know if you would like to be informed when it goes into print.

Outlook

Members of the programme have founded MBRiG, Marine Biofouling Research i Göteborg AB, to provide a solid organisational basis for a continuation of the research activities. In order to put their research results to practical use, Marine Paint and MBRiG are currently in contact with several biocide and paint companies (including I-Tech), as well as an antifouling programme driven by the Chinese Ministry of the Environment and the United Nations Development Programme in China.
The problem

Fouling of surfaces – a natural phenomenon

When a surface comes into contact with seawater, dissolved and particulate organic matter will immediately foul it. Natural organic compounds dissolved in the seawater adhere to the surface within milliseconds. Living particles, such as bacteria and unicellular algae, start to colonise the surface and are readily detectable within a few hours when the surface becomes slippery and slimy. After a week or more, the surface is colonised by a variety of microorganisms, algae and animals. The attached way of life is an important survival strategy for many organisms in the marine ecosystem, and there are some 4,000 marine species known to colonise submerged surfaces in the marine environment.

All submarine surfaces are affected – both natural and those introduced by man: ships’ hulls, offshore installations, bridges and other structures at sea. The fouling gives rise to many different kinds of problems and high costs. Finding strategies to prevent fouling on marine surfaces without impacting on the environment is challenging and engages many research scientists, companies and authorities throughout the world.

What is the problem with fouling, and how big is the problem?

Fouling on ships increases the surface roughness of the hull, and its frictional resistance increases when the vessel moves through water. The increased resistance leads to increased fuel consumption. The cost of increased fuel consumption is substantial – after six months, a ship without an appropriate antifouling coating can suffer a 80% increase in fuel consumption in order to maintain normal speed. A medium-sized ship with a 20% increase in fuel consumption and 150 days under way per year will increase annual fuel costs by about SEK 3 million.

Maintenance costs also increase with fouling. The ship must be dry-docked more often, and requires additional surface treatment and/or re-painting. In addition, fouling has a negative effect on a ship’s manoeuvrability. To prevent fouling, over 80,000 tonnes of antifouling paint are used every year – with a total market value of €1 billion. The total cost of fouling is, however, significantly higher. The US Navy faces annual costs from fouling of over €1 billion, including maintenance and increased fuel consumption.

The environmental problem is evident and serious. Increased fuel consumption leads to increased emissions of carbon dioxide, nitrogen oxides, sulphur oxide, hydrocarbons and particles. In addition, there is scientific evidence showing that fouling can play an important and undesirable role in spreading marine species from their natural areas of distribution to new areas where they potentially constitute a threat to the ecological balance, becoming what are called “alien species”. In addition, to prevent fouling, non-sustainable countermeasures are taken. Hence, there is a trade-off between the adverse effects of fouling and the adverse effects resulting from the use of toxic antifouling paints that are hazardous to marine ecosystems.
The International Maritime Organisation (IMO), a UN organ, agreed in two on a convention to ban on tributyltin (TBT)-based paints. TBT has been shown to have severe ecotoxicological effects. As of two, it is forbidden to apply new TBT-containing coatings, and from eight there is a ban on the presence of such paints on ship hulls for those states that adhere to the convention. Five states representing seven percent of the world tonnage have ratified the convention in November one. There are many lessons to be learned from the introduction and the later ban of TBT. One is the long process from the first warning signs to effective international sanctions – see table. When developing new antifouling agents it is of the utmost importance to rigorously anticipate and assess the risk of long-term effects on the environment.

What is fouling?
The particular species adhering to and growing on a hull depends on the waters through which the vessel moves, the season, and how much time the vessel spends in port. The first colonisers are unicellular organisms. Bacteria, cyanobacteria, diatoms (unicellular algae), and protozoans (unicellular animals) are common species in the initial microfouling. Diatoms excrete large quantities of extracellular polymeric substances (EPS), which contribute to the sliminess of the surface. Following the microfouling, a macrofouling community establishes itself, consisting of soft or hard foulers. Soft foulers include higher algae, such as the green algae Ulva intestinalis. Ulva releases spores which, on touching a surface, secrete an adhesive consisting of glycoproteins to ensure that the algae adhere to and grow on the surface. Other types of soft foulers are sea squirts, sea anemones or soft corals. Hard foulers include mussels, tube worms and barnacles, all of which have highly developed abilities to adhere strongly to the surface. The species use different types of chemical adhesives, although they all have the same function; to allow the species to attach itself strongly to the surface.

Consequently, the fouling on a ship’s hull becomes a unique ecosystem in itself, but one that creates major problems for both commercial shipping and leisure boating.

The legislative pressure
The necessity to develop antifouling strategies with low environmental impact, has led to a substantial commitment from national and international authorities.

1850s Organotins first prepared
1950s TBT biocidal activity discovered
1960s TBT introduced as antifouling agent
1976 TBT + Self polishing Coating (SPC) patent
1983 First report on malformation of oyster shells round marinas
1986 First report of imposex in molluscs
1989 EU ban on TBT on boats < 25 m
2001 IMO Anti-fouling system convention re. TBT
2008 No ships may enter an EU port with TBT
2008 The IMO Anti-fouling system convention enters into force
2012 TBT still in use in several countries
In the EU, the Biocidal Products Directive (BPD) was implemented in 2000. The EU is reviewing all biocidal products including antifouling paints. Of 46 notified antifouling agents in 2002, only ten have entered the BPD registration process. At the moment it is not known how many of the ten biocides will be deemed acceptable. Unacceptable biocides will be removed from the EU market. In addition, there are also national restrictions on antifouling paints in non-European countries. In Canada, antifouling paints containing copper must have a very low copper release rate, and Sweden has banned most biocide-based antifouling paints for leisure craft in the Baltic Sea.

### Stakeholders

Shipping companies and boat owners looking for a better solution to the problem of fouling are the primary stakeholders of the Marine Paint research programme. Government authorities are also crucial stakeholders, since there is considerable pressure from their side for new and better solutions to be brought onto the market and used. In addition paint companies as well as biocide companies are sharing an interest in developing environmentally optimised paints. The greatest stakeholder, however, is the marine environment itself.

### Many attempts to prevent fouling

Over the years, a wide range of methods have been tried to protect ship hulls. From the very beginning, the principal approach has been to make the hull toxic by coating it with tar or using iron or copper sheathing to protect the wood. When iron hulls came into use, it was no longer possible to use copper sheathing, due to the galvanic corrosion problems that would arise.

The first antifouling paint patent was filed in the 17th Century and was based on iron powder, copper and cement. The development of bottom paints really took off in the nineteenth century, with several patents granted in that era. The paints at that time contained everything from lead and mercury to arsenic and tin compounds, and were the precursors of the paints used today.

#### Current technologies and the search for new solutions

Current antifouling technologies follow two routes, the chemical approach and the physical approach. The chemical methods involve coating of the hull with a paint containing an active substance – a biocide – to prevent fouling. Formerly, organic tin compounds such as tributyltin (TBT) were the dominant biocides, but they are being phased out because their use is extremely hazardous to the marine environment. Copper, often in combination with additional organic biocides, is the most commonly used biocides today.

The coating formed after the paint has dried can be of several types:
1. A matrix, which slowly dissolves in seawater, releasing the biocide.
2. An insoluble matrix through which the biocide moves freely by diffusion out into the water.
3. A self-polishing coating (SPC) producing a soluble microlayer at the surface, resulting in a continuous polishing of the surface, and a release of the biocide.

Other physical approaches to inhibit fouling include micro- or nanostructures in the coating and on the surface of the coating. Microstructures in the order of several hundred microns have proved effective in preventing the adhesion of barnacles. AMBIO, an integrated project funded by the European Commission, focused on modern molecular engineering of the surface to create nanostructures that prevent or reduce the adhesion of fouling organisms.

These three types of paint represent the chemical approach to antifouling. The physical methods rely on effects other than the leakage of chemical/toxic substances. Fouling-release technologies involve protecting the hull by a coating with a very low surface energy. Low surface energy means that the marine organisms adhering to the hull have a very low strength of adhesion, and are dislodged by the hydrodynamic forces generated when the vessel moves through the water. Silicone is a suitable basis for this kind of coating. The coating is effective only at relatively high velocities through the water (12–15 knots and above), which generate the hydrodynamic forces necessary to scour off the fouling.

A highly effective and environmentally optimised method of controlling fouling could be to remove it mechanically. Brush systems are now on the market, which can clean the hull without requiring the boat or ship to be taken out of the water.

There are many research initiatives to find new and better solutions to fouling. In the search for new biocides, several substances produced by marine organisms have been identified. These substances are used by specific marine organisms to avoid being fouled by other marine organisms.

The development of bottom paints really took off in the nineteenth century, with several patents granted in that era. The paints at that time contained everything from lead and mercury to arsenic and tin compounds, and were the precursors of the paints used today.
Medetomidine – a new marine biocide

The marine biocide market

The industrial market for marine biocides is integrated with the marine coatings industry and although the active biocides are represented by other industrial actors than the coating products the two industries have to work hand in hand to develop and distribute optimised coating products for the end customers, i.e. ship and boat owners. As the shipping industry is a truly global operation, the suppliers to this industry also need to work with a global perspective on their products and customer offerings. This brings about specific requirements in terms of presence, distribution, language and cultural awareness and, of course not least, regulatory know how.

As part of the total chemical biocides market the marine section is a relatively small niche. Biocides used for the agricultural industry, personal care and water treatment are much larger segments. In view of the limited requirement for marine biocides it is not surprising that these are chemicals with applications in other industrial segments as well, and where the marine applications have been developed when the product is already in industrial use. Indeed, given the time and cost involved in developing a complete registration dossier for a new chemical which complies with all necessary regulations, it is unrealistic to develop new marine biocides without applications in other business areas. In that regard, medetomidine is an exception to the rule for which the limited use can be financially compensated for to some extent through the existence of a complete medical file in which a substantial part of the costs associated with developing a biocide dossier has been accumulated.

Copper and copper products dominate the marine biocide market to a very large degree following the ban of TBT. According to industry sources, more than 95% of all antifouling paint used is based on using copper products as the principal biocides. Copper has a number of features which make it attractive as a marine antifoulant; a relatively broad biocidal effect and chemical properties suitable for ablative and self-polishing coating systems. The marine paint companies have refined and optimised the use of copper by developing special polymer systems with the ability to bind and release copper at the same rate as the degradation of the paint layer, making it possible to design coating systems with a predetermined functional life-span, typically two and a half or five years depending on the dry-docking intervals for the ship.

As copper has a limited biocidal effect on algae and slime, the antifouling coating needs to be complemented with other biocides for complete fouling protection. These biocides are often referred to as co-biocides by the industry. After the EU authorities required the industry to submit complete dossiers in accordance with the requirements laid down by the
BPD, only a small number of marine biocides remain. This has created a somewhat inflexible situation for the marine paint industry, which needs to be able to offer antifouling solutions for all possible fouling challenges.

The regulatory challenge

Biocide legislation is largely national. The EU is an exception in that all member states have decided to harmonise their legislation in a unified set of requirements, the Biocidal Products Directive, BPD. The legislation covers the life cycle of the biocides, taking account of its effect on paint factory workers’ health and of discharge after the end of the product’s service life. For marine biocides, particular emphasis is put on avoiding risk to operatives during the application of marine antifouling paint, i.e. amateur and professional painters, and on avoiding risk to the aquatic environment. Since marine biocides disseminate directly and without discrimination between target and non-target organisms into the marine environment, it is difficult to balance requirements on efficacy and safety. Medetomidine is, on the one hand, exceptionally potent as a sedative for vertebrates and as a deterrent to the most troublesome marine fouling organisms, on the other hand it is relatively benign to non-target organisms, making the total risk assessment favourable in view of the predicted low concentrations generated for different marine scenarios.

The application of marine paint obviously takes place in the countries where ships are built and dry docked for maintenance. Over the last ten years these activities have been increasingly concentrated in Asian countries. The European Community countries are less important than they used to be as shipbuilding and maintenance nations. As the regulations in most Asian countries are less far-reaching than those in the EU and in USA, some feared that the stringent regulations in western countries would diminish into empty gestures if the industry were to concentrate its activities in Asia. However, this has not happened, since the marine paint companies have adopted internal policies dictating that the marine biocides used must comply with BPD requirements. The industry is consequently driven by both regulatory requirements and by self-regulation. In view of the respect the industry pays to the EU legislation it is discouraging that the corresponding respect is not paid to the industry by the system. The BPD review process of the dossiers for marine biocides mandatorily submitted at the end of 2006 was scheduled to have been completed by the end of 2008. After almost five years the process is however still ongoing, leaving the industry in a planning vacuum. The BPD process is also unnecessary lengthy for new biocides: the review processes by the competent authorities in the individual countries are needed and should be allowed ample time to ensure that safety and efficacy requirements are met. However, the lack of trust between the regulators from the different member states has resulted in excessively long handling processes on the EU level. To make things worse, the administrative handling time within DG Environment further extends the registration process. The way the system is managed at present does not encourage the industry to introduce new biocides even if they have a more favourable environmental profile than those in current use.

In addition to scientific investigations carried out by Marine Paint, approximately 20 new investigations have been carried out by I-Tech, using Good Laboratory Practice (GLP) in line with the requirements of the regulatory authorities. These studies relate to ecotoxicological risk assessment, as well as to human health.

The industrial development process

The marine paint manufacturers have extensive legal and moral warranty obligations for antifouling paint performance in respect of ship owners. The cost of unplanned underwater grooming or dry docking with consequent loss of revenues is substantial to the ship owner. Reliable antifouling protection is thus a must to manage an efficient shipping operation. The development processes required from the marine paint manufacturers are, therefore, extensive and lengthy before a new antifouling paint formulation is released to the market. Furthermore, by nature the shipping industry is global, ships are traded between ship owners in all parts of the world and larger ships in particular must be equipped to operate in any waters. Consequently, the antifouling system applied must demonstrate adequate performance independent of geographical region. In line with these market requirements, the marine paint manufacturers strive to develop global products, taking account of both regulatory and performance aspects. Field testing on static panels, rotating panels and on ships provides
the knowledge base to evaluate efficacy. These field tests have to be performed in all of the different geographies where the antifouling coating is eventually going to be used. In order to mimic the life cycle of the antifouling coating, these trials often have to go on for years before enough confidence in performance is built up. In parallel with this, the coating is tested in the laboratory for colour stability, storage stability and a myriad of other technical aspects.

Medetomidine is currently at the core of the laboratory benches and in the field testing stations of most of the marine paint manufacturers. The compound is attractive as an antifoulant due to its potency as a barnacle deterrent and to its favourable chemical binding properties, which fit well with the self-polishing copolymer systems developed for the controlled release of marine biocides. However, as the amounts of medetomidine added to the paint system are minute compared to e.g. cuprous oxide, the controlled release of the compound from the paint matrix is critical to guarantee long-term performance. If too strongly bound to the matrix, there will be no biological effect and the coating will fail at an early stage. If, on the other hand, the minute amount of the substance is allowed to release too easily, the biological effect will be short lived and fouling will occur after a short period of time when the medetomidine in the coating is depleted.

Through the pivotal research by the Marine Paint consortium, I-Tech has gained knowledge of a suitable leach rate to maintain sufficient efficacy, at least for cold waters. The marine paint companies have applied the compound in a large number of coating systems and in combination with different co-biocides, enabling them to optimise the use of the compound in coating systems for global use. Extensive field tests have been in progress for a number of years, and increasingly larger ships have been painted with larger test patches for the ultimate validation of in-service performance. The development process is going hand in hand with regulatory developments for the compound. At present the substance is approved for use in South Korea and Japan, and approvals for China and the EU area are predicted for 2012.

The future for medetomidine and for I-Tech

After ten years of research and development, it has proven its functionality as a marine biocide. Thanks to the development work taking place in the Marine Paint academic programme, the extensive formulation development and validation with marine paint companies, and the endeavours of the company itself, together with contracted research organisations, the technology stands at the threshold of commercial use. The main competitor to medetomidine, cuprous oxide, has an exceptionally strong position on the marine biocide market, with a market share exceeding 90% of the antifouling paint volume, so it would be naive to expect a swift technology shift from this technology to pure organic biocides such as medetomidine or, possibly, tralopyril (from Janssen PMP). On the other hand, marine paint formulators have demonstrated that their skills in formulating biocide-based coatings have found ample
applicability for medetomidine formulations. Their experience and innovation have interacted beautifully to make the most of the fundamental pharmacological properties of medetomidine.

Prices of metals and oil-based products have increased dramatically over the last few years, putting the anti-fouling coating products in a price squeeze, while the shipping industry is facing difficult conditions, and is not prepared to accept price increases for coating systems. This development favours I-Tech’s offering of an organic product that is less exposed to the volatile and unpredictable fluctuations of the raw materials markets.

With the regulatory permissions for South Korea and Japan in hand, and with the corresponding approvals for China and the EU area due during 2012, I-Tech will soon be in an excellent position to assist the marine paint industry to launch regulatory compliant products. In addition, the scale-up of the chemical synthesis of the compound has taken quantum leaps towards reliable supply at realistic prices, thanks to the development systems.

All-in-all, the future looks bright for I-Tech and the marine paint market. Their self-reliance and persistence over the long development period. It is still too early to pop the champagne and celebrate science towards a sustainable future and also in recognising the fundamental importance of factors such as of funding, patience and appropriate agreement structures to taking a vision through the research phase to a finished technology or process to benefit society.

I-Tech was founded by Professor Hans Elwing and his co-workers in 2000 as a holding company to exploit the discovery that medetomidine could be used as an antifouling agent, and the subsequent patent. Without the economic resources to verify medetomidine as a new antifouling agent, it was impossible to develop the patent further towards more applied research. MISTRAS overall strategy of acting as a partner in such processes enabled the establishment of the Marine Paint research programme.

The collaboration between Marine Paint and its commercial partner, I-Tech, has been influenced at times by the different demands put on academia and industry respectively, and these seemingly conflicting requirements have sometimes resulted in less-productive periods. In particular, finding a balance between scientific independence and legally binding agreements has proven to be a challenge. Another challenge has been the inherent conflict between finding a balance between spending resources on industrially mandatory verifications and those initiated by the researchers. It is a sad fact that, in the academic setting of eco-toxicology, a published non-observed effect carries little academic merits whereas the same non-effect data has often proven to be critical to I-Tech. One would hope that research in this field will adhere to the principles set up in pharmacology, where non-effect data (absence of negative side effects) are critical research parameters.

A second important actor besides MISTRAS has been GU Holding, Gothenburg University’s holding company. At the time when Marine Paint was funded, but the collaboration terms between Marine Paint and the company were unclear, and the commercial possibilities for I-Tech were impossible to quantify in view of the early stage of the development, GU Holding was able to offer commercial expertise and excellence, and took a major responsibility in financing and operating I-Tech, allowing the company to work on commercial premises. On reflection, the importance of infrastructures such as MISTRAS and GU Holding, who have had the ability to act on both commercial and scientific perspectives and premises, cannot be overestimated. The interface between science and enterprise can easily become a minefield of misunderstandings and preconceptions, and this has often prevented transfer of scientific knowledge to commercial products. Having the integrity and the ability to act on both commercial and scientific perspectives is critical research parameters.

Research is often driven by a vision to find solutions for societal problems. In the case of scientific research, this often revolves around medical, environmental or technological issues. Ideally, the researchers and industrial representatives should work towards a common goal, i.e. to bring about change to a better technology. Even where all the good intentions to cooperate in the chain from research to industrial development are present at the time the two parties come together to formulate an application for financial backing, there is often less than perfect understanding of the preconditions faced by each partner and the particular demands on the individual partners. The academic partner is circumscribed by the absolute requirement to produce publications, and the industrial partner is exposed to the specific requirements of the actual industry. Each collaboration project is unique, and the road map often has to be redrawn in line with new and varying requirements, and success depends on having sufficient time and energy to adapt to new circumstances. These adaptations need to be considered in terms of expectations and agreements.

Few scientific funders take this important prerequisite into account, but assume that the world will be roughly the same throughout a lengthy project. MISTRAS is an exception who has taken a leading position both in supporting science towards a sustainable future and also in recognising the fundamental importance of factors such as of funding, patience and appropriate agreement

Reflections on I-Tech and Marine Paint research group collaboration

Per Jansson
Lena Lindblad
I-Tech AB
As outlined in previous chapters, fouling is caused by a complex community of different organisms, comprising – amongst others – barnacles, bryozoans, macroalgae, sea squirts and complex microbial biofilms ("slime"). The perfect antifouling biocide would be equally effective against all these creatures. However, each fouling species has a unique biology and, therefore, a typical biocide is not equally effective against all foulers. This phenomenon can be described by the species sensitivity distribution which is unique to each biocide. Figure 1 provides an example.

For this reason, while a few grams of a compound in a litre of paint might be enough to prevent fouling by a certain species, ten times as much of this compound might be necessary to prevent all the other organisms settling on the hull of a ship. Consequently, antifouling paints that rely on only one active ingredient inherently lead to overdosing, as the more sensitive organisms are "killed twice over" (Figure 2).

One obvious solution to this problem would be to compose an antifouling paint using only biocides that very specifically affect only one particular part of the fouling community, and nothing else. A paint could then contain just enough of each compound to take care of the fouling by this organism group. Unfortunately, although compounds such as medetomidine or Irgarol come close to this ideal, most antifouling biocides do not show a similar specificity and selectivity.

For this reason, the task of the optimisation project within Marine Paint was to provide an approach that systematically explores the feasibility of "intelligent mixtures", i.e. combinations of biocides with complementary efficacy profiles (Figure 3). The aim was to provide a collection of biocide recipes that are all fully competent (i.e. effective against all fouling organisms), while avoiding unnecessary overdosing, thereby providing the basis for an environmentally-optimised paint system.
Empirical mixture optimisation

Mixture optimisation is a well-established concept in the production of food, pharmaceuticals, solvents, concrete and other industrial mixtures. Combinations of process variables such as heat, temperature and pressure are often optimised in a similar fashion.

It is, however, a major problem for any optimisation that the number of possible combinations rapidly becomes too big for direct experimentation if the mixture contains more than a few compounds. Assume, for example, a mixture of a mere 4 compounds, which are supposed to be mixed in combinations that differ in steps of 10% relative content (i.e. the first conceivable mixture is composed of 10% compound A, 10% compound B, 10% compound C and 70% compound D. The second mixture would then comprise 10% compound A, 10% compound B, 20% compound C and 60% compound D, and so on). Already, under these simple conditions, 282 combinations are possible, each of which would then also have to be tested at various concentrations. This is not feasible most of the time. Accordingly, instead of systematically testing all possible alternatives, typical designs for mixture optimisation focus on testing just a few selected mixtures, and then extrapolate the results to all untested mixtures. Such “component-based empirical approaches” for mixture optimisation always proceed in the following three principal steps: first, the compounds used in the mixture are selected; second, a selected subset of the possible combinations is tested; and finally, the results from these trials are used to extrapolate to untested mixtures, one of which might provide the optimal solution to the given mixture problem.

Although these approaches have proven powerful, they suffer from at least two severe drawbacks. Firstly, the ratio between the pool of all possible mixtures and those few mixtures that actually can be tested becomes increasingly unfavourable with an increasing number of components. Consequently, there is a growing risk of overlooking promising combinations.

Secondly, all conclusions are strictly limited to mixtures of exactly those compounds that were initially selected for a particular trial. Should the mixture composition need changing, for example because one of the compounds is withdrawn from the market, the whole optimisation process has to be restarted from the beginning. This might be especially problematic for biocide combinations: the substitution principle embedded in the upcoming new biocide regulation basically requests that a substance be withdrawn from the market as soon as a superior compound is available. This might considerably increase the dynamics of the European biocide market.

The Marine Paint approach: predictive mixture modelling

In order to overcome these limitations of classical optimisation approaches, Marine Paint built its strategy on predictive mixture modelling, using the classical concept of “Independent Action”, which was initially used for describing the joint action of insecticide combinations. In contrast to the previously outlined approaches, this method is based on the specific assumption, that all compounds act independently (i.e. they do not influence each other’s efficacy in a mixture), but at the same time all contribute to the common aim (prevention of fouling). The concept of Independent Action then links the amount of the individual components and their potency to the total efficacy of the mixture at a given concentration. It therefore enables the efficacy of any mixture type to be predicted, avoiding the need to test an often overwhelmingly large number of mixture ratios and mixture concentrations.

Such an approach, however, requires detailed knowledge on the potency of each compound against each of the fouling species under consideration over its complete concentration-response curve (CRC). Marine Paint therefore invested considerable effort into the compilation of a library in which the CRCs for all the biocides and fouling organisms involved are documented.

Minimising the environmental risks of biocide combinations

Biocides are, by their very nature, biologically highly biocide substances, as there is no such thing as a non-toxic poison. Their use for antifouling purposes involves an inherent environmental risk, which is described for each biocide as the ratio between its Predicted No Effect Concentration (PNEC, describing an “acceptable” environmental concentration) and the Predicted Environmental Concentration (PEC, which is the concentration in the environment that is expected to result from a certain typical use). A PEC/PNEC ratio below 1, therefore, indicates a use pattern with an acceptable environmental risk. Marine Paint used PEC/PNEC ratios that were provided by the Swedish Chemicals Agency and I-Tech (medetomidine only).

The two specific aims set for the optimisation project were (i) to identify those mixtures from the infinite number of possibilities that are fully effective against all fouling organisms, and then (ii) to rank those mixtures according to their predicted environmental risk. This ranked list of biocide recipes then allows for specific mixtures to be cherry-picked, for example by their technical performance, costs and existing license agreements.
An overview of the optimisation algorithm is provided in Figure 4. It should be emphasised that the whole optimisation process can be carried out in silico. No experimental work is needed, given that the CRC library can provide the necessary input information. This allows for simple re-runs of the optimisation for various scenarios, which is a major advantage in comparison to the classical approaches to mixture optimisations outlined above.

The optimisation starts with the selection of the compound set that is to be included in a particular optimisation run. For Marine Paint these were copper, medetomidine, DCOIT (Sea-Nine), Cu-pyrithione, tolyfluanid and Irgarol (Cybutryn). 2,998 mixtures with different component ratios can be composed from these six compounds, if their relative proportions in the mixtures are systematically changed in 10% intervals.

This mixture pool ranges from simple 2-compound mixtures to mixtures comprising all 6 compounds. Each of them can contain varying total concentrations.

The next step is to identify the optimum concentration for each of the 2,998 mixtures, i.e. the mixture concentration that is predicted to inhibit settling of even the most resilient organism. Concentrations that are too low to ensure full antifouling activity are discarded, as well as concentrations that are unnecessarily high.

The mixtures are then finally ranked according to their predicted environmental risk. This is approximated by attributing a penalty (a risk weight) to the concentration of each compound in the mixture. Marine Paint used the PEC/PNEC ratio for this purpose and the final risk estimate for each combination is, therefore:

\[
\text{Risk} = \frac{\text{PEC}}{\text{PNEC}} \times \text{conc} + \frac{\text{PEC}}{\text{PNEC}} \times \text{conc} + \ldots
\]

This approach is systematic and unbiased, all possible combinations are considered and no compound is favoured for any other reason than their estimated environmental risk. The approach is also highly flexible. Should the PEC- or PNEC-estimates change due to changes in use pattern or because new data on the environmental hazard of a compound become available, the optimisation can simply be re-run with different input values. Figure 5 shows the final risk ranking for all the 2,998 mixtures that were modelled in Marine Paint, with risk values covering a broad range from 191 to 21,500.

Emerging new biocides or additional groups of fouling organisms can easily be added to the CRC library at any time and then included in the optimisation.

Åsa Arrhenius
Thomas Backhaus
Hans Blanck
Åke Granmo
Annelie Hilvarsson
Paint Formulation

Any marine antifouling paint comprises different chemicals, the most important being solvent, binder, filler, pigment, stabiliser, and, of course, the biocides that are responsible for the antifouling efficacy as they are released from the paint. Depending on the application and/or customer, all these compounds are chosen on the basis of price, mechanical properties and environmental aspects. Optimising paint ingredients in order to achieve good mechanical properties is, therefore, a primary concern for paint companies. However, relatively little time and effort has been invested in optimising the release of antifouling biocides from the paint, and this may imply not only increased environmental risks, but also unnecessarily high costs of the paint.

A common antifouling approach is to use biocides in a self-polishing coating (SPC). When these coatings are exposed to seawater, they erode as the water penetrates the top coating layer, which is usually termed the “leached” or “erosive layer” for that reason. The formation, structure and thickness of the erosive layer depends on paint parameters such as type of pigment, type of self-polishing polymer and on external parameters such as water velocity, salinity, temperature and pH. There are, however, coatings that do not rely on the self-polishing mechanism but rather on continuous biocide release. These coatings are not as common, as their release properties are inferior to those of self-polishing paints.

Controlled Release Technologies

It is of crucial importance to prevent an early depletion of the biocide pool that is embedded in the paint. Hence the release of biocides from the coatings needs to be decelerated in a controlled fashion, which is usually achieved by binding the biocides to various coating components and thus preventing them from leaking out too rapidly from the paint film. We worked with different controlled release strategies through Marine Paint. The first two technologies (binding to paint polymers and metallic nanoparticles) are specifically tailored towards controlling the release of medetomidine, while the third technology – which is based on microencapsulation – is suited for any biocide or mixture of biocides.

Binding to Polymers

The first of Marine Paint’s controlled-release technologies is based on electrostatic interactions between the biocide, medetomidine, and a sulphate-containing polymer. Polymers are large molecules that are immobile in the coating and can, therefore, serve as convenient biocide anchors. Medetomidine, due to electrostatic interactions of its imidazole functionality, binds very strongly to the sulphate-functionality in the polymer: the proton from the sulphate of the polymer prototates one of the nitrogens in the imidazole-containing medetomidine, creating a very strong ion-ion interaction which makes the small medetomidine molecule stick to the large polymer chain.
Experimental techniques such as nuclear magnetic resonance (NMR) diffusometry and Fourier transform infrared (FTIR) spectroscopy provided the experimental data that actually proved that there was a strong binding between medetomidine and the polymers. Medetomidine demonstrated good compatibility to the paint binder and a slow release rate, providing prolonged fouling properties, in current paint systems. The results were first patented by I-Tech and subsequently published.

Medetomidine was also successfully bound to another polymer, making use of a different interaction between the imidazole-functionality of medetomidine and the polymer. By introducing a transition metal ion to the system, medetomidine was bound very strongly to the polymer, due to the coordination to the metal-polymer complex.

**Binding to Nanoparticles**

Inspired by this coordination chemistry, Marine Paint developed a second technology for controlling biocide release. We found that a very effective means for immobilising medetomidine was to adsorb it onto the surface of microparticles of transition metal oxides (zinc- and copper-oxide), which was experimentally demonstrated using NMR and high-performance liquid chromatography (HPLC). The strong adsorption is also caused by the imidazole functionality of medetomidine and the binding is, therefore, specific for medetomidine, as other antifouling biocides do not contain the necessary imidazole moiety.

The nanoparticle concept turned out to work in our favour, especially because the release of medetomidine from the paint is only triggered on contact with water. This drastically decreases biocide loss during production, storage and handling of the paint, while at the same time providing sufficient biocide close to the ship’s hull to ensure the anti-fouling efficacy of the paint after contact with water. With this mechanism, the nanoparticle based release technology lends itself quite naturally to self-polishing coatings.

**Biocide mixtures – challenges**

Medetomidine alone is not sufficient to counteract the fouling pressure from all the different groups of fouling organisms. Marine Paint worked with the whole pool of biocides that were judged potentially able to pass the registration process of the European biocidal products directive (medetomidine, DCOIT, Zn- and Cu-pyridoxine, Irgarol, tolylthiazolid and Cu-Oxide).

This puts extra demands on the coating systems as it requires a solid concept for a coating that contains as many as six different biocides simultaneously at sufficiently high concentrations (see also previous chapter on Paint Optimisation).

There are a number of issues to be resolved in order to achieve this goal. Obviously, interactions between the biocides need to be circumvented. But the coating system itself must also be protected from the biocides, as some of them are efficient softeners, rendering the paint too soft and of insufficient mechanical strength. Furthermore, the release system needs to be applicable on an industrial scale in a cost-efficient way. With the health and environmental footprint of future paints in mind, Marine Paint finally decided that the release system should also be usable not only for commonly used solvent-borne paints, but also for water-based formulations, which are vastly superior in terms of occupational health and environmental performance.

**Microencapsulation**

With these challenges in mind, Marine Paint decided to use microencapsulation techniques to provide a system that can harbour multiple biocides. Microencapsulation technology is based on particles in the size range of 0.1 µm up to several µm, which can be of any material type, but most often comprise a high molecular weight polymer. The biocide in question is either solubilised directly into this polymer, resulting in a microsphere, or an inner core of biocide-containing oil is surrounded with a protective polymeric shell, known as a microcapsule. Finally, the microcapsules are added to the wet paint.

In both cases, the two main components of the microcapsules are a polymer and the antifouling biocide. The interactions between these components are determined by the porosity of the polymer, the state of the active substance (amorphous, crystalline, or molecularly dispersed) and the spatial distribution of the compounds in the particle. All these parameters taken together determine the release rate of the biocide from a particular micro-system.

Compared to ordinary formulated paints, where the biocide(s) are directly formulated into the paint system, microcapsule-based system usually show a significantly slower release rate, which offers a prolonged lifetime and more robust protection against surface growing organisms. However, although the use of microspheres and microcapsules for controlling biocide release has been discussed for many years in both the patent literature and in scientific publications, there are still only a few examples of paints containing microspheres or microcapsules on the market.

One of the reasons for this is the highly specific partitioning of the biocide into the high molecular weight polymer of the particles. It is pivotal to understand and finally control this partitioning, as it drives the release behaviour of the biocide from the microcapsule or microsphere. A central focus of the microparticle work in Marine Paint has, therefore, been the physicochemical evaluation of the particle components, in order to understand how the different antifouling compounds interact with the microcapsule components.
Finally, Marine Paint has also reduced the environmental impact of the encapsulation process itself. This was achieved by replacing the chlorinated solvent dichloromethane with ethyl acetate. The latter is vastly superior in terms of occupational health and environmental impact. It also meets the demands of industrial-scale production of microparticles, which led Marine Paint not only to describe the use of ethyl acetate for microencapsulation purposes in the scientific literature, but also to cover it with a corresponding patent.

**Future activities**

Copper pyrithion and zinc pyrithion are highly hydrophilic compounds and were, therefore, found unfavourable for encapsulation. However, Marine Paint is working to develop microparticles with these important metallo-organic biocides using a more elaborate approach to encapsulation.

We started to explore the feasibility of large-scale production of microparticles with the Kinematica, a company in Lucerne, Switzerland – a work that was carried out in cooperation with the Gothenburg-based company, Capeco AB. Highly promising results make us confident that encapsulation on an industrial scale is achievable at reasonable cost, a perspective that is also shared by the experts at Kinematica.

Lars Nordstierna
Magnus Nydén
The rationale for the optimisation of biocide mixtures has been outlined in the Paint Optimisation chapter, and the technologies that we developed for the incorporation of such mixtures into paint systems in the Paint Formulation chapter. The next step was then to evaluate the performance of the resulting novel paint formulations under real-life conditions, for which we followed the internationally-acknowledged ASTM standard D5653 (“Standard Test Method for Testing Antifouling Panels in Shallow Submergence”). Obviously, the Paint Performance evaluation had to follow in time after Optimisation and Formulation, and so we were able to evaluate paints over two seasons only, with the final panel testing ongoing as this report is finalised. These investigations were performed in a bay near the Sven Lovén Centre for Marine Sciences at Kristineberg on the Swedish west coast, using panels that were painted with a range of different paint formulations and then submerged for a period of 4 to 6 months at a depth of one to three metres. In 2010, Marine Paint based these field studies on an existing paint system that was stripped of any biocide or metal prior to the experiments, and which was kindly provided by Lotréc AB, a Stockholm based company which has been producing boat paints for more than 30 years. The optimised mixtures of encapsulated (e.g. tolyfluanid) and non-encapsulated (e.g. Cu-pyrrithione) biocides were then mixed into these base paints in amounts that ensured near-hull concentrations that were predicted to be sufficiently high for complete anti-fouling activity during a certain time of period. For comparative purposes, mixtures containing only non-encapsulated biocides were also tested.

Five different combinations, at three concentrations respectively, were evaluated and their comparative performance evaluated after four and six months. We learned four important lessons from this first field trial. First, and most important, the optimised combinations were indeed fully effective over the test duration, providing a strong case for our approaches (Figure 1). Second, mixtures of encapsulated biocides provided superior anti-fouling activity over a longer time than free biocides. As expected, encapsulation dampens the initial burst of biocide release, given a biocide release from the paint that is more constant over time. This enables an extended service life from the same initial biocide amount in the paint. Third, the paint used show defects in mechanical properties due the stripping of metals and follow-up studies were, therefore, necessary. This rather simple stripping treatment must be replaced by a more comprehensive formulation of non-metal marine paint which includes biocide mixtures and microcapsules. And finally, we gained experience on the practical preparation and replication of panels, construction and handling of field equipment, documentation and assessment of the result.

A new set of field tests was conducted in 2011, and is still ongoing as this report is finalised. For these studies, we used a commercial paint from Lotréc AB (Lefant TF) as a basis, in order to improve the mechanical stability of the resulting paint formulation. This paint, intended for the Baltic Sea, is biocide-free but contains zinc oxide at a concentration of 20–30% in the wet paint. Additionally, we also investigated a commercial water-based acrylic varnish (Hempel) as a test matrix for the biocide mixtures, to explore the feasibility of developing a completely metal-free paint system. We decided to test two optimised combinations of biocides experimentally: DCOIT and medetomodine, and DCOIT, medetomodine and copper. Both were tested in the paint and the varnish based system respectively, and all were freely dissolved in the paint/varnish. A duplicate set of panels with coatings containing one-tenth of the optimised concentrations was also evaluated.

The anti-fouling performance of these paint and varnish formulations was documented after two and four months respectively (Figure 2), during which heavy fouling occurred on the reference panels with no added biocides, including numerous barnacles of different sizes from newly settled to older ones. The varnish system did not work well enough to protect against fouling, there was visible macro-fouling even when combinations of biocides were added. The results for the optimised combinations were promising, using Lefant’s paint system as a basis. The optimised paints worked almost perfectly except for some micro-fouling (dime), which was easily removed and might not pose a major problem on ships and boats that are in use regularly. However, the mechanical stability of the paint still seems to be slightly impaired, most likely due to the addition of DCOIT. Nevertheless, the field results provided us with good examples of efficient anti-fouling paints where the biocide formulations was based upon optimisation calculations, laboratory release experiments, and release models.

Åsa Arrhenius
Thomas Backhaus
Hans Blanch
Åke Granmo
Annelie Hilvarsson
Åsa Arrhenius
Magnus Nydén

36  Paint Performance

Paint Performance 37
Results from 2010

Figure 1: Result from first round of panel testing with optimised paints in 2010 after 6 months at sea. Substantial fouling on the reference panel and the optimised paint performing equally to the commercial paint.

A: Reference paint with no biocides added.
B: Paint with optimised combination of biocides.
C: Commercial copper based paint.

Results from 2011

Figure 2: Result from second round of panel testing in 2011 after 4 months at sea. Heavy fouling was growing on the panels with biocide free coatings. As seen the varnish with optimised combinations did not perform well. However the optimised paints show very promising results with only a loose slime layer covering parts of the panels. No commercial paint were included in this survey.

A: Control paint.
B: Optimised paint with DCOIT, medetomidine and copper.
C: Control Varnish.
D: Optimised Varnish with DCOIT, medetomidine and copper.
There is no such thing as a non-toxic antifoulant: each compound that is highly efficacious in preventing fouling on the ship’s hull, also has the potential to damage environmental organisms as the antifoulants leave the ship’s hull and enter the surrounding marine ecosystem.

Even fouling organisms are worth protection when they occupy their natural habitats in the ecosystem. For that reason, all antifoulants – including those considered in the Marine Paint project – are regulated in the European Union under the Biocidal Products Directive (98/8/EC) and are only approved for use after an environmental risk assessment. This regulatory system involves a set of mandatory tests for the marine environment, describing both the fate and toxicity of the compound in question. However, the history of fouling protection indicates that degradation is often overestimated and the sensitivity of marine biota underestimated. If the compounds do not degrade fast enough, they may accumulate in the environment and threaten organisms that are particularly vulnerable due to their physiology and their way of life. Persistent and/or bioaccumulative compounds must therefore be avoided, and the toxic effects of the compound in questions should be investigated for a broad set of species and life forms.

When the sensitivity of only a few species is known, it is likely that more sensitive as well as less sensitive species also exist. However, medetomidine seems to be an exceptional case: barnacle settling (the targeted process near the ship’s hull) is close to 100% inhibited even at low concentrations (1 nM = 0.2 µg/L) of medetomidine in laboratory experiments. However, the thorough check conducted by Marine Paint showed that only a very few ecotoxicological endpoints are of similar sensitivity. By comparing other effects to this efficacy of medetomidine, we can illustrate (Figure 1) the relatively lower sensitivity of most non-target species in the marine environment. This means that there seem to be few non-target organisms with higher sensitivity than the target organisms – which of course is a great advantage for the application of medetomidine as an antifouling biocide.

**Test strategy for medetomidine**

The basic idea behind the Marine Paint Ecotoxicology approach was to go beyond the formal requirements in order to provide an in-depth environmental risk profile for medetomidine. The developed test battery included several species of fish, molluscs, crustaceans and communities of marine microalgae and bacteria. The toxicity parameters were chosen on the basis of our knowledge on medetomidine’s mode of action as an agonist to neuropeptidase receptors, and – in addition – on key processes or behaviours of the test organisms. We were searching for expected effects, without ignoring the unexpected. This is a cautious approach to environmental hazard assessment, and a large number of ecotoxicological endpoints were evaluated.

**Figure 1**: Efficacy and ecotoxicity of medetomidine (Selektape). Medetomidine completely inhibits barnacle cyprid settling at a concentration of 1 nM (= 0.2 µg/L) on the ship’s hull. Algae, mussel larvae and bacteria are about 10,000 times less sensitive. The most sensitive endpoint is fish pigmentation, which is affected at concentrations between 0.5–10 nM (0.1–2 µg/L). Due to the dilution and degradation in water, the predicted environmental concentrations (PECs) of medetomidine are below these values.
However, the environmental risk presented by a compound depends not only on its ecotoxicological effects, but also on its release and fate in the environment – which in turn depends on the transport and degradation processes both in the physical environment and within exposed organisms. Fate studies with medetomidine in the Marine Paint Programme included investigations on bioaccumulation in fish, mussels, brown shrimp and microbial periphyton communities, and a set of preliminary degradation experiments considering the role of water and sediment, biodegradation in toxic and anoxic conditions, as well as photodegradation. There was little indication of bioaccumulation, and no conclusive evidence of degradation.

The periphyton test system consists of natural communities of microalgae, bacteria, ciliates and many other groups of microbiota growing together on an experimental surface – it is the slimy microbial layer on ship hulls. Periphyton were exposed to medetomidine and effects on photosynthesis protein synthesis were measured. Medetomidine had very little effect on the algae and bacteria in periphyton communities although they are sensitive to many other antifoulant biocides. There seem to be no sensitive receptors in the microorganisms, and strong effects do not occur even after long-term exposure. The microbial communities tested seem to be at least 10,000 times less sensitive than the barnacles tested.

A set of tests related to reproduction was set up. Spores of the sea lettuce Ulva sp were affected but only at 10,000 times higher concentrations than barnacles. The embryonic development of blue mussel Mytilus edulis eggs to the veliger larva was equally unaffected by exposure to medetomidine.

A variety of vertebrates and invertebrates were tested with medetomidine. Mussels of the species Abra nitida feed on organic matter in sediments. Their physiological status and behaviour can be observed by their ability to dig into and rework the sediment. Medetomidine affected this behaviour of small mussels at 4 nM (0.9 µg/L), i.e. Abra is 4 times less sensitive than barnacles.

The typical decolorising effects of medetomidine on pigmentation of fish scales and skin (Karlsén et al 1989) were observed in all our studies: Lumpfish (Cyclopterus lumpus) larvae changed from dark to a paler yellowish colour at 4 nM thus being 4 times less sensitive than barnacles. Also other fish species showed this response at low concentrations. Bottom-dwelling flatfish use colour changes for disguise, by mimicking their background substrate, and turbort (Psetta maxima) was also the most sensitive of the tested species responding at 0.5 nM (0.2 µg/L), i.e. this reaction of turbort was 2 times more sensitive than barnacle settling (Lennquist et al 2010, Lennquist et al 2011). Rainbow trout initially responded at this low concentration. However, there are indications of decreasing sensitivity of the melanophores to medetomidine over time while other responses to medetomidine exposure have been reported to be reversible over time. The contamination pattern will determine whether or not an avoidance reaction followed by recovery is a survival strategy. Fish in their natural habitat cannot migrate easily to a clean sea.

The respiration rate of lumpfish larvae (Cyclopterus lumpus) was reversibly affected at concentrations above 10 nM (2 µg/L), indicating an effect of medetomidine on metabolic activity of the fish at elevated medetomidine levels. Breathing of turbort also decreased, indicating again a transient down-regulation of metabolism in fish at low medetomidine concentrations. Indications of changes in glucose metabolism in fish have also been observed.

The study of physiological or biochemical changes (biomarkers) in fish was part of a strategy to detect response patterns indicative of the target organ or process affected by medetomidine (Lennquist et al 2008). Four species of fish showed a weak induction of EROD (ethoxyresorufin-O-deethylase) activity indicating that the organisms had mobilised some anti-chemical defence, at in vivo exposure levels corresponding to 5 nM (1.2 µg/L) of medetomidine in water. Sensitivity differed somewhat among species, with turbort as the more sensitive fish species. It is chemically unlikely that medetomidine itself is a substrate to the AH-receptor involved, and the response pattern became even more complicated with the observation that medetomidine in the 35–110 nM (8–26 µg/L) range is a potent inhibitor of EROD activity in vitro. The conclusion is that medetomidine may interfere, directly or indirectly, with CYP1A-dependent metabolism of man-made toxicants in tested fish species turbort, rainbow trout and Atlantic cod.

Bioaccumulation of medetomidine has been investigated in a selection of marine species: periphyton communities, two mussel species (Mytilus edulis and Abra nitida) and in brown shrimp (Crangon crangon). Medetomidine was shown to have a maximal bio-concentration factor of 1,255 µg/kg FW in periphyton (mainly caused by adsorption), 134 in mussel and 2.8 in shrimp. Medetomidine should not be classified as bioaccumulating according to the Biocidal Products Directive (<2000 µg FW).

As with every biocide, there are two sides to the coin. The risk situation is both promising and of some concern.

Promising...

The target species of barnacles are very sensitive in their settling stage. Cyprid settling is inhibited at 1 nM (0.2 µg/L) however lethal effects occur at 100,000 times higher concentrations (Dahlström et al 2000). There are few signs of lethal effects among studied species and there are several examples of reversible effects after continued medetomidine exposure. The main effect of medetomidine is indeed the inhibition of barnacle settling, and there are indications that similarly sensitive ecotoxicological endpoints are only triggered transiently, i.e. are reversible after discontinued medetomidine exposure. There seem to be no life cycle effects in fish, and no effects on algae or bacteria at relevant concentrations. The observed effects confirm the proposed mechanisms of action, although medetomidine affects different receptors in vertebrates (adrenergic α2-receptor) and invertebrates (octopamine receptor).
Antifouling paints contain mixtures of biocides

Medetomidine is highly efficacious against barnacles and a tube-forming polychaete, but much less so against other fouling animals, algae and against the microbial slime communities. This means that any antifouling paint product will need to contain more than medetomidine alone if it is to prevent all fouling. With the exception for some copper-only paints, this requirement to contain biocide mixtures holds true for antifouling paints in general. As described in Paint Optimisation, the Marine Paint Programme has made considerable progress in the optimisation of antifoulant combinations that contain between 2 and 7 biocides.

Under these circumstances, data on environmental risks are needed not only for medetomidine, but also for all the biocides that make up the final mixture. For this purpose, we analysed the available information e.g. from the open scientific literature and risk assessment reports – and completed them with our own data for phytoplankton, bacterioplankton, zooplankton, and sediment-living mussels (Figure 2). Together with the efficacy data for the fouling organisms (Figure 1, page 26), this provided an in-depth view on the ecotoxicology of all biocides in the mixtures.

A computer tool called MAMPEC – Marine Antifoulant Model to Predict Environmental Concentrations – was used to estimate environmental concentrations of the antifoulants used. MAMPEC is suggested for use in the BPD to perform the exposure assessment and was developed by Deltarom and the IVM Institute for Environmental Studies at Vrije Universiteit Amsterdam (http://delftsoftware.wldelft.nl). This chemical fate model predicts environmental concentrations of antifoulants in waters such as marinas, harbours, and estuaries. The advantage of the MAMPEC model is that it accounts for important environmental processes like degradation and partitioning that are both crucial for the fate of environmental pollutants. One can argue that it is a conservative approach to estimate the environmental load for the harbour per se in immediate proximity to the emissions. However, since the model operates with high water exchange rates, dilution is the major factor dominating the fate processes. In our minds, this is a drawback that will not give sufficient credit to compounds with a positive environmental profile (e.g. degrades rapidly). Compounds with a strong affinity for suspended matter will be exported from the harbours, and will (if they are not readily biodegradable) accumulate in the environment outside the harbour. It might be that an estimate of the concentration in water and on suspended matter (instead of in sediments) would provide a better priority instrument for the longer term perspective, by favouring the unstable toxicants.

<table>
<thead>
<tr>
<th>Biocide</th>
<th>Phyto- and bacterioplankton</th>
<th>Zooplankton</th>
<th>Sediment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medetomidine</td>
<td>&lt;5% effect</td>
<td>&lt;5% effect</td>
<td>&lt;5% effect</td>
</tr>
<tr>
<td>SeaNine® 211N</td>
<td>&lt;5% effect</td>
<td>&lt;5% effect</td>
<td>&lt;5% effect</td>
</tr>
<tr>
<td>Telyfluanid</td>
<td>&lt;5% effect</td>
<td>&lt;5% effect</td>
<td>&lt;5% effect</td>
</tr>
<tr>
<td>Copper Pyrithione</td>
<td>&lt;5% effect</td>
<td>&lt;5% effect</td>
<td>&lt;5% effect</td>
</tr>
<tr>
<td>Irgarol</td>
<td>~10% effect</td>
<td>&lt;5% effect</td>
<td>&lt;5% effect</td>
</tr>
<tr>
<td>Copper (II)</td>
<td>&lt;5% effect</td>
<td>&lt;5% effect</td>
<td>&lt;5% effect</td>
</tr>
</tbody>
</table>

...but also of some concern

All animals tested were affected to some extent by exposure to medetomidine. The ecological consequences of pale fishes at low concentrations are not clarified, although it has been demonstrated that fish with impaired ability to adjust pigmentation have lower survival rates (Kohlishi et al 1991). It has also been argued that the low presence of albino fish in the environment is due to their increased visibility to predators (Gartner 1986). Sedation and down-regulation of respiration occurs in fish. Growth hormone/growth stimulating effects of medetomidine and clonidine have previously been reported for humans and fish respectively. However, although we observed a slight decrease in growth and growth hormone levels in rainbow trout, this was not significant (Lennquist 2010). The influence on cytochrome systems is significant for the degradation of biogenic and anthropogenic compounds that occurs at low concentrations (Lennquist 2008). Medetomidine is not readily biodegradable. Degradation seems to be slow and there is no ultimate mineralisation as judged by the release of labelled carbon dioxide from 14C-medetomidine. Medetomidine shows high surface activity (binding to surfaces) beyond the hydrophobic interaction coupled to the KOW, which is positive from the paint formulation point of view since it allows for an inherent slow release mechanism, but this might also lead to a higher particle affinity than expected from the hydrophobicity. The imidazole ring in the medetomidine molecule also shows affinity for transition metals like copper and zinc and to nanoparticles of their oxides (ZnO, CuO).
Conclusions

Marine Paint ecotoxicology provides an in-depth account of the ecotoxicology of medetomidine, and provides tools and understanding for evaluating the environmental risk of paint products and exposure scenarios containing mixtures of antifouling biocides. Medetomidine seems to be a highly specific compound that does not cause any lethality or growth impairment. It could, however, potentially interfere with pigmentation in fish.

Together with the mixture-modelling approaches outlined in Paint Optimisation, Marine Paint now has an in silico instrument for evaluating the environmental risks of biocide mixtures for a variety of purposes:

– Comparative evaluation of individual paint formulations, either generated in Marine Paint or already on the market.
– Evaluation of the collective risk generated by the current use patterns in a harbour, region or country.
– Evaluation of alternative decisions of product approval e.g. nationally or for the European market.

References used


Åsa Arshenius
Thomas Backhaus
Hans Blanck
Lars Förlin
Åke Granmo
Annelie Hålverson
Anna Lennquist
Fundamental Research

One of the goals of Marine Paint has been to find a reversible antifouling mechanism that does not kill the barnacle larvae (cyprids), but instead inhibits their settling on a ship hull. In Marine Paint Fundamentals, we focused on the interaction between barnacles, the worst of all foulers, and medetomidine. The overall aim was to provide fundamental biological understanding of the modes and mechanisms of action of medetomidine, which is not only required for its registration as a new antifouling biocide, but is also required for future work with the compound.

The barnacle species in focus for the experimental work in Marine Paint has been Amphibalanus improvisus (previously named Balanus improvisus (Darwin 1954)); the name issue is still debated. It has been cultivated regularly at the Sven Lovén Centre for Marine Sciences at Tjärnö.

The life stages of barnacles

The barnacle develops through six naupliar stages, until it finally molts into the cyprid larval stage (Figure 1). Cyprids swim freely in the water, do not feed and are driven by the overriding objective of selecting a surface suitable for settling and thus allowing development into an immobile adult animal that starts building the well-known, volcano-like, hard structure, strongly attached to the outside of the cell to the inside, where they inducing a biological response, such as an increased swimming activity. The cyprids then have difficulties in holding on to a surface and the success of their exploration of the surface is effectively inhibited by medetomidine.

Medetomidine activates octopamine receptors in the cyprids and thereby causes changes in the motility of the larvae

The part of the barnacle life cycle during which cyprid larvae search for a settlement site is critical. Cyprids are passively transported over long distances by the currents in the ocean but also have extended appendages for passively transported over long distances by the currents in the ocean but also have extended appendages for swimming (Figure 2). Hence the cyprid larva is a good swimmer and can swim (twice its length each second (average speed of movement is about 1 mm/s)). This is how cyprids explore their immediate surroundings and find a suitable site for settlement and metamorphosis.

We found that the cyprid larvae respond to the presence of medetomidine by increased leg movement (Lind et al 2010), resulting in increased swimming activity. The cyprids then have difficulties in holding on to a surface and the success of their exploration of the surface is effectively inhibited by medetomidine.

The fundamental question is then: how do cyprid larvae sense and respond to the presence of medetomidine? All cells in an organism are connected by different communication systems, which can be either neuronal or be based on circulating hormones. The signal molecules, neurotransmitters or hormones, act through binding to specific receptors on the surface of a cell. Accordingly, these receptors transmit the signal from the outside of the cell to the inside, where they inducing a biological response, such as an increased swimming activity.

One important class of biological receptors are known as G-protein coupled receptors (GPCRs), which are protein complexes that are inserted into the membranes of a cell. Early on in Marine Paint, we found that several adrenoceptor compounds (classified from their action in vertebrates, medetomidine being one of the compounds tested) were very efficient at preventing the settlement of cyprid larvae of A. improvisus (Dahlström et al 2000). Further experiments using highly specific antagonists indicated that the main target of medetomidine would be to receptors analogous to alfa-2-adrenergic receptors (Dahlström et al 2001). Thus, pharmacological research indicated that medetomidine was detected by a specific class of GPCRs, the so-called octopamine GPCR (octopamine receptors). These receptors are analogues

![Figure 1: The life cycle of barnacles. Adults reproduce sexually and release nauplii larvess. These feed on plankton and go through six stages before being transformed into a cyprid. This life form is a non-feeder living exclusively on reserves accumulated during the nauplii stages. Its only role is to swim and search for a good place to settle, such as a boat hull. After settlement, the metaplasmosis into the adult stage is rather quick and is completed within a day.]

![Figure 2: Reproduce, Stop eating, Find place & partners, Settle & Metamorphose, Nauplii: 5 – 6 days, Cyprids: weeks, Ca 24 hours]
of the alpha-2-adrenergic receptors that are common in vertebrates, including humans. Octopamine receptors are found not only in barnacles, but also, for example, in insects.

In order to get a better understanding of the molecular pharmacology of barnacles reaction to medetomidine, we have cloned five genes of these octopamine receptors from _A. improvisus_. _A. improvisus_ is the most common barnacle species around Swedish waters. In particular, this species is noteworthy for its great capacity to inhabit low salinity waters and is, therefore, also a problem for boats in the Baltic Sea. It turned out that barnacle octopamine receptors are composed of roughly 500 amino acids, and showed the typical GPCR topology with seven membrane spanning regions. They can be clearly distinguished in five sub-types, one alpha-like and four beta-like octopamine receptors that are also quite different from the ones found in insects (Lind et al 2010).

This indicates that one cannot simply extrapolate from insects to understand the pharmacology and functional role of these barnacle receptors.

Our research clearly shows that all five octopamine receptors are active in both cyprid larvae and adult barnacles. All of them also seem to be involved in the biological action of medetomidine. This indicates that the likelihood of developing resistance to medetomidine is rather low, as a resistant barnacle would need to develop five altered octopamine receptors simultaneously.

To characterise the actual biological function of the barnacle receptors we used molecular techniques to introduce the cloned genes into mammalian cell lines. This part of our study was conducted in collaboration with Professor Mika Scheinin at Åbo University, Finland. We found that all cloned receptors were activated by the natural hormone (octopamine) and medetomidine, resulting in increase of different intracellular signal molecules (cAMP or calcium). The different receptors consequently appear to trigger different response types within a cell.

We also discovered that medetomidine activated the alpha-like octopamine of _A. improvisus_ better than even the natural ligand octopamine (Figure 3). This certainly provides a molecular explanation of why medetomidine acts at very low concentrations as a settling-inhibiting compound.

Using our data we developed a three-dimensional model of the octopamine receptor (Figure 4), which will provide a good starting point for the future development of medetomidine derivatives with, for example, further enhanced binding and activation properties.

Finally we also compared the molecular response of barnacles to medetomidine with that to exposure to copper, by investigating the reaction of 2,000 different genes in DNA microarrays. It turned out that these compounds provoked a wide range of reactions in exposed barnacles, with some of them being distinct while others related to general stress being induced by both compounds. Future studies utilising advanced, genome-wide technologies will be important to understand the specific cellular targets during various antifouling regimes.

Figure 2: A cyprid larva. The image is taken by an ordinary light microscopy. One can easily see the legs (thorax) to the right, and the antennules for sensing the environment (to the left). The length of the cyprid is roughly 750 µm.

Figure 3: The graph displays the stimulation of the calcium signal via activation of the alpha-like octopamine receptor encoded by the OctR1 gene in _A. improvisus_. The gene is expressed in a mammalian cell system for functional characterisation. Different concentrations of the ligands octopamine and medetomidine have been tested and the increase in calcium levels in the cells is measured via a fluorescent calcium assay. The maximum response with medetomidine is set to 100%.

Figure 4: This is a 3-dimensional model of the binding pocket of one of the beta-like octopamine receptors from _A. improvisus_. The model is built using homology modelling based on the structures obtained from other organisms. Some potentially important amino acids are denoted as well as the corresponding transmembrane (TM) regions. The binding pocket shape is indicated with the blue surface. Medetomidine is predicted to dock in a conformation similar to that of octopamine with strong electrostatic and hydrogen bonding interactions between its imidazole ring and asparagine 123 (D123/3.32).
A cDNA library of *Amphibalanus improvisus* provides the basis for the future development of novel antifouling biocides

A cDNA library was constructed from a population of cyprid larva. Such a cDNA library is a collection of cloned complementary DNA that represents the active genes of a population. Using various molecular techniques (based on DNA sequencing), we identified several important genes/proteins that are involved in the signalling responses to medetomidine.

In addition, we have identified several other genes that are of fundamental importance for barnacle settlement, e.g. a gene repertoire that is responsible for the secretion of cement components, and proteins known to play a communication role between individuals during barnacle settlement (known as settlement-inducing proteins). Furthermore, we find a huge variability between alleles (gene variants) of different individuals, which is about tenfold higher than in humans.

This emerging knowledge of the barnacle genome will be used to search for novel molecular targets for antifouling biocides and will open up completely new avenues for studies and antifouling developments in the near future.

References used


Anders Blomberg
Linda Hasselberg Frank
Ulrika Lind
Lena Lindblad

The research has been conducted at six different departments in Gothenburg at the University of Gothenburg and at Chalmers University of Technology. In addition, there has been collaboration with The Norwegian Institute for Water Research (NIWA, working group of Kevin Thomas), The Faculty of Science at the University of Gothenburg hosted the programme. The field studies were performed at The Sven Lovén Centre for Marine Sciences at Kristineberg and at Tjörn.

Board

The Board had overall responsibility for the programme, and linked the programme to the anticipated end users.

Carl Henrik Wendt, Chairman of the Board 2003–2006. Mr Wendt is the former Technical Director of PLM. He now acts as a consultant to companies and governmental organisations.

Göran Dahlberg, Chairman of the Board 2007–2011. Mr Dahlberg is a former Director of Corporate Strategy for Chemicals at Akzo Nobel.

Ulf Alexanderson (2003–2007). Mr Alexanderson is the former Technical Director of Wallenius Lines, one of Sweden’s largest ship-owners.


Anna Joborn (2007–2011). Dr Joborn was the Research Manager at IVL Swedish Environmental Research Institute. She is now Director of the Science Affairs Department at the Swedish Agency for Marine and Water Management.

Ingvar Lindgren (2003–2007). Mr Lindgren, Emeritus Professor of Physics from Chalmers, has been Managing Director of the Swedish Foundation for Strategic Research.

Ann-Christin Thor (2003–2011). Ms Thor is Head of Faculty Administration at the Faculty of Science, University of Gothenburg.

Göran Wessman (2003–2011). Mr Wessman is the CEO of Mintoage Scientific AB.

Management

Over the years, the Programme Directors have had operational responsibility for the programme; Professor Kristo Holmberg (2003), Anders Carlberg (2003–2004), Dr Björn Dahlbäck (2004–2009) and, finally, Professor Thomas Backhaus (2010–2011) who was assisted by Dr Annika Söderpalm (2010) and Dr Åsa Arhennius (2011) as Deputy Programme Directors. Together with the respective project leaders, they constituted the Management Team.
Mistra solves key environmental problems

Marine Paint was financed by Mistra, the Swedish foundation for strategic environmental research (www.mistra.org). Mistra supports environmental research in a long-term perspective, aiming to solve major environmental problems. The bulk of Mistra’s funding is focused on broad-based interdisciplinary programmes. An endowment of more than SEK 3.6 billion (January 1, 2006), made it possible to allocate an annual amount of about SEK 100 million (€ 20 million, $ 25 million) to research funding. This makes Mistra one of the largest sources of funding for environmental research in Sweden.

Some personal reflections from the Programme Directors

I. Krister Holmberg

When Marine Paint started in January 2003, we knew, mainly through Hans Elwing’s initial results, that medetomidine was very effective in inhibiting settling of barnacle larvae. We formulated three main tasks: (i) to develop a proper route for synthesising medetomidine, (ii) to understand the mechanism behind its biological effect, and (iii) to assess the ecotoxicological profile of the substance. During the initial period the work was very focused on barnacle fouling. The interest in formulations with broader antifouling efficacy came later. The initial testing at Tjärnö went very well, and attracted considerable attention. We started discussions with paint companies, in particular with I-Tech. A consortium of researchers was set up to bring together all the intellectual property rights that arose within the programme. The researchers waived their teachers’ exemption for the benefit of joint ownership. This meant that the consortium could enter into agreements with I-Tech regarding the transfer of intellectual property rights from research to I-Tech. The time it takes to establish a structure that can support commercial collaboration should not be underestimated. It also takes time to learn and understand each other’s perspectives, which differ between academia and industry. It is important that both sides adopt an open view of the different conditions and ways of thinking that exist in academia and the industrial world. Applications to Mistra must be evaluated on the likelihood that the research group has the capacity to participate, and that the programme host can harbour the programme in a professional way.

Being clear that it is possible to lead research is important in an academic environment. Mistra has as a starting point the principle that better leadership can produce better research. We attempted to establish an attentive, facilitating management team. Experience from Marine Paint has shown that the aim of having solid leadership has been good for both the quantity and quality of the research. Leadership has focused on “creating the prerequisites” for good research and cooperation. Such prerequisites could include the capacity to communicate internally and to understand each other’s research approach, the capacity to resolve conflicts as they arise and a functioning management team that adopts a holistic view of the programme. (Björn Dahlbäck, the second Programme Director of Marine Paint 2004–2009)

II. Björn Dahlbäck

The programme was assigned the task at an early stage of presenting a commercialisation plan. The fact that these plans were in place early in the programme was crucial to the development of contacts with companies, and in particular with I-Tech. A consortium of researchers was set up to bring together all the intellectual property rights that arose within the programme. The researchers waived their teachers’ exemption for the benefit of joint ownership. This meant that the consortium could enter into agreements with I-Tech regarding the transfer of intellectual property rights from research to I-Tech. The time it takes to establish a structure that can support commercial collaboration should not be underestimated. It also takes time to learn and understand each other’s perspectives, which differ between academia and industry. It is important that both sides adopt an open view of the different conditions and ways of thinking that exist in academia and the industrial world. Applications to Mistra must be evaluated on the likelihood that the research group has the capacity to participate, and that the programme host can harbour the programme in a professional way.

Being clear that it is possible to lead research is important in an academic environment. Mistra has as a starting point the principle that better leadership can produce better research. We attempted to establish an attentive, facilitating management team. Experience from Marine Paint has shown that the aim of having solid leadership has been good for both the quantity and quality of the research. Leadership has focused on “creating the prerequisites” for good research and cooperation. Such prerequisites could include the capacity to communicate internally and to understand each other’s research approach, the capacity to resolve conflicts as they arise and a functioning management team that adopts a holistic view of the programme. (Björn Dahlbäck, the second Programme Director of Marine Paint 2004–2009)

III. Thomas Backhaus

The Marine Paint programme started more than half a decade before I got involved. Being the successor to Björn Dahlbäck and the final Director of the programme was certainly a special challenge. Not only did we need to organize the finalisation of the experimental work, lay the foundation for the final publication and dissemination activities, but the commercial activities of I-Tech reached an all-time high. All-in-all, the final years were challenging times—and I learned a lot about synergies and goal conflicts between applied and fundamental environmental research, about the involvement of academic organisations in applied research and about the proverbial difficulties of “herding cats”.

Marine Paint’s activities, although deeply scientific in its core, were aimed at “applied research” in the most positive sense. That is, making research results available for improving the environmental performance of antifouling paints and, consequently, for limiting the environmental footprint of current shipping activities. Did we reach that goal? You’ll be the judge.

All the activities of a programme such as Marine Paint ultimately depend on the quality and quantity of its fundamental scientific activities. For that reason, I would like to take the opportunity to thank all the field assistants, master students, PhD students, Post-Docs, technicians, external contributors and senior scientists involved. They all spent countless hours in the lab, behind the computer and in the field in order to provide the high-quality data that Marine Paint so much depended on—and always went the extra mile if necessary. Special thanks are due to Marine Paint’s steering group, which was pivotal for the organisation, vision and implementation of Marine Paint. Without all of you, Marine Paint would not have been as successful as it is today. Stort tack! (Thomas Backhaus, Programme Director 2009–2011)
Key researchers in the programme

**Applied Surface Chemistry, Chalmers University of Technology**
- Magnus Nydén, Professor, Project leader
- Kristers Holmberg, Professor
- Camilla Fant, PhD
- Dan Isaksson, PhD
- Lars Nordsterna, PhD
- Mohammad Mizanun Rahman, PhD
- Lyuda Shtytkova, PhD
- Lars Swanson, PhD
- Atta Allah Abdallah, PhD student
- Markus Andersson, PhD student
- Paul Hans, PhD student
- Alireza Movahedi, PhD student
- Alberta Mok, Technician

**Cell and Molecular Biology, University of Gothenburg**
- Paul Handa, PhD student
- Atta Allah Abdallah, PhD student
- Mohammad Mizanun Rahman, PhD
- Lyuda Shtytkova, PhD
- Lars Swanson, PhD
- Atta Allah Abdallah, PhD student
- Markus Andersson, PhD student
- Paul Hans, PhD student
- Alireza Movahedi, PhD student
- Alberta Mok, Technician

**Chemistry, University of Gothenburg**
- Hongjun Liu, Associate Professor
- Martin Ogmard, Technician

**Plant and Environmental Sciences, University of Gothenburg**
- Thomas Backhaus, Professor, Programme Director 2010–2011
- Hans Blanck, Professor, Project leader
- Björn Dahlbäck, PhD, Programme Director 2004–2009
- Asa Arhenius, PhD, Programme Director 2004–2009
- Goran Birygsson, PhD
- Kristina Holm, PhD
- Cecilia Ohlauson, PhD student
- Ida Wendt, PhD student
- Erik Norin, Technician

**Marine Ecology, University of Gothenburg**
- Per Jonsson, Professor
- Åke Granmo, Associate Professor
- Annelic Hilverdsson, PhD
- Kent Bernstorf, PhD
- Rolf Ekelund, PhD
- Juan Bellas, PhD
- Martin Ogmard, Technician
- Norwegian Institute for Water Research
- Kevin Thomas, Professor
- Katherine Langford, PhD

**Zoology, University of Gothenburg**
- Lena Mårtensson Lindblad, Associate Professor, Project leader
- Lars Förlin, Professor
- Margareta Wallin, Professor
- Linda Hasselberg Frank, PhD
- Nora Kerekes, PhD
- Anna Lennequist, PhD
- Kristin Ödling, PhD student
- Elisabeth Norström, Technician
- Ulla Svedin, Technician

**Dissemination activities**

Members of Marine Paint were constantly carrying out dissemination activities in order to increase awareness and knowledge within the field of marine biofouling and antifouling. We targeted a broad audience, including the public, schoolteachers, boat owners, chemical regulators, the biocide and paint industries and scientists from a wide range of fields.

**Some recent outreach activities**

- Organisation and implementation of a special session on Marine Coatings at the European Coatings Conference in Nuremberg, with an audience mainly from regulatory authorities, biocide industry, research laboratories and academia.
- Sponsoring and participation in SETAC’s special science symposium on “Recent Developments in Biocide Risk Assessment”, 2011 in Brussels. Participants came from regulatory authorities, biocide industry, research laboratories and academia.
- Inspirational evenings for secondary teachers about Fouling and Antifouling in Gothenburg.
- Organisation and implementation PhD courses on Fouling and Antifouling at University of Gothenburg.
- Giving advice on antifouling principles to the United Nations Development Programme (UNDP) and the Office of Foreign Co-operation at the Ministry of Environmental Protection (MEP-FECO), China.
- Funding of Marine Biofouling Research in Göteborg AB (MBRG AB) in 2009.
Some recent presentations

**European Coatings Conference – “Marine Coatings”, 28 – 30th March 2011, Nuremberg, Germany**


**SETAC Europe Conference in Milano, 2011. Special session on Marine antifouling – perspectives and recent developments**

2. Thomas Backhaus: Employing classical mixture toxicity concepts for the optimisation of biocide combinations for antifouling paints. Oral presentation.

**15th International Congress on Marine Corrosion and Fouling (ICMCF), July 25 – 29 2010. Newcastle, United Kingdom.**

- Åsa Arrehnsius: Combined effects of antifoulants – synergistic, additive or antagonistic effects? Poster presentation.
- Thomas Backhaus: Employing classical mixture toxicity concepts for the optimisation of biocide combinations for antifouling paints. Oral presentation.
Acknowledgements

For the work on optimised mixtures of biocides we depended on good relations with biocide producers, and we would like to thank Arch Chemicals, Dow Chemicals, Ciba Specialty Chemicals GmbH, I-Tech AB and Lanxess for providing biocides and information about their products. For the panel testing, we gratefully acknowledge the help we received from Hempel A/S and Lorté AB in providing many buckets of paint. Please note, the companies had no influence on the actual work nor on how we interpret and use the results.

The Sven Lovén Centre for Marine Sciences at Fiskebäckskil and Tjärnö and their staff provided excellent working facilities for working with marine fouling organisms and performing panel testing, for which we offer our warmest thanks.

Finally we would like to thank Mistra for funding Marine Paint’s research over the past 9 years.

Acronyms used

- BPD – the EU’s Biocidal Products Directive (98/8/EC)
- cAMP – Cyclic adenosine monophosphate
- cDNA – complementary DNA
- CRC – Concentration response curve
- DCOT = Sea-Nine; 4,5-dichloro-2-n-octyl-4-isothiazoline-3-one
- EROD – ethoxyresorufin-O-deethylase et al – Latin for "and others"
- FTIR – Fourier transform infrared; method used to evaluate the paint formulations developed
- FW – fresh weight
- GLP – Good Laboratory Practice
- GPCR – G-protein coupled receptor
- HPLC – high-performance liquid chromatography
- In vitro – Latin for “within glass”, refers to studies conducted using only parts of an organism
- In vivo – Latin for “within the living”, referring to a study performed with a whole organism
- l/kg – litres per kilogram
- MEP-FECO – Ministry of Environmental Protection, Foreign Economic Cooperation Office
- nM – nanomolar, 10^-9 moles per litre, a concentration unit
- NMR – nuclear magnetic resonance; method used to evaluate the developed paint formulations
- PEC – Predicted environmental concentration
- PNEC – Predicted no-effect concentration
- SEM – Scanning Electron Microscopy
- SIPC – settlement-inducing protein complex
- SPC – Self-polishing Coating
- TBT – Tri-butyltin
- µg/L – microgram per litre, 10^-6 gram per litre
- UNDP – United Nations Development Programme