The Scientific and Patent Landscape for Marine Genetic Resources in Southeast Asia

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Chapter 1

Acknowledgements

The WIPO Report on the Scientific and Patent Landscape for Marine Genetic Resources in South East Asia, was written with the generous financial support of the Patent Office of Japan (JPO).

The report is based on data from a combination of Clarivate Analytics Web of Science Core Collection, Clarivate Analytics Derwent Innovation patent collections and the EPO World Patent Statistical Database (PATSTAT, October 2017 edition). The report is made possible by the increasing availability of digital information on biodiversity and the development of tools to access this data. We thank the World Register of Marine Species which made available the list of marine species used in this research, and the Global Names Index for data on variations on species data. Environmental information on marine species for the WoRMS database was available thanks to the API made available by Lifewatch Belgium. Additional taxonomic information and species occurrence data was obtained from the Global Biodiversity Information Facility (GBIF). The GBIF API was accessed using the ROpenSci R package `rgbif` and the resolution of taxonomic names was performed using the ROpenSci `taxize` package (Chamberlain, 2018; Chamberlain et al., 2018). Name cleaning and text mining was performed using VantagePoint from Search Technology Inc and additional text mining performed in R using the tidytext package (Robinson and Silge, 2018). General data analysis was performed in the R programming language in RStudio using packages within the tidyverse (R Core Team, 2018; Wickham, 2017). The report was written in R markdown with Bookdown (Allaire et al., 2018; Xie, 2018).

1.1 Authorship

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Chapter 2

Introduction

This landscape report examines the scientific and patent landscapes for marine genetic resources in South East Asia (ASEAN region).[1] The aim of the report is to advance knowledge and understanding of the importance of research and innovation involving the marine environment in the ASEAN region.

It has recently been estimated that South East Asia is home to around a third of the world's population and that 70 percent of its residents live in coastal areas (Olewiler in Olewiler et al., 2016). While encompassing approximately 10% of the world's land mass, the ASEAN region includes an estimated 30% of the world's coral reefs and 33% of its mangrove forests (Olewiler et al., 2016). Fisheries are also central to the livelihoods of many people within the ASEAN region with recent estimates suggesting that the region accounts for 21 million tonnes of fish production, or a quarter of global production (Ferrer in Olewiler et al., 2016). As this suggests the marine environment and the ecosystem services that it provides are central to the economies, livelihoods and welfare of people throughout the ASEAN region. Recent years have witnessed growing research and awareness of the threats to the marine environment in the form of pollution, over-exploitation of marine resources and climate change (Olewiler et al., 2016).

Growing awareness of human impacts on the marine environment has also been accompanied by increased recognition of the opportunities that the marine environment presents for advancing human welfare through the development of new products such as pharmaceuticals, cosmetics, novel foods and tools for use in biotechnology. Awareness of the actual and potential contribution of the marine environment to economic well being is increasingly taking shape through the adoption of policies directed towards the 'Blue economy' within ASEAN and the wider East Asia region (Gamage, 2016). Thus, in 2012 countries from across the region issued the *Changwon Declaration: Towards an Ocean-based*

[1] ASEAN stands for the Association of Southeast Asian Nations

Blue Economy which stated that:

> "We understand the Blue Economy to be a practical ocean-based economic model using green infrastructure and technologies, innovative financing mechanisms and proacticve institutional arrangements for meeting the twin goals of protecting our oceans and coasts and enhancing its potential contribution to sustainable development, including improving human well-being and reducing environmental risks and ecological scarcities."[2]

On a wider level, growing awareness of the threats to the marine environment and its role in human welfare and global ecosystem services is reflected in ongoing work under the marine programme of work of the United Nations Convention on Biological Diversity and negotiations under the United Nations General Assembly on a new treaty on biodiversity in Areas Beyond National Jurisdiction.

This landscape report seeks to contribute to understanding scientific research and patent activity involving marine genetic resources in South East Asia. The landscape is based on a review of data from 391,181 scientific publications from the South East Asian region and 461,380 patent documents. The research involved text mining these documents for over 398,000 marine species recorded in the World Register of Marine Species[3] and access to millions of species occurrence records from the Global Biodiversity Information Facility (GBIF).[4]

The research reveals that marine genetic resources are a growing focus of attention among research communities within the ASEAN region. Research on marine genetic resources within the region is primarily oriented towards the aquaculture sector but extends to the exploration of the potential of marine organisms as sources of new pharmaceuticals, cosmetics and other products. In addition, a significant body of research is dedicated to understanding the basic biology of marine organisms and the environmental impacts of human activity. The report reveals that marine genetic research in the ASEAN region is increasingly international in nature. We identify collaborations between researchers from over 130 countries and an emerging network of funding agencies from within and across the region. While marine organisms have attracted an increasing amount of commercial interest as sources of potential new products in recent years, as in many regions of the world, patent activity is presently emergent for marine genetic resources in the ASEAN region and concentrates on the aquaculture and, to a lesser degree, the pharmaceutical sectors.

The report begins with a general overview of biodiversity data for the ASEAN region to orient the reader on available knowledge about the region. We then move into analysis of the scientific and patent landscapes for marine genetic research within the ASEAN region.

The report is organised into four sections.

[2] http://www.pemsea.org/sites/default/files/changwon-declaration.pdf
[3] World Register of Marine Species
[4] Global Biodiversity Information Facility (GBIF)

1. Biodiversity Data in the ASEAN region
2. The Scientific Landscape
3. The Patent Landscape
4. Conclusions

Annex 1 presents a summary of activity for some of the major species identified in the report and links to additional resources. Annex 2 presents details of the methodology used to prepare the report. The bibliography provides details and links to the research reviewed for this report.

Chapter 3

Biodiversity in the ASEAN Region

ASEAN countries are the home to an extraordinary range of biodiversity with Indonesia, Malaysia and the Philippines classified as megadiverse countries in terms of the number of endemic species. We obtained the available records on biodiversity for each ASEAN country using the Global Biodiversity Information Facility (GBIF) data portal. As of March 2018 GBIF contained 6,350,017 occurrence records for ASEAN countries covering a total of 147,036 species. Occurrence records are recorded observations of a species and are commonly accompanied by georeference data notably latitude and longitude. Figure 3.1 displays a summary view of the available biodiversity data for the ASEAN region focusing on species counts and counts of occurrences.

Figure 3.1 reveals that the available species data for ASEAN countries is dominated by information on animal (Animalia) species followed by plants (Plantae) and fungi. GBIF does not consistently include data on viruses and this will therefore be under-represented in this data. Turning to the class of organisms, the data is dominated by a class of plant species (Magnoliopsida) which also account for a large number of observation records, followed by insects (Insecta), snails (Gastropoda), Liliopsida (a class containing the Lily Family) and Malacostraca such as crabs, lobsters, and shrimps. In reviewing this data note that a common feature across GBIF data is that observational data (occurrences) are dominated by birds (Aves) because humans display a marked tendency to record and submit bird observations

Figure 3.1 also reveals that the availability of data on biodiversity within the ASEAN region varies considerably between countries with Indonesia coming top in terms of both the number of recorded species and observations in GBIF with Brunei recording the smallest numbers. This will reflect the size of countries and also the extent to which the scientific community and taxonomic collections

Figure 3.1: Species Occurrence Records in ASEAN Countries

have made their basic taxonomic data available to GBIF.

Recent years have witnessed dramatic improvements in the availability of species information in digital form. However, it is important to bear in mind that this data will almost always represent a limited set of the overall data and of actual biodiversity within a country or region. This is particularly true for marine species with the marine environment representing one of the least explored and documented environments on earth.

3.0.1 Marine Species in the Biodiversity Data

Marine species are a subset of the biodiversity data for the region. However, it is important to recognise that the description of a species as marine is not straightforward in practice because they may exist in multiple habitats. Specifically, using the classification adopted by the World Register of Marine Species (see below) a species may occupy one or more of the following environments:

- terrestrial
- freshwater (aquatic)
- brackish (freshwater/saltwater boundary)
- marine

A species may therefore be found in multiple environments, or it may occupy a particular habitat at one stage of its life cycle and another habitat at a later stage. This makes the strict isolation of marine species difficult. As we will see below the common plant pathogen *Fusarium oxysporum* is widespread in soils but is also a marine organism according to the World Register of Marine Species (WoRMS). This presents the difficult challenge of distinguishing between terrestrial fungi and marine fungi. A second example is provided by mosquitoes (genus Anopheles) that have been a major focus of attention in the scientific and the patent literature. These insects are aquatic in the early stage of their life cycle and lay eggs in water during the adult stage. Similarly, in the case of animal organisms some fish may breed in freshwater but spend the majority of their life cycle in a salt water marine environment. In the case of plants these may be found in salt marshes, lagoons, beaches and other coastal environments and extend into underwater habitats.

As this makes clear, drawing a distinction between marine and non-marine organisms can be a challenge and requires close attention to detail. In this report following exploration of the species data we adopt the approach of excluding terrestrial species wherever possible. Based on investigation of some plant species and fungi we limit plant species to those with a coastal distribution (such as mangroves) and generally exclude fungi except where they are demonstrably of marine origin.

To identify Marine species in the GBIF data we used a reference list of marine species binomial names from the World Register of Marine Species that we reduced to 398,000 binomial names for text mining purposes. We identified

28,000 marine species names in GBIF data that appear in the reference list from WoRMS. We then retrieved the available environmental data about those species using the Lifewatch Belgium web service. GBIF data on marine species appearing in WoRMS is summarised in Figure 3.2.

Figure 3.2 reveals, as we might expect, that the number of species is dominated by Animalia, notably gastropods, followed by Actinopterygii, ray-finned bony fish, Malacostraca (crabs, shrimp, lobster), molluscs (Bivalvia), Anthozoa (marine invertebrates including corals and gorgonians) and Hexanauplia or crustaceans such as copepods. Interestingly, while the rankings for country level data only undergo minor change with Singapore moving up one ranking, the Philippines moves to the top ranking in terms of the number of recorded occurrences for marine species. However, as we will see in the next section, in recent years marine research in the Philippines has displayed a declining trend.

3.0.2 Conclusion

In this section we have provided a brief overview of the available data on biodiversity and marine biodiversity in the ASEAN region. As we have emphasised our ability to interrogate the scientific and patent landscapes for marine biodiversity in the ASEAN region is fundamentally constrained by access to data about biodiversity in the region. In many countries this is improving as countries recognise the value of digitising their biodiversity data and make it available through the Global Biodiversity Information Facility (GBIF).

As we will see in the following sections, the availability of taxonomic information or biodiversity informatics is also important for our ability to map and understand research and research and development involving marine species within and beyond the ASEAN region.

3.0.3 References

GBIF occurrence datasets as used in this report are publicly available for download as follows and should be cited using the supplied DOIs.

1. Brunei darussalam, DOI 10.15468/dl.ny8aam
2. Cambodia, DOI: 10.15468/dl.22e1ct
3. Indonesia, DOI: 10.15468/dl.cwwjsn
4. Lao people's democratic republic, DOI: 10.15468/dl.x7kr9j
5. Malaysia, DOI: 10.15468/dl.3b9yw3
6. Myanmar, DOI: 10.15468/dl.2czwzg
7. Philippines, DOI: 10.15468/dl.fi2kit
8. Singapore, DOI: 10.15468/dl.ribxsw
9. Thailand, DOI: 10.15468/dl.vzhaey
10. Viet Nam, DOI: 10.15468/dl.8qivwd

Figure 3.2: Occurrence Records for Marine Species in ASEAN Countries

11. South East Asia and Pacific bounding box, DOI: 10.15468/dl.e7bm2i. Polygon: ((89.296875 -11.591978551846823, 89.296875 30.388035892267144, 161.71874999999997 30.388035892267144, 161.71874999999997 -11.591978551846823, 89.296875 -11.591978551846823))

Chapter 4

The Scientific Landscape for Marine Genetic Resources in the ASEAN Region

In this section we examine the scientific landscape for research involving marine species. In total we identified 6,659 scientific publications in Clarivate Analytics Web of Science Core Collection that contained a marine species listed in the World Register of Marine Species (WoRMS) database. ASEAN researchers were co-authors on 77% (5,109) of the publications. The 6,659 records contained 3,685 marine species after the exclusion of common model organisms.

Figure 4.1 displays a snapshot overview of activity for marine species in the region. [1]

In Figure 4.1 we can immediately see that marine research in the ASEAN region encompasses countries within and outside the region. This reflects the increasingly international nature of modern scientific research and marine research. We can also observe significant variation in levels of marine publications between ASEAN countries with respect to trends that reflect the underlying emphasis and strength of each country with respect to marine research. Finally, information on the subject area of research reveals the prominence of Marine & Freshwater Biology (as we would expect) along with more applied fields such as Biotechnology & Applied Microbiology and Parasitology or Immunology that provide an indication of potentially more commercially oriented research areas.[2]

[1] This data can be explored interactively in an online Tableau Public workbook

[2] Subject Areas refer to Web of Science Subject Categories which seek to describe the subject area of journals where articles are published. A single journal may fall into more than one category and are used here as a proxy for summarising research subjects

Figure 4.1: Overview of Research Activity for Marine Species in ASEAN countries

4.0.1 Trends by Country

The presentation of trends by country in Figure 4.1 has the effect of pressing countries with lower level marine research outputs to the bottom of the graph. We gain a clearer view of country level trends in Figure 4.2 where the data for each country is presented in separate panels. In Figure 4.2 we present the data as a scatterplot and then add a smoothed trend line (using Loess or locally weighted smoothing) between the data points.

Figure 4.2: Country Trends for Research on Marine Genetic Resources in the South East Asia Region

This reveals, that in general all countries within the region have displayed an increase in publications on marine research over time with Myanmar, Laos, Cambodia and Brunei exhibiting less than 10 publications per year across all years. For countries with higher levels of activity, Thailand emerges as the leading country for research involving marine species. However, research outputs plateaued from 2010 onwards before staging a more recent increase in 2016. In the meantime, as can more clearly be seen in Figure 4.2, Malaysia has displayed a steeply rising trend in research outputs that has overtaken Thailand. In contrast with countries throughout the region that display a rising trend, the Philippines displays a declining trend from approximately 2008 onwards that may reflect either a change in the orientation or research outputs (for example with a more applied focus that place less emphasis on publications) or a decline in research investment in marine research.

Research outputs, in the form of peer reviewed research articles and scientific publications, reflect underlying investments and incentives for scientific research in the marine and terrestrial aquatic environments. As we have seen, while varying in intensity, in the majority of ASEAN countries marine organisms are an increasing or emerging focus of scientific publications. We now take a closer look at the nature of research activity.

4.0.2 Marine Species Research

Figure 4.3 presents an overview of marine research in the ASEAN region from the perspective of the species that are a focus of research.[3] For the top ten species we provide a set of short fact sheets in Chapter 6 of the report. Here we present a short summary for the top species.

Figure 4.3: Top Marine Species Overview

[3]This dashboard can be explored interactively Tableau Public workbook

In considering Figure 4.3 a number of the top species are shrimps associated with the rapid growth of aquaculture in the region from the late 1990s onwards (Hishamunda et al., 2009).

Figure 4.3 reveals that the species that the Giant Tiger Shrimp (*Peneaus Mondon*) is a major focus of research activity that reflects the economic importance of the species in the aquaculture sector within the ASEAN region. Research with respect to *Peneaus Mondon* is directed towards maximizing yields. A significant proportion of the literature focuses on understanding *P. mondon* immune responses to viral and bacterial pathogens that are responsible for large scale mortality in tiger shrimps, notably White Spot Syndrome Virus, Yellow Head Virus and *Vibrio harveyi* (Wongteerasupaya et al., 1995; Ponprateep et al., 2011; Jaree et al., 2012).

The second ranking animal species in the data also relates to aquaculture. *Macrobachium rosenbergii* (the Giant River Prawn and the Giant Freshwater Prawn) is widely fished and is the main freshwater shrimp cultivated within the commercial aquaculture industry (De Grave et al., 2012).[4] While this is a freshwater species, females move into brackish estuarine waters to lay their eggs. As with *P. mondon* research is directed towards maximizing yields and reducing mortality from pathogens such as White Tail Disease virus (Bonami and Widada, 2011). Improvements to broodstock genetics (Karaket and Poompuang, 2012; Thanh et al., 2015, 2010) as well as improvements to prawn feed (Kangpanich et al., 2016) have been a significant focus of research activity.

Oreochromis niloticus is a species of Tilapia, a cichlid fish native to the Nile basin in Africa and coastal rivers of Israel.[5] It is an economically important species introduced into the ASEAN region and elsewhere because it is fast growing. The literature focuses on issues such as genetic improvement (Bentsen et al., 1998), options for rice paddy field polyculture in conjunction with other species (Vromant et al., 2002) , and salt tolerant hybrids for aquaculture in coastal ponds for this freshwater species (Kamal and Mair, 2005).

Litopenaeus vannamei is the world's dominant cultivated shrimp. It grows as a juvenile in estuarine environments and lives in marine salt water as an adult. South East Asia has witnessed dramatic growth in aquaculture for this species, notably in Thailand and China. Improving breeding stocks (Nimrat et al., 2006), protection against infectious myonecrosis (da Silva et al., 2010), and alternatives to the use of antibiotics such as the use of probiotics (Nimrat et al., 2011) feature prominently in the literature for this major species.

Lates calcarifer is the Barramundi or Asian seabass and is a widely distributed demersal fish ranging from the Persian Gulf through South East Asia and Papua New Guinea.[6] It is typically found in estuaries, coastal waters, lagoons and rivers. Research has focused on aquaculture for this species including under-

[4] IUCN Redlist at http://www.iucnredlist.org/details/197873/0

[5] Encyclopedia of Life at http://eol.org/pages/356343/data?toc_id=4#1448

[6] Demersal fish are bottom feeders in what is known as the demersal zone

standing the natural history of the species (Shadrin and Pavlov, 2015) and fish feed (Shansudin et al., 1997; Mohd-Yusof et al., 2010) including the use of local seaweed species (Shapawi and Zamry, 2015).

Ascaris lumbricoides is the large roundworm and is responsible for causing ascariasis in humans. While *A. lumbricoides* is aquatic and recorded by WoRMS as a marine species it is excluded from further analysis because the focus of the scientific literature in the ASEAN region is on soil transmitted helminth infections in humans, including in coastal areas, rather than the marine environment as such (Montresor et al., 2007).

Perna viridis is commonly known as the Indian Green Mussel. Research in relation to this species in ASEAN countries focuses on issues such as the impacts of metal concentrations, notably heavy metals on speciation, the implications of contamination for human health and the potential use of the species for wider biomonitoring of heavy metal contamination (Yap et al., 2002, 2004, 2003). Other research addresses concentrations of shellfish toxins and *Vibrio parahaemolyticus* in *P. viridis* (Marasigan et al., 2001) along with issues such as suspension feeding behaviour (Hawkins et al., 1998; Tan and Ransangan, 2016) and genetic diversity (Ye et al., 2015). As this suggests, land based run offs of contaminants into the marine environment in the ASEAN region has become a significant focus of research for this economically important species.

Epinephelus coioides is the Orange Spotted Grouper or Estuary Cod. This is an IUCN Red List near threatened species that in its juvenile stage is found in estuaries and mangroves and as adults in brackish water and coastal reefs. [7] It is a commercially important species including in aquaculture. Research in the ASEAN region has included work on cell lines (Qin et al., 2006), feeding performance (Doi et al., 1997; Eusebio et al., 2004) and the immune system of this important commercial species (Zhou et al., 2011; Guo et al., 2012).

Two bacteria feature prominently in marine research in the ASEAN region. The first of these is *Vibrio parahaemolyticus*, a gram negative bacteria that is found in estuarine, coastal and marine waters. *Vibrio parahaemolyticus* is now a globally distributed species associated with vibriosis through the consumption of raw shellfish or exposure to contaminated water (Nair et al., 2007). Within the literature for ASEAN countries the main focus is on the impact of contamination in aquaculture, including detecting strains associated with infection(Rahman et al., 2006) and vaccines (hua Hu and Sun, 2011). The risks of mortality in shellfish stocks and consequent mortality rates are combined with increasing awareness of the problem of antibiotic resistance and the quest for alternatives such as botanical extracts sourced from ASEAN countries (Sivasothy et al., 2013; Nguyen et al., 2016; Tinh et al., 2016).

The second major bacterial species is *Vibrio harveyi*, a Gram-negative, bioluminescent and common marine bacterium in the same genus as *V. parahaemolyticus*. It is common in the gut of many tropical marine organisms with a small

[7] http://www.fishbase.org/summary/6465

number of strains being pathogenic. While the bacteria is normally benign, pathogenic sub-strains are particularly associated with impacts on shrimps such as *P. mondon*, with the ASEAN literature focusing on detection and the use of natural compounds, including from marine cyanobacteria (Ponprateep et al., 2009; Maneechote et al., 2016,?)

Rhizophora apiculata is a widespread intertidal mangrove species in the ASEAN region. The species is used for firewood and is also a focus of commercial mangrove silviculture in the region (Rhi, 2015). A second important mangrove species is *Avicennia marina*, known as the grey or white mangrove that is widely distributed throughout the ASEAN region and beyond. It takes form as a shrub or tree and has a range of uses as a food source, in construction and medicine (Duke et al., 2008). Research on this species in the ASEAN region has focused on issues such as genetic structure and variation (Arnaud-Haond et al., 2006; Giang et al., 2003), the impacts of aquaculture water on mangroves (Vaiphasa et al., 2007), biodiversity (Zhila et al., 2013), mangrove restoration (Aung et al., 2011) and new plant extract for alopecia treatment (Jain et al., 2015, 2014).

As this brief summary of the major species suggests, the marine data is dominated by species that are commercially important in aquaculture within the region. This comes into clearer focus if we examine the relationship between research on species grouped on the genus level and the subject areas of publications.

Figure 4.4 presents a Sankey diagram of the flow between research on the species and Subject Areas presented in 4.3. A Sankey diagram is typically used to display the flow of energy, in this case investments in research on species grouped on the genus level, and the intended audiences represented by the subject areas.

We can clearly see in Figure 4.4 that research on Penaeus (e.g. Tiger Prawn) genus primarily flows into fisheries followed by Marine and Freshwater Biology. The link between research on Penaeus and Vibrio is represented by Immunology and Veterinary Science. In contrast work on mangroves (represented by Avicennia and Rhizophora) is more concentrated in Environmental Sciences (for Avicennia) and additionally Marine and Freshwater Biology, Ecology and Plant Sciences for Rhizophora. This suggests a more basic research orientation for our mangrove species as discussed above.

Figure 4.4 provides the first indication that marine research may be directed in multiple directions, from basic taxonomic and ecological research, to commercially oriented research that focuses on enhancing productivity and addressing problems such as pathogens for commercially valuable species.

In practice, research on species takes place in networks that can be explored on multiple levels.

First, researchers are typically performing research on more than one species. For example, work on pathogens of *P. mondon* and other shellfish will include reference both to the source species (*P. mondon*) and the target species.

Figure 4.4: Flows of Publications on Species into Subject Areas

Second, there has been a growing trend towards the internationalisation of research collaborations represented by collaborations between researchers outside their home countries and regions. This is typically supported by national research institutions, such as research councils, and home institutions administering funds on behalf of national organisations. These investments form a network of collaboration between countries that are underpinned by financial investments in research, typically by national research councils or their equivalent.

Third, collaboration networks between researchers involve inter-institutional relationships including flows of research funding, equipment, students and postdoctoral researchers.

Finally, there are the networks of relationships between researchers who build the wider inter-institutional network and communities of researchers working on particular marine species and particular problems.

To gain a fuller understanding of the characteristics of research on marine genetic resources in the ASEAN region we will explore each of these networks in turn.

4.0.3 The Species Network

Figure 4.5 displays the network relationships between publications involving marine species where there are more than 10 publications referencing the species. The dots represent nodes in the network and are sized based on the number of records. The lines or edges are based on the number of publications where the species appear in the same publication with thickness representing the number of shared links. The colours in this case refer to the kingdom for each organism as in Figure 4.3.

What is powerful about this form of visualisation is that we can immediately see that a strong relationship between the Vibrio pathogenic viruses and important aquaculture species, notably prawns and shrimps such as *Penaeus mondon*, *Macrobrachium rosenbergii* and *Litopenaeus vannamei* among others such as *Penaeus vannamei*. We can also see that research on plants, dominated by mangroves (in green) forms a distinctive cluster of research but also links through *Avicennia marina* and *Rhizophora apiculata* to research on *Peneaus mondon* and related species (Hai and Yakupitiyage, 2005).

We can apply this same approach to a broader overview of the scientific landscape for marine research at the level of the analysis of international and regional level research collaborations to which we now turn.

4.0.4 Country Networks

In total 136 countries appeared in the ASEAN data for research involving marine genetic resources (see Figure 4.1 above). Collaborations between countries involved in marine research can be visualized as a network. Figure 4.1 below

Figure 4.5: Network of Species that are the Focus of Research

displays the country collaboration network where there are two or more publications involving researchers from those countries. Once again the size of the nodes reflects the number of publications.

Figure 4.6: Country Collaboration Networks for Marine Genetic Research in the ASEAN region

In Figure 4.6 the country nodes are sized based on the number of records that involve a publication with an author from the country. The lines (edges) represent publications by authors from both countries with the weight of the lines indicating the number of publications. The colours denote communities of collaborating countries based on the calculation of the strength of the links between them compared with the strength of connections between all other nodes (countries) (Blondel et al., 2008). This allows us to see the distinctive network connections between ASEAN countries and other countries.

Figure 4.6 reveals 4 main country network clusters. The largest network cluster

is represented by Thailand with strong connections with Japan, the United States, Australia, the UK and China along with the Philippines. Malaysia displays weaker links with a number of these countries but is distinctive for its links with India, neighbouring Brunei, Bangladesh, Pakistan and Sri Lanka. Singapore displays a weaker but wider set of connections with other countries, while Vietnam forms part of a network with South Korea, Denmark, Norway, Laos and Cambodia. The importance of mapping these collaboration networks is that they reflect underlying financial investments in the form of research funding, investments in student training, equipment and materials.

4.0.5 The Funding Network

This network of relationships between countries reflects underlying national investments in the driving force behind all research: research funding. Data on research funding is difficult to access and has only been available in *Web of Science* from 2008 onwards and suffers from a lack of uniformity in the data requiring extensive cleaning. However, we can gain a partial insight into the major funding agencies involved in marine genetic resources in the ASEAN region in the network map in Figure 4.7. This network displays funding organisations that appear in the acknowledgements of more than 20 publications in the ASEAN Web of Science dataset.

In considering Figure 4.7 we immediately observe the dominant position of the Thailand Research Fund and the Commission on Higher Education in Thailand (officially the Office of the Higher Education Commission or OHEC) along with universities in funding marine research in Thailand. While this network displays rankings based on the number of publications, rather than the size of investments, it suggests that the strong trend in publications in marine research in Thailand reflects dedicated funding investment. Looking outside Thailand, a network of external funding bodies emerges in connection with publications from Thailand in the form of the United States National Science Foundation (through the Thailand National Research Fund and the BIOTEC centre) as well as joint publications with research funding from Germany. Funding Agencies from Japan appear particularly prominently in the funding network notably through the Ministry of Education, Culture, Sports, Science and Technology (MEXT) and the Japan Society for the Promotion of Science. Funding organisations from China are also emerging as a major funding source on marine research publications.

As noted above, our ability to view funding networks is presently partial. However, we can also gain an insight into the subject areas where research investments are being made. Figure 4.8 aggregates the funding agencies by country and displays the subject areas of research outputs focusing on the top subject areas.

Three points stand out in Figure 4.8. The first of these is a clear investment stream in fisheries research in the case of Thailand that is also strong in the

Figure 4.7: Major Funding Networks for Marine Genetic Research in the ASEAN region

Figure 4.8: Funding Flows through Publications on Marine Genetic Resources in the ASEAN region

case of Marine & Freshwater Biology. The second point is the that Vietnam's research investment is marked by an emphasis in Chemistry and Pharmacology (as are research investments from Korea). Investment by Japan is more evenly balanced but also includes Chemistry and Pharmacology while investments from the European Union (through the European Commission programmes) are focused on Fisheries, Marine & Freshwater Biology and Zoology. While we must emphasise that our ability to view the data is partial, and constrained by data variability, we can nevertheless detect the main orientations of research investments as we will see in more detail below.

4.0.6 The Organisational Landscape

Collaborative research relationships between countries in marine research reflect underlying collaborations between individual researchers and research teams based in organisations. In total, approximately `xxx` organisations were involved in marine research linked to the ASEAN region. Advances in the availability of geomapping tools, in this case the Google Maps API, made it possible to geocode the nearly 4,000 organisations involved in marine genetic research. Figure 4.9 displays the results along with a selection of linked records from the National University of Singapore. [8]

Figure 4.9 reveals, as we might expect, that the major clusters of research activity is found within the ASEAN region extending through to Japan, Australia and China. However, we can also observe a wider set of connections including with India, Africa, Europe and the United States that make clear the global nature of research on the marine environment in the ASEAN region.

As with the country networks, this data can also be visualised as a network. Figure 4.10 displays the network of collaborating organisations for organisations with 20 or more publications involving marine species. The nodes in the network are sized on the number of publications associated with the organisation. The lines represent the connections (in the form of co-authored articles) between the organisations with heavier lines representing stronger collaborative links. Finally colours seek to identify communities based on the strength of the co-author linkages between the actors in the network using the modularity class algorithm in Gephi for community detection (Blondel et al., 2008). This suggests that researchers at the National University of Singapore lead a networked community of researchers involving Nanyang Technology University in Singapore, the Chinese Academy of Sciences and the University of Queensland (Australia) among others. In contrast, Mahidol University, Chulalongkorn University and Prince Songkla University in Thailand are all prominent in conducting research involving marine genetic resources but have stronger links with Tokyo University of Marine Science and Technology, Deakin University (USA) and the University of California at Davis (USA). For the Philippines, a strong connection emerges

[8] The interactive version of this figure is accessible INSERT here and will display the results by institution

Publications by Organisation

Publications by Organisation

locations	Title
Natl Univ Singapore, Singapore, Singapore	A BLASTOCYSTIS SPECIES FROM THE SEA-SNAKE, LAPEMIS-HARDWICKII (SERPENTES, HYDROPHIIDAE)
	A cost-effective approach to enhance scleractinian diversity on artificial shorelines
	A developmental model for predicting handedness frequencies in crabs
	A female-specific pentraxin, CrOctin, bridges pattern recognition receptors to bacterial phosphoethanolamine
	A first record of anchialine crab of the genus Orcovita Ng and Tomascik, 1994 (Decapoda : Brachyura : Varunidae) from Japa
	A FIRST RECORD OF FRESHWATER SPONGE FROM SINGAPORE AND REDESCRIPTION OF EUNAPIUS CONIFER (ANNANDALE,
	A genome-scale metabolic model of Methanococcus maripaludis S2 for CO2 capture and conversion to methane
	A high-resolution linkage map for comparative genome analysis and QTL fine mapping in Asian seabass, Lates calcarifer

Figure 4.9: Geographic Distribution of Organisations Publishing on Marine Genetic Resources in the ASEAN Region

with the University of Tokyo. For Vietnam, which appears on the outer edges of the network a relationship emerges between the Vietnam Academy of Science and Technology and the Russian Academy of Sciences with other links in the Vietnam community to Seoul National University and Gyeongsang National University in South Korea.

Figure 4.10: Collaboration Networks for Organisations publishing on Marine Genetic Resources in the ASEAN region based on shared publications

These networks are revealed through the analysis of the institutional affiliation of authors, but they are generally hidden networks in so far that only the parts of a network that a researcher is involved with will be visible to them while institutional knowledge of these connections may be limited. However, these networks are important in so far that they represent exchanges and transfers of knowledge, the joint generation of new knowledge and financial investments in personnel and research in the form of research funding. One question, to

which we will return in the analysis of the patent data, is the extent to which organisations involved in research networks on marine genetic resources in the ASEAN region are also involved in patent activity.

We can perform a similar analysis for the researchers whose collaborations establish these networks. Figure 4.11 visualises the network of authors with 20 or more publications involving marine organisms and uses a community detection algorithm to identify clusters of collaborating authors. We will return to this analysis in more detail in consideration of the patent data. However, for the moment we observe the prominence of Anchalee Tassanakajon at Chulalongkorn University in Thailand who has conducted extensive research on the tiger shrimp (*Penaeaus mondon*) and on the outer edge of the network Nobel Prize winner Sydney Brenner who has collaborated with Byrappa Venkatesh from the Institute for Molecular & Cell Biology in Singapore in ground breaking research on the puffer fish genome (*Fugu rubripes*) (Brenner et al., 1993).

We can gain a clearer picture of the relationship between the leading researchers in these clusters and the species involved in their research by placing the researchers and the species that are the target of their research in the same network graph. Figure 4.12 displays the top species, based on the number of records in green and the main researchers in pink.

In terms of the overall ranking based on publications Peter Ng Kee Lin is the leading researcher on marine species within the ASEAN region according to our data. However, in Figure 4.12 no prominent connections emerge to species. This reflects the fact that Professor Ng Kee Lin is a biologist and taxonomist who has worked on a wide range of species (notably freshwater and marine crabs) (Cai and Ng, 2002; Shih et al., 2007). As such, viewed from a species perspective his research is dispersed across a range of species and therefore not immediately visible.

In contrast Figure 4.12 reveals that Anchalee Tassanakajon at Chulalongkorn University in Thailand is a leading researcher working on *Peneaus mondon* with links to work on *Penaeus vannamei*, *Litopenaeus vannamei*, *Haliotis asinina* (a large sea snail known as ass's ear abalone) and the main *Vibrio* pathogens (Wongteerasupaya et al., 1995; Supungul et al., 2004; Kaewkascholkul et al., 2016). Professor Prasert Sobhon in the Department of Anatomy at Mahidol University shows a similar pattern but with an additional focus on *Macrobrachium rosenbergii* (the giant freshwater prawn), *Fasciola hepatica* (parasitic trematodes or liver flukes) and crabs (*Scylla olivacea*, *Scylla serrata*) (Meeratana et al., 2006; Duangprom et al., 2017; Preyavichyapugdee et al., 2008). Professor Boonsirm Withyachumnarnkul at the Department of Anatomy at Mahidol University also specialises in *Penaeus mondon* with a particular focus on selective breeding and disease screening using DNA based techniques (Wongteerasupaya et al., 1995) with recent work focusing on the use of a protein extract from red seaweed to prevent hepatopancreatic necrosis in shrimp (Boonsri et al., 2016). In practice all three researchers while leading distinct groups have collaborated on a number of publications in the past (Wongteerasupaya et al., 1995; Pongtippatee et al.,

Figure 4.11: Collaboration Networks for Researchers publishing on Marine Genetic Resources in the ASEAN region based on shared publications

penaeus monodon
macrobrachium rosenbergii
vibrio harveyi
vibrio parahaemolyticus
litopenaeus vannamei
penaeus vannamei
oreochromis niloticus
lates calcarifer
rhizophora apiculata
epinephelus coioides
fusarium oxysporum
Ng, Peter K L
perna viridis
ascaris lumbricoides
Sobhon, Prasert
Tassanakajon, Anchalee
Withyachumnarnkul, Boonsirm
Klinbunga, Sirawut
Panyim, Sakol
Chavisuthanadura, Parin
Longyant, Siwaporn
Van Minh, Chau
Van Kiem, Phan
NGUYEN, Hoai Nam
magnaporthe grisea
Cuong, Nguyen Xuan
Ho, Hon Young
NGUYEN, Phuong Thao
Todd, Peter Alan
Jones, Evan Benjamin Gareth
anopheles gambiae
Ching, Chang Ving
Chu, Ching Yi
Tan, Siew Guan
Arshad, Aziz
Upatham, ES
Yuzuki, Tatsushi
Yuzuki, Fatimah Md
Nakayama, Tohru
Yap, Chee Kong
Nishibuchi, Mitsuaki
Hyde, Kevin D
Wei, Chaoguang
Huang, Xiaohong
Lumyong, Saisamorn
Chaiyanan, Niraj
Chou, Chie Ming
Kimura, Takashi
Sorgeloos, Patrick
Rukayadi, Sombat
Rosa, Sybil Dra
Kuatrachua, Malesya
Vuddhakul, Varaporn
Berkjak, Suttawat
Hara, Reiko
Panzer, Raul W.
Bossier, Peter
Amparo, Pilo
Na-Nakorn, Uthairat
Sithigorngul, Paisarn
Sithigorngul, Pasham
Supiwong, Wuwarapith
Wu, Shaua
Huang, Yuchai
Hirowa, Iwao
Aid Ghafar, Mazian
Venkatesh, Byrappa
Srikrishnaraj, Kanaya
Bowman, Sydney
Senapin, Saengchan
Meeanwea, Piamsak
Rajal, Timothy W
Tanasitikul, Aduljaded
Phongdara, Amornrat
Wanichanon, Chalip
Bhassu, Subha
Hayashidani, Yasemasa
Anekpong, Jesu
Ariffin, Zainiyah
Ahmad, Ismail
Ramasamy, Kalai
Ng, Kim Lian
Ng, Kwee Siong
Ng, Kwee
Ng, Kwee Siong
Ng, Kwee Siong
Ng, Kwee Siong

2007; Wongteerasupaya et al., 1997).

This form of network analysis usefully displays the relationship between researchers and the species they are researching. However, the prominence of aquaculture focused research in the ASEAN research landscape can also, as we saw in the case of Professor Ng Kee Lin, disguise other areas of research.

Figure 4.11 revealed a research cluster focused around Chau Van Minh at the Vietnam Academy of Science and Technology (VAST) in Hanoi whose work, mainly conducted in collaboration with Phan Van Kiem (now at Chungham National University in South Korea), has included an explicit focus on pharmaceutical compounds from Marine Natural Products (Minh et al., 2017; Quang et al., 2011; Thao et al., 2015a,b). As we saw in Figure 4.8 this appears to reflect the underlying research investments by funding organisations in Vietnam. We can gain a clearer view of the genera involved in research directed towards chemistry, pharmacology and biotechnology by removing dominant genera such as Peneaus and restricting subject areas to those in chemistry, pharmacology and biotechnology. This data is displayed in Figure 4.13.

Figure 4.13: Pharmaceutical Focused Research for Marine Genetic Resources in the ASEAN region

The top genus emerging in this area are sea snails (gastropods) in the Conus

genera with a total of 37 publications in the ASEAN data. Top cited research on Conus includes collaborative research between the University of the Philippines and the University of Utah in the 1990s to identify a Novel Alpha Conotoxin and Omega Conotoxin from *Conus striatus* Venom, along with other research on a delta conotoxin from *Conus gloriamaris* (Ramilo et al., 1992; Shon et al., 1994). More recent work at the University of the Philippines with the University of Utah has involved characterisation of the complete mitochondrial genome of *Conus tribblei* and the structural features of conopeptide genes focusing on gene encoded peptide toxins (Barghi et al., 2015,?). In Vietnam, members of the Conus genus have also been a focus of research between the University of Nha Trang and CNRS in France concentrating on the identification of novel venom compounds including the use of novel proteomic approaches (Nguyen et al., 2013, 2014b,a,c)

A second important genus in research directed towards pharmaceuticals and similar products are members of the Channa genus or snakehead fish which includes a range of species found in brackish or freshwater. Research at the University Putra Malaysia has focused on comparative analysis of the protein content of Channa species with a focus on levels of DHA as an explanation for their use in traditional knowledge practices for reducing pain, inflammation and wound healing in Malaysia (Zuraini et al., 2006). More recent research by the University Putra Malaysia has focused on the antidepressant like effects of a lipid extract from *Channa striatus* and investigation of wound healing (Abdul_Shukkoor_2016; Baie and Sheikh, 2000; Isa et al., 2016).

As this brief summary of research in two genera suggests, while the marine research data is dominated by fisheries and aquaculture related research there is also an important strand of research in Chemistry and Biochemistry focusing on the medical properties of organisms and linking through to using traditional knowledge as a lead for research.

4.0.7 Conclusion

In this section we have mapped and explored the landscape of over 6000 publications on marine genetic resources for the ASEAN region involving 3,685 marine species. The global research network for research on ASEAN marine species has involved approximately 17,625 researchers from nearly 4,000 organisations distributed in 136 countries. As we have seen in this section research activity for marine species in the ASEAN region is growing in the majority of countries. Research activity ranges from basic taxonomic and ecological research to a major concentration of research effort in the aquaculture sector and important concentrations of research in marine natural products directed towards biotechnology and pharmaceuticals. We have also seen that funding for marine research in the ASEAN region is critically dependent on national research funding agencies and an important network of international funding agencies from Japan, China, the United States and Europe who support collaborative research with researchers

within and outside the region. In the next section we turn to analysis of the available data on patent activity involving marine species in the ASEAN region with a particular focus on identifying patent activity by researchers from the region.

Chapter 5

Patent Activity for Marine Genetic Resources in the ASEAN Region

In this section we focus on patent activity involving researchers and marine genetic resources in the ASEAN region. Our aim is to understand the nature of patent activity exhibited by researchers from within the region working on marine genetic resources and to situate their research in the wider context of research and development for marine genetic resources.

We begin the section with a brief overview of patent activity in the region and consideration of the challenges involved in examining patent activity in ASEAN countries. We then move into analysis of patent activity that includes a marine species originating from or making reference to an ASEAN country.

5.0.1 Patent Overview

There are two primary sources for global patent data for statistical purposes. The first of these is the European Patent Office World Patent Statistical Database (known as PATSTAT) and the second are commercial databases, such as Derwent Innovation from Clarivate Analytics. For statistical research PATSAT is preferred as the international baseline. However, our research exposed significant problems with the use of PATSTAT in the case of ASEAN countries.

We initiated research with PATSTAT (Autumn 2016 edition) by identifying:

a) patent applications where an ASEAN country was the application authority (210,972 records). This data captures priority filings from the ASEAN region even where they are not published or published outside the region.

b) patent applications where an ASEAN country is the publication authority (173,461 records).
c) patent applications anywhere in the world where an applicant or inventor is listed from an ASEAN country (109,744 records).

These documents may contain duplicates and were deduplicated to 299,830 applications. This data is presented in the left panel of Figure 5.1.

It is immediately clear from Figure 5.1 that the data is irregular across countries. For Indonesia, PATSTAT data is limited to information from the late 1990s and early 2000s. The Philippines displays a pattern of an early peak in the 1990s followed by a long trough until the late 2000s while information for Thailand and Vietnam is very limited and is absent for Brunei, Cambodia and Laos. At first sight the data for Malaysia and Singapore appears to be more consistent however, the presence of major peaks or troughs is typically a sign of missing or incomplete data.

To test levels of data completeness, the same query was performed using Derwent Innovation from Clarivate Analytics (formerly Thomson Innovation). Derwent Innovation includes the full text collections for the majority of ASEAN countries (Malaysia, Singapore, Vietnam, Thailand and the Philippines). Datasets were downloaded and deduplicated to 461,380 distinct patent applications. Trends based on Derwent Innovation data are displayed in the right hand panel of Figure 5.1. This approach yielded an additional 162,000 applications and had a dramatic impact on the availability of data from ASEAN countries. Data for Singapore radically improves for recent years with improvements in data for Thailand on a more modest level. Data for Vietnam, again for recent years, also improves markedly.

Comparison of the data between PATSTAT and Derwent Innovation exposes two problems. The first of these in the case of PATSTAT is the problem of data availability. Put simply, the ASEAN collections are effectively not present in PATSTAT data (Autumn 2016). The second is the problem of data completeness. While Derwent Innovation radically improves coverage, the presence of peaks and troughs also suggests a lack of data completeness. Presumably, this reflects the lack of availability of patent documents in electronic form for earlier years. It is also likely that for later years there are lag times in the availability of electronic records.

The practical consequence of these issues is that data for ASEAN countries is presently incomplete. We are therefore obliged to work within the constraints of the available data. However, we would note that the availability and completeness of the patent collections for the ASEAN region will also affect the ability of ASEAN countries to fully understand and assess the economic significance of patent activity for their country and region.

Figure 5.1: PATSTAT and Derwent Innovation coverage for ASEAN countries

5.0.2 Search Strategy

The aim of our search strategy was to capture two areas of patent activity:

1. Patent activity for marine genetic resources originating from within the region
2. Patent activity for marine genetic resources that could involve marine genetic resources collected from the region.

This aim required us to examine activity from within the region and wider activity. To achieve this we used a three part methodology.

a) Text mining the titles, abstracts and claims of Clarivate records from the ASEAN collection for binomial species names from the World Register of Marine Species (WoRMS) in VantagePoint. This identified an initial 730 first filings for 302 marine species.

b) Combining the data with existing data on marine patent activity within the ABSPAT index linked to ASEAN countries. The ABSPAT index consists of 6.5 million sentences from patent documents from the full texts of the EPO, USPTO and PCT collections until 2013 that contain a country name and a separate table containing 21.4 million sentences containing a species names. The ASEAN country names were identified in the country table and then cross referenced with the species table yielding 15,376 documents containing a species name and an ASEAN country name. This data was deduplicated to 6,521 first filings. Text mining of this set for marine species names revealed 2,033 first filings containing an ASEAN country name and a marine species.

c) A keyword based search strategy. We aimed to capture additional records outside the Clarivate search of ASEAN jurisdictions and the historic ABSPAT data for the US, EP and WO. As the WoRMS data consists of over 390,000 marine species names a search strategy was required that would capture those names. This strategy was advanced by developing a query that captured species names without directly using a species name. Experimentation with the texts of the 6,521 first filings for the ASEAN region mentioned above from ABSPAT revealed that the following search strategy captured 98% of documents in the dataset.

   "species" OR "genus" OR "family" OR "order" OR "phylum" OR "class" OR "kingdom" OR "tribe" OR "DNA" OR "nucleic" OR "nucleotide" OR "amino" OR "polypeptide" OR "sequence" OR "SEQ ID" OR "protein" OR "proteins" OR "peptides" OR "peptide" OR "enzyme" OR "enzymes" OR "plant" OR "plants" OR "animal" OR "animals" OR "mammal" OR "mammals" OR "mammalian" OR "bacteria" OR "protozoa" OR "virus" OR "viruses" OR "fungi" OR "animalia" OR "archaea" OR "chromista" OR "chromist" OR "chromists" OR "protista" OR "protist" OR "protists" OR "plantae" OR "eukaryotes" OR "eukaryotes" OR "eukaryote" OR

> "prokarya" OR "prokaryote" OR "prokaryotes" OR "microorganism" OR "microorganisms" OR "organism" OR "organisms" OR "cell" OR "cells" OR "gene" OR "genes" OR "genetic" OR "viral" OR "biological" OR "biology" OR "strain" or "strains" or "variety" or "varieties"

Beyond these terms the addition of new terms produced diminishing returns. If used across the full texts of the Derwent Innovation collection, the above search query produced 30 million publications. However, patent applicants typically include references to species and related terms in the Title, Abstract or Claims of documents. As our aim was to capture documents for marine species that may have originated from the region we therefore adopted a strategy of:

a) searching for ASEAN country names in the description section of the patent documents.
b) searching the title, abstracts and claims for the species related terms

The search query was run in two sets (1990-2009 and 2010-2017) focusing on the US, EP, JP and WO and the ASEAN jurisdictions.

> (PY>=(1990) AND PY<=(2009)) AND DSC=("brunei" or "cambodia" or "indonesia" or "laos" or "lao" or "malaysia" or "philippines" or "myanmar" or "burma" or "singapore" or "thailand" or "vietnam") AND CTB=("species" OR "genus" OR "family" OR "order" OR "phylum" OR "class" OR "kingdom" OR "tribe" OR "DNA" OR "nucleic" OR "nucleotide" OR "amino" OR "polypeptide" OR "sequence" OR "SEQ ID" OR "protein" OR "proteins" OR "peptides" OR "peptide" OR "enzyme" OR "enzymes" OR "plant" OR "plants" OR "animal" OR "animals" OR "mammal" OR "mammals" OR "mammalian" OR "bacteria" OR "protozoa" OR "virus" OR "viruses" OR "fungi" OR "animalia" OR "archaea" OR "chromista" OR "chromist" OR "chromists" OR "protista" OR "protist" OR "protists" OR "plantae" OR "eukaryotes" OR "eukaryotes" OR "eukaryote" OR "prokarya" OR "prokaryote" OR "prokaryotes" OR "microorganism" OR "microorganisms" OR "organism" OR "organisms" OR "cell" OR "cells" OR "gene" OR "genes" OR "genetic" OR "viral" OR "biological" OR "biology" OR "strain" or "strains" or "variety" or "varieties" or "common name");

This dataset consisted of a raw 73,164 documents that were deduplicated to the first application numbers to 38,120 first filings. The available full texts for these documents were downloaded and text mined for marine species names using a tidy text mining approach (Robinson and Silge, 2018).

In total, this approach yielded 5,742 applications based in 3,587 first filings either originating from the ASEAN region or referencing an ASEAN country within the text and containing a marine species. These documents were text mined by document section (title, abstract, description and claims) in R using a tidy text mining approach as the basis for the analysis in this section.

An important constraint with this data is that while the documents contain a reference both to a marine species and to an ASEAN country, the reference to the ASEAN country may occur for reasons that are not related to the origin of the marine species. For example, a country may be referenced as the source of a commercial supplier of material. As such, while it is a precondition of the data that it either originate from an ASEAN country and contain a marine species or reference an ASEAN species and a marine species, there is a fuzzy element to the outlines of this data.

5.0.3 An Overview of Filing Trends

Figure 5.2 presents an overview of the first filings of patent applications involving marine genetic resources linked to the ASEAN region. Trends in first filings refer to the original filing of an application (anywhere in the world) and displays a characteristic *data cliff* the closer we move towards the present day. This reflects the lag time between the first filing of a patent application and its publication (typically 24 months after filing).

The panel on first filings by region aggregates the first filings displayed by country using the United Nations regional division and reveals that Eastern Asia (Japan, China and South Korea) account for the majority of first filings followed by North America (dominated by filings in the United States). Patent instruments (notably the European Patent Convention through the European Patent Office) and the Patent Cooperation Treaty rank third and will reflect an EP or PCT first filing strategy on the part of applicants.[1]

Within the ASEAN region filings are evenly spread between Indonesia, Singapore and Malaysia, with a lower level of first filings from Vietnam, the Philippines and Thailand. As we will see below, in practice activity from researchers in ASEAN countries is higher than is suggested by reduction to the earliest filings.

5.0.4 Patent Family Trends

The first filings of patent applications lead to follow on applications and grants (family members) within the country of filing and, using international instruments, in other countries. Patent Family analysis allows us to identify the markets where applicants are seeking protection. Figure 5.3 displays follow on filings around the world by individual country and summarises the data by major United Nations region. The data on family members has been adjusted to remove search reports from the data for the European Patent Office and the Patent Cooperation Treaty to avoid counting purely administrative documents.

[1] United Nations Statistical Division Standard country or area codes for statistical use (M49)

Figure 5.2: Trends in First Filings for Marine Species linked to the ASEAN region

Figure 5.3: Overview of Patent Family Members world wide for Marine Species linked to the ASEAN region

Figure 5.3 demonstrates that demand for patent rights is highest within North America followed by Eastern Asia (China, South Korea and Japan) with regional and international patent instruments playing an important role in enabling the pursuit of protection in multiple markets. The ASEAN region itself is not a major focus of demand for patent rights based on the available data.

Figure 5.4 displays the available data on trends in demand for patent rights, broken down by the main regions for ease of visibility. In *Figure 4.5* a major spike is immediately visible for North America that starts at the end of 2001 and peaks in 2003. This is an artefact from the transition in the United States from the publication of patent grants prior to 2001 to the publication of both applications and grants after 2001 leading to an apparent, rather than real, surge in activity.

Figure 5.4: Trends in Family Publications by Major Region for Marine Species linked to the ASEAN region

We can also observe that activity for the ASEAN region in the lower panel of Figure 5.4 is at a significantly lower level, across the period 2000-2017 and peaking with 100 records in 2015. As this suggests, demand for patent rights involving marine genetic resources that can be linked to the ASEAN region is best classified as emergent.

5.0.5 Top Species

A single patent document may contain a range of species. Figure 5.5 presents an overview of the top species by counts of applications and species counts.

In total 3,114 species from the World Register of Marine Species appeared in the patent documents. We have excluded species where they were classified as terrestrial, or where environment information was not available. We have also excluded Fungi from the display of species as they are not normally sourced from a marine environment (see below).

Figure 5.5 illustrates that a number of the top species in the overall marine data are plants. This also illustrates some of the challenges involved in identifying marine species that cross environments. *Apium graveolens* is better known as Celery and is included within the marine data because it was originally a marsh plant that can grow in salt water conditions and features in patent activity for herbicide resistance (JP2013046624A). *Phleum pratense* is a widespread invasive grass that can be found in brackish conditions and appears in patent activity for control of plant pathogens (IN200800137P1). *Phragmites australis* is a perennial wetland grass with patent claims that focus on the use of the species, among others, as feedstock in methods for producing cellulose pulp (WO2017178849A1). *Ammophila arenaria* is commonly known as beach grass and typically appears as a passing reference in the description of patent activity focusing on genetic engineering to increase yields in a wide range of plants, rather than as the focus of an invention (EP2316956A2).

As noted in the discussion of the scientific landscape, fungi such as *Fusarium oxysporum*, *Aureobasidium pullans*, *Fusarium solani*, *Aspergillus terreus* and *Alternaria alternata* among other fungi in the data are extremely widespread in soils and other habitats and patent activity is not typically directly linked with these organisms from a marine environment. We have therefore excluded fungi from the display of species in Figure 5.5 while noting that marine fungi are an increasing focus of interest in the wider scientific literature (see for example, Kim and Li, 2012). It is therefore important not to second guess categories of organism that are of interest in the marine environment.

Figure 5.6 presents the data above in terms of the technology areas that are the focus of activity by the number of species and the number of applications. The definition of technology areas is based on the use of Subclasses from the International Patent Classification. The International Patent Classification is used by patent offices worldwide to classify the technical content of patent documents and consists of alphanumeric codes. Because the descriptions associated with a code may be very long the Subclasses have been edited to short versions for ease of presentation.

Figure 5.6 reveals that species and applications across the dataset are concentrated in the fields of biotechnology and pharmaceuticals. However, as we will see in more detail below fields such as aquaculture are also prevalent but dis-

Figure 5.5: Summary Marine Species linked to ASEAN countries in Patent Data

Figure 5.6: Summary of Marine Species linked to ASEAN countries in Patent Data

persed across the fields of Animal Husbandry (A01K), Animal Foods (A23K) and Water/Waste Water/Sewage Treatment (C02F).

5.0.6 ASEAN Researchers as Inventors

In the previous section we examined the research activities of the approximately 17,625 researchers involved in research on marine species linked to the ASEAN region. We now focus in on the analysis of those researchers within the scientific literature who are also inventors.

In order to identify researchers who are also inventors we combined the names of the 17,625 researchers from the scientific literature together with the inventor name field containing 9,382 cleaned names. Name matches and close name matches were then examined against the criteria of the appearance of co-authors who are also inventors, author affiliation and applicant name matches and matches on species names between the scientific and patent literature linked to an author name. Where one or more of these criteria were met the author was classified as an author inventor.

In total we identified 290 authors who are also inventors in patent applications involving marine genetic resources. Taken together author inventors accounted for 369 applications that referenced 446 marine species.

Figure 5.7 displays the rankings for species appearing in patent documents based on counts of applications. The smaller panels display details for certain kingdoms that would otherwise be hidden.

In considering Figure 5.7 we can readily see that animal species are dominant with shrimp genera (Penaeus) in the aquaculture sector dominating the rankings with *Paralichthys olivaceus* or Japanese halibut also appearing high in these rankings. Bacteria in the Vibrio genus, again reflecting the aquaculture sector, dominate the rankings for bacteria with *Bacillus thermus*, a high temperature and alkaline tolerant bacterium, among others such as *Geobacillus kaustophilus* (a deep sea bacterium reportedly isolated from the Mariana Trench)[2] and *Photobacterium damsela* (associated with Pastereullosis in fish) appearing in a list of 35 bacteria in the patent documents.

In the case of plants, they typically appear in the description section of patent documents within the dataset rather than as the focus of the invention. *Sporobolus virginicus* is a shoreline couch grass, *Bruguiera gymnorhiza* is the black mangrove, *Hippomane mancinella* is a coastal tree that is often found in association with mangroves (WO2013137822A1), *Kandelia candel* is a mangrove native to South East Asia and *Manilkara zapota* is a widely grown coastal fruit tree. *Phleum pratense* is a widely distributed coastal grass, and *Rumex crispus*, or yellow dock, is a widespread plant with a coastal sub species.

[2] https://microbewiki.kenyon.edu/index.php/Geobacillus_kaustophilus

Figure 5.7: Summary of Marine Species linked to ASEAN countries in Patent Data

Figure 5.8 displays a summary for researchers as inventors based on counts of the number of patent applications associated with a researcher.

Figure 5.8: A summary of author-inventors by number of applications, organisations and technology areas

We can clearly see in Figure 5.8 that while overall applications are low, there are clear leaders with organisations representing a mixture of universities, government research organisations and private companies across a number of countries including the United States, China and Japan.

In the analysis of the scientific literature we approached the data in terms of networks of authors and organisations. We will adopt the same approach for the analysis of the patent data. Note that collaboration networks in patent data, notably between organisations, are typically sparser than in the case of the scientific literature.

Figure 5.9 displays the network clusters for author inventors where node size is based on the number of applications associated with a researcher. Figure 5.10 displays the network of organisations (applicants) associated with the applications.

Figure 5.9 reveals clear clusters of researchers who also appear as inventors on patent applications involving marine species. As we will see below, in prac-

Figure 5.9: Author-Inventor Networks for Marine Genetic Resources in the ASEAN Region

Figure 5.10: Author-Inventor Applicant Networks for Marine Genetic Resources in the ASEAN Region

tice the data for researchers reveals three basic sets of circumstances where researchers submit patent applications.

a) Cases where a researcher has a pre-existing patent portfolio (that may be in a different subject area such as plant biotechnology) who then joins a research collaboration in the new area;
b) Cases where researchers jointly submit patent applications arising from their joint research;
c) Cases where members of a research group go on to form a sub-cluster and file patent applications arising from their research;

In the case of data on applicants we can see that as expected, applicants are typically sole applicants. However, we can see cases of collaboration in patent filings around the National University of Singapore, the University of Utah and the University of Tokyo. In other cases such as Guangdong Ocean University in China, a significant number of filings are observed as a sole applicant.

For ease of exploration of the patent data we will approach the analysis using the clusters of author-inventors starting with the larger clusters and then exploring the patent data based on the number of citations received as a measure of impact and areas of research. In approaching the data note that in some cases patent activity involves a researcher outside the region who has collaborated with a researcher within the ASEAN region.

1. The most prominent and top cited cluster in the inventor network is represented by Baldomera Olivera who is a graduate of the University of the Philippines and Distinguished Professor of Biology at the University of Utah. He pioneered research on cone snail toxins (conotoxins).[3] His work on cone snails appeared on the front cover of Science magazine in 1990.[4] Research on *Conus magus* by his team led to the development of the severe pain analgesic Ziconotide (SNX-111; Prialt) that was approved for use by the US Food and Drug Administration in 2004 under the trade name Prialt and subsequently by the European Commission in 2005.[5] Professor Olivera's research proved to be a major spur to research on cone snails and members of the cluster, notably Lourdes Cruz (below) have gone on to further research in this area.

2. The second major cluster is represented by Cheng-Bo Sun at Guangdong Ocean University in China who has conducted research on the *Penaeus mondon* immune system. The research has been conducted in collaboration with JA Benzie who lists collaborations with the University of Cork in Ireland and WorldFish in Penang, Malaysia. Cheng Bo Sun submitted two sets of filings in 2015. The first set, filed on the 9th of June 2015, consists of 8 applications and includes methods for cultivating parent fish in waste water from prawn cultivation (CN104839079A), a mass

[3] https://www.ncbi.nlm.nih.gov/pubmed?term=Olivera%20BM
[4] Science magazine
[5] Wikipedia entry for Ziconotide

scale outdoor cultivation method and facility (CN104839070A), and a low soil prawn pond (CN104938381B). A specific focus of these filings is the cultivation of *Sillago sihama* (northern whiting fish). The second set, filed on the 12th of December 2015, focuses on a method for controlling white spot syndrome by polyculture of sea bass and *Marsupenaeus japonicus* (CN105494189A), a method for controlling bacterial diseases in blue fish and Japanese prawn breeding (CN105409848A), a method for cultivating mixed *Epinephelus oanceolutus* (Giant grouper) and *Marsupenaeus japonicas*(Kuruma prawn) to control white spot syndrome (CN105309360A) and a method for controlling prawn liver pancreas gland necrosis disease by mix breeding of desmodium and Japanese capsule prawn (CN105532522A).

3. The third major cluster (consisting of 10 applications) is Dustin John Loy associated with Harris Vaccines, and associated with researchers at the University of Iowa, who has published research on therapeutic antiviral treatments against myonecrosis virus in *Litopenaeus vannamei* based on the spread of the virus from Brazil to Indonesia (Loy et al., 2012, 2013). A set of filings in 2011 and 2012 in Brazil, China, the European Patent Office and the United States include PCT filings focus on methods for rapidly producing vaccines for protecting an animal (in general) from a pathogenic micro-organism (VN45743A, US2013122025A1, US2013064839A1, US2012107355A1, WO2013066665A1, WO2012058072A1, US2012108649A1, US20130045223A1, WO2012058073A2, WO2013103434A1).

4. Justinus M Vlak (known as Just Vlak) is at the University of Wageningen and has collaborated with NX Tuyen, who is affiliated with the University of Wageningen and the Institute for Aquaculture Research in Ho Chi Minh City, Vietnam (see Tuyen et al., 2014). Justinus Vlak had previously filed for patents in 1999 and 2000 including for Proteins derived from White Spot Syndrome Virus (WO2001009340A1), antigenic proteins of shrimp white spot virus (WO2002022664A2), and a White Spot Syndrome Virus Vaccine (WO2003000900A1) with Akzo Nobel NV and Intervet Iinternational BV.

5. Husband and wife research team Professors Hu Bow and Ding Jeak Ling at the National University of Singapore (NUS) received the 2012 Outstanding NUS Innovator Award for what was described as the one of the NUS's most successful commercialised technologies.[6] The focus of the technology is a cloned Horseshoe Crab *Carcinoscropius rotundicauda* recombinant cDNA Factor C (rFC) that can be used to remove endotoxins from a sample and subsequently for use in endotoxin assays (WO1999015676A1, US6645724B1, US5716834A). Filings have also been made for recombinant polypeptides for endotoxin biosensors and removal (US2004175388A1) and treatment of bacterial infections (US2008085865A1). The University reports that the recombinant Factor C was licensed to Lonza. Work on

[6]Factor C: Saving Humans and Horseshoe Crabs

Sushi peptide technology was licensed to BioDTech.

6. Dr. Serena Teo is a researcher at the St. John's Island National Marine Laboratory of the National University of Singapore. Her research has focused on barnacles (*Balanus amphitrite*) associated with surface fouling or biofouling (Phang et al., 2009; Guo et al., 2011; Petrone et al., 2013). Patent filings focus on an organic antifouling compound that is an alternative to existing technologies involving copper. The application claims that the invention provides "cheap, easy to prepare additives that do not contain metals and therefore have reduced toxicity in marine environment"(SG166436A1, EP2294144B1, WO2009139729A1). A second filing focuses on functionalised anti-fouling compounds as environmentally benign anti-fouling compounds that can be applied in seawater conditions including cooling towers and desalination plants (SG183158B, US2012301423A1). A third document focuses on biocidal and/or biostatic treatments for biofilms and biofouling (US2006110456A1). Marine biofouling is a major cost associated with marine transport and infrastructure (Callow and Callow, 2011). Dr. Teo's work is an example of an effort to promote green technology to address the environmental impacts of metal and other toxic biofouling treatments in aquaculture and wider maritime applications (Callow and Callow, 2011; Floerl et al., 2016)

7. Luc Grisez has conducted research on Scale Drop Virus in the Asian seabass *Lates calcarifer* that began to affect aquaculture in South East Asia from 1992 onwards. The research involved near complete genome sequencing to identify the source virus (a Megalocytivirus genus of the Iridoviridae family) and the development of a vaccine (de Groof et al., 2015). Patent activity, which pre-dates this published research, includes an immune stimulant for use in a vaccine against the causative viruses for Big Belly Syndrome in fish (WO2008074783A1, CN1904034B) and a vaccine against Rickettsia-like organisms (WO2007138036A1). The recent publication on Scale Drop Disease was immediately preceded by patent filings on the isolated virus and derivatives (WO2014191445A1, VN46347A).

8. Michelle Grilley at Utah State University has worked in collaboration with colleagues at the University of the Philippines on conus peptides (and forms part of the wider group above) demonstrated that the contryphan family of peptides is widely distributed in venoms of the fish-hunting cone snails. (JACOBSEN et al., 2009, originally published 1998). Patent filings focused on the contryphan peptides (US6153738A, WO1999033865A1) with later filings focusing on kappaA conopeptides for use in combating multiple sclerosis and similar disorders (WO2000020018A1, US2003181368A1, US2006014673A1).

9. Professor Tragoonrung Somvong at Kasetsart Univ is a plant genomics specialist who was a member of the International Rice Genome Sequencing Project for Thailand and presently director of BIOTEC in Thailand. His research has included collaboration in identifying microsatellite mark-

ers in *Penaeus mondon* (Wuthisuthimethavee et al., 2003). Professor Somvong's patent activity reflects his focus on plant biotechnology in the form of filings on transgenic plants with increased grain aroma to enhance flavour (JP2011004752A, IN200600050I1, US2006168679A1, US2009170202A1, EP1683869A2)

10. Shao-wu Yin has worked with colleagues at Hainan University and Nanjing Normal University in China on the isolation of microsatellite marker loci in the marble goby fish *Oxyeleotris marmoratus*. *Oxyeleotris marmoratus* is found in freshwater and brackish waters in the Mekong River and all ASEAN countries plus China.[7] The species is commercially important both in terms of fisheries, aquaculture and the aquarium trade. Patent activity by this team from China focuses on microsatellite markers to identify *Oxyeleotris marmoratus* and *Odontobutis potamophila* fry in aquaculture (CN102653795A and CN102134586A), and a fish hybridization breeding method for river sand bostrichthys and oxyeleotris (CN103651219A).

11. Professor Mahiran Basri at the Department of Chemistry at the Universiti Putra Malaysia (UPM) has mainly focused on enzymes. Her research with colleagues at UPM and Tokai University in Japan involving marine species focused on the nutraceutical potential of the commercially important edible jellyfish species *Acromitus hardenbergi*, *Rhopilema hispidum* and *Rhopilema esculentum* (Khong et al., 2016). Other research has focused on a novel *Geobacillus zalihae* thermophylic lipolytic bacterium that was isolated from the effluent of a palm oil mill in Malaysia (Rahman et al., 2007). The research highlights that Geobacillus species are found in hydrothermal vents, oilfields, soils and compost from hay. Their research focused on the identification of the new strain Geobacillus zalihae sp. nov. TIT (= DSM 18318(T); NBRC 101842(T)) (Khong et al., 2016). Patent activity arising from this research includes a Lipase from a biologically pure Geobacillus strain for use in food processing to flavour dairy products, as a digestive in medical use or to improve fats and oils (US2006024789A1, JP2006042820A) and a separate application for lipase gene from a biologically pure culture of *Bacillus sphaericus* strain 205 isolated from soil (US20050260737A1). A European patent grant is also part of the portfolio for a novel thermostable lipase from Geobacillus sp. strain ARM and A. thermoaerophilus strain AFNA for use in the food industry, surfactants, processing oil, detergents, pesticides, and the leather industry (EP2450458B1).

12. Guang-Hsiung Kou while at the Institute of Zoology at the National Taiwan University in collaboration with researchers at the National University of Singapore and Tokyo University of Marine Science and Technology conducted research on the comparative genetics of *Panaeus mondon* in-

[7] Allen, D.J. 2011. Oxyeleotris marmorata. The IUCN Red List of Threatened Species 2011: e.T181009A7657958. http://dx.doi.org/10.2305/IUCN.UK.2011-1.RLTS.T181009A7657958.en

fected with White Spot Syndrome Virus. The research focused on identifying differences in gene expression in infected and non-infected shrimps using DNA sequencing to create Expressed Sequence Tag libraries (Leu et al., 2007). Later research was also performed on White Spot Syndrome Virus (WSSV) in shrimp broodstock in collaboration with colleagues from other universities in Taiwan and Jie-Cheng Chuang at the Uni President Vietnam Co company (Chang et al., 2012). Guang-Hsiung Kou's patent activity in this area dates to the late 1990s and includes DNA primers and probes to screen for the virus WSBV (baculovirus associated with white spot syndrome) in shrimps (US5824535A, EP785255A2, US6190862B1 originally filed in 1996) and a later 2005 filing on promoter sequences for WSSV early genes and their use in recombinant DNA techniques (US7429480B2).

13. Prakash Kumar Pallathadka is a Professor of Biological Sciences at the National University of Singapore with research focusing on plant sciences. His research has focused on proteomics in connection with the mangrove tree *Avicennia officinalis* to understand salt tolerance in mangroves. This has led to the identification of Expressed Sequence Tags (ESTs) linked to salt stress tolerance and additional work on the role of root hydrophobic barriers in salt exclusion (Krishnamurthy et al., 2014; Jyothi-Prakash et al., 2014; KRISHNAMURTHY et al., 2014). Patent activity is not directly linked to this research but includes filings from 2007 on a putative cytokinin receptor for modulating the expression of traits in plants (EP2124522B1). In a separate area of research a family of filings is observed on a novel snake toxin (originally filed in 2004 and published as US2009285825A1, SG132985A1 and WO2006068625A1).

14. Lo Chu Fang is affiliated with the Institute of Zoology, National Taiwan University and the Institute of Bioinformatics and Biosignal Transduction at National Cheng Kung University in Taiwan. She is presently a Professor in the Department of Biotechnology and Bioindustry Sciences at the National Cheng Kung University. A series of research articles have focused on viral infection in *Penaeus mondon* and related commercially important species with a notable focus on proteomics (Suraprasit et al., 2014; Rattanarojpong et al., 2007; Gonnet et al., 2008). Patent activity includes a 1996 filing for the identification and detection of WSBV virus (US5824535A, US6190862B1) a 2005 filing for Promoter sequences for WSSV early genes (US7429480B2) and a 2006 filings for a highly expressed WSSV peptide (US20070269453A1).

15. Siew-Moi Phang is the Director of the Institute of Ocean and Earth Sciences at the University of Malaya and her research focuses on algal biotechnology. Her research includes work on the Kappaphycus Doty and Eucheuma J. Agardh genera of algae as sources of commercially important carrageenan in Malaysia (Tan et al., 2012). Patent activity has involved a 2010 filing (MY2010PI5261A) introducing a vector into

algae that express modified V28 peptides that when ingested elicit an immune response to WSSV virus among shrimps in the Penaeida family (WO2012064181A1, US9475844B2) and a related filing for a vaccine against White Spot Syndrome that can be added to shrimp feed (US20140170181A1, WO2012064180A1).

16. Raymond S Norton is Professor of Medicinal Chemistry at Monash University in Australia and has conducted research in collaboration with Nonlawat Boonyalai at Kasetsart University in Thailand along with colleagues from China and elsewhere in Australia focusing on the cone snail *Conus imperialis* (Ye et al., 2012). Earlier research by Norton focusing on the sea anemone *Stichodactyla helianthus* led to a filing in 1996 on ShK toxin compositions from the sea anemone (US6077680A, WO1998023639A2). The granted patent US6077680A has attracted 87 citations.

17. Ocky Karna Radjasa at Diponegoro University in Indonesia has been active in research on the chemical properties of marine invertebrates, notably corals and their bacterial symbionts, and extending to recent work on the role of bacteria in diseases in seaweeds (Ayuningrum et al., 2017; Trianto et al., 2017; Syafitri et al., 2017). Patent activity arising from this research includes a 2013 filing in Indonesia involving a *Virgibacillus salarius* strain for producing d-carotene as an alternative bio-pigment health product (ID201403020A). An earlier filing in 1996 focused on a wood preserving composition derived from the soft coral Sinularia sp. that would inhibit biofilm forming and wood boring organisms (WO1997034747A1).

18. Ratih Pangestut at the Indonesian Institute of Science and Se-Kwon Kim at Pukyong National University in South Korea have conducted research on the highly valued and widely traded sea horse *Hippocampus trimaculatus* (Pangestuti and Kim, 2015). The scale of the trade in the sea horse in dried form for traditional medicines and in live form for the aquarium trade, along with the impact of shrimp and trawl fisheries on habitats and capture as bycatch is such that the IUCN Red List categorises the species as vulnerable [8]. Research by Pangestus and Kim has focused on the isolation of bioactive peptides targeting Alzheimers disease (Pangestuti and Kim, 2015). This is reflected in a 2012 patent filing focuses on a composition containing a bioactive peptide for preventing or treating neurodegenerative disorders (KR2014042148A, US20140094414A1).

19. Yannick Gueguen is a researcher at IFREMER in France who has conducted extensive research on marine organisms in the ASEAN and Pacific region. Research in collaboration with Anchalee Tassanakajon at Chulalongkorn University has focused on a recombinant expression and anti-lipopolysaccharide factor (ALF) from the black tiger shrimp Penaeus monodon (SOMBOONWIWAT et al., 2005). Earlier research by Yannick

[8] Wiswedel, S. 2015. Hippocampus trimaculatus. The IUCN Red List of Threatened Species 2015: e.T10087A17252219. http://dx.doi.org/10.2305/IUCN.UK.2015-2.RLTS.T10087A17252219.en. Downloaded on 24 March 2018.

Gueguen on the genome sequence of *Pyrococcus abyssi* led to a 1999 filing on genome sequences involved in replication with potential industrial use (FR19995034A, WO2000FR1065A, EP1196583A2).

20. Chau Van Minh and Phan Van Kiem from Vietnam have conducted extensive research on the bioactive properties of a range of marine organisms including sea urchins, marine sponges, corals and starfish (Thao et al., 2015a,b; Kiem et al., 2017; Ngoc et al., 2017; Vien et al., 2016). The available patent data suggests that patent filings have not been a substantive focus of attention, although this may be affected by the availability of information from the national collection in English. However, Chau Van Minh is listed as an inventor on a 2015 filing in Vietnam for an antimicrobial compound from the marine actinobacteria Nocardiopsis sp.G057 (VN10017267B). Phan Van Kiem is listed in a separate filing in Vietnam from 2011 for a pyrrole oligoglycoside compound extracted from the starfish *Asterina batheri* collected from Vietnam's seas that has strong anti-inflammatory activity.

5.0.7 Conclusion

In this section we have focused on providing an overview of patent activity involving marine genetic resources in the ASEAN region. As we have seen patent activity can be described as emergent. We have concentrated our analysis on the emerging clusters of researchers from within the region, or with links to the region, who have been involved in filing patent applications. Two significant success stories, from the Philippines in the case of research leading to the drug Ziconitide from cone snails, and from Singapore in the case of recombinant Factor C from the Horseshoe Crab were identified. Looking beyond these examples of successful commercialisation of research we have observed patent activity in relation to aquaculture, nutraceuticals, industrial biotechnology, pharmaceuticals and vaccines, and marine biofouling. It remains unclear whether these other emerging areas of patent filings have led to successful commercial products and processes. However, the researchers who have pursued patent protection also represent a pool of people who have developed experience with the patent system as they seek to commercialise their work. That pool is presently small but encompasses researchers from Indonesia, Malaysia, the Philippines, Singapore, Thailand, Vietnam and other countries, including the United States and China, who could serve as a resource for consultation on appropriate strategies for research groups interested in the practical and commercial dissemination of the results of their work in the ASEAN region.

Chapter 6

Annex 1: Species Profiles

In this section we provide additional reference material for top species covered in this report. Links to patent collections in the Lens database are provided to facilitate exploration of wider patent activity for the species.

6.1 *Clarias macrocephalus*

- **Species name:** *Clarias macrocephalus*
- **Kingdom:** Animalia

- **Phylum:** Chordata GBIF

Brief Description of the Species:
Clarias macrocephalus lives in lowland wetlands and rivers - occurs in shallow, open water including sluggish flowing canals and flooded fields of the Mekong, and is capable of lying buried in mud for lengthy period if ponds and lakes evaporate during dry seasons. *Clarias macrocephalus* can move out of the water using its extended fins (http://eol.org/pages/211498/overview). Spawns in small streams between May and October (http://www.fao.org/docrep/field/003/ac231e/AC231E03.htm).

There are 5 catfish species found in Thailand with two of them being eaten by people: *C.macrocephalus* and *C. batrachus*. *C.macrocephalus* is considered to be the tastiest of the 2 by Thai people but is the more difficult of the two to cultivate (http://www.fao.org/docrep/field/003/ac231e/AC231E03.htm). Presently a hybrid created using *C.macrocephalus* females and males of the African *C. gariepinus* are farmed in Thailand on a large-scale coming 1st in terms of farmed freshwater fish with a production of 86 475 tonnes or 30 percent of total production. It has recently been suggested production of the hybrid catfish is decreasing which may be due to the quality of the male African catfish which was intro-

duced into Thailand a long time ago.[National Aquaculture Sector Overview Thailand]](National Aquaculture Sector Overview Thailand).

C.macrocephalus is listed as near threatened by the IUCN - populations have been impacted by the loss of suitable wetland habitat through drainage and clearance for urbanisation and agriculture, as well as exploitation for aquaculture. In addition escaped hybrids from cultivation, are causing some concern.IUCN Redlist

Known Distribution of the Species
Clarias macrocephalus is native to the Indochina peninsular: Vietnam, Cambodia and Laos as well as Thailand, and Malaysia. (http://www.fao.org/docrep/field/003/ac231e/AC231E03.htm)(http://www.iucnredlist.org/details/full/166020/0). *Clarias macrocephalus* has also been recorded in Myanmar, Japan, China, Indonesia (Sumatra), Guam and the Philippines, but these are considered misidentifications or introductions (http://www.iucnredlist.org/details/full/166020/0). It is not commonly cultivated - although a hybrid of it is - but interest in farming it is on the increase.(http://eol.org/pages/211498/overview).

Figure 6.1: Photo of *C.macrocephalus* by FiMSeA, on http://ffish.asia"

First description
Clarias macrocephalus, commonly known as the bighead catfish, was first described by Günther in 1864.

6.1.1 Scientific Research on the Species in the ASEAN Region

Research categories
Much of the research on *Clarias macrocephalus* in the region is categorised as Fisheries (20), Marine and Freshwater Biology (15), and Biochemistry & Molecular Biology (4).

Research summary
Clarias macrocephalus is an economically important fish in Thailand and is increasingly being cultivated in aquaculture settings(10.1016/j.aquaculture.2004.08.001). However *C. macrocephalus* doesn't cultivate well and also has a near threatened status across its wild population range because of habitat loss; as such much of

the research effort is at identifying ways to increase production in aquaculture and minimise harm to the wild population.

A genetic population study examined the success of crosses between males of various strains of the fast growing African catfish *C. gariepinus* and females of strains of *C. macrocephalus* - which has tastier flesh - and found some hybrid strains had greater absolute growth rate than others (10.1016/j.aquaculture.2013.12.023). The use of hybrids has led to some conservation concerns in Thailand regarding the wild population of *C. macrocephalus* becoming back crossed with artificially created hybrids that have escaped from cultured systems. A study in Thailand took DNA samples from 25 natural populations of *C. macrocephalus* from across the country - they found 12 of the populations contained alleles in them from the African *C. gariepinus*(10.1016/j.aquaculture.2004.08.001). The hybrid is able to breed with both species which could lead to species extinction and also grows faster than *C. macrocephalus* and so might out-compete the native stock for resources (Na-Nakorn 2004).

Hara, M. et al., 1998, examined genetic distance in 4 wild populations in Thailand, they found two population groups, which were Chiangrai-Prachinburi and Pattani-Yala group and genetic distance was larger within the first group than those within the second group.

Much of the research literature is focussed on maximising yield in aquaculture settings through studying immunity to pathogens, as well as factors affecting growth and reproduction. Bacterial infection by *Aeromonas hydrophila* increased expression of the gene 'HSC70-2' in the tissues of *C. macrocephalus* which may relate to the role of HSC70-2 in the immune response of the species (10.1111/are.12076). Poompuang, S. et al 2012 found the C3 protein produced in the liver of *C. macrocephalus* had an essential role in immunity – furthermore an increase in C3 was induced by beta glucan in the diet of the fish.

The effect of stocking densities in aquacultures was investigated and found to be density dependent - *C. macrocephalus* fry reared at 285 m(-3) in tanks and at 114 m(-3) in ponds had significantly faster growth rates than fish reared at higher densities (10.1046/j.1365-2109.2002.00763.x). Myostatin levels were found to have a negative feedback effect, rising levels reducing growth rate in larvae of *C. macrocephalus* when they were fasted for a period of time (10.1007/s10695-014-0015-8).

Methods of increasing reproduction, whilst minimising numbers of broodstock were investigated in the literature - as numbers of *C. macrocephalus* are limited. One study examined 5 forms of Gonadotropin releasing hormones to see the efficacy at stimulating ovulation in *C. macrocephalus*. Chicken GnRH was most effective as identical to catfish Gn RH (10.1016/0167-0115(92)90024-O). Another study looked at the success of using irradiated sperm of another fish species for gynogenesis - creating offspring with only the mothers DNA (10.1016/j.aquaculture.2004.02.032). Another study examined the properties

required to create artificial seminal plasma to be able to dilute *C. macrocephalus* milt whilst still giving high fertilisation success of eggs -so less males are sacrificed during artificial insemination (10.1016/S0044-8486(98)00402-5). *Clarias macrocephalus*, harvested from irrigated rice fields in Malaysia, showed that spawning changes with water level (10.1007/BF00014311).

What to feed *Clarias macrocephalus* in culture was looked at by Bolivar, M. and Fermin, AC., 1996, who found that catfish larvae can be given a dry diet, but growth rate is higher if live feed - artemia - is given prior to the dry formula diet.

Aquatic or marine?
In a sector review of aquaculture in Thailand by the FAO *Clarias macrocephalus* and its hybrid with *C. gariepinus* are listed as freshwater species, not listed within the commercial brackish water production section of the report. [There has been some discussion of the possibility of introducing some catfish species] (https://www.researchgate.net/profile/Douglas_Clay/publication/313167412_Preliminary_observations_on_salinity_tolerance_of_Clarias_lazera_from_Israel/links/58d73761aca2727e5ee94ab6/Preliminary-observations-on-salinity-tolerance-of-Clarias-lazera-from-Israel.pdf) into brackish water aquaculture to make use of available coastal locations, but I didn't find any reference to this having occurred for this species.

Is there a description of any research locations that you can identify?

A conservation biology study in Thailand took DNA samples from 25 natural populations of *C. macrocephalus* from across the country including- 12 populations from provinces located in the Chaophraya river basin in the centre of the country, 5 from the Mekong river basin, 1 from the east and 7 from the south of Thailand - they found 12 of the populations contained alleles in them from the African *C. gariepinus*(10.1016/j.aquaculture.2004.08.001). Another genetic study in Thailand OF *C. macrocephalus*, by Hara, M. et al in 1998, assayed 14 proteins across 4 wild populations from the north (Chiangrai), central (Prachinburi) and south (Pattani and Yala) of Thailand.

In 1987, *C. macrocephalus* were sampled monthly from the rice fields, sump ponds and irrigation canals of North Kerian area up to about the latitude 5°45', Northwestern Peninsular Malaysia the fish are considered as one population 10.1007/BF00014311.

6.1.2 Patent activity

There are only 2 patent documents for *C. macrocephalus*, the most commonly cited patent being for a specialized feed for sensitive organisms, especially larvae or juvenile forms of farmed aquatic organisms and the method of producing the feed..

The other *C. macrocephalus* patent document is for the use of vitamin K3 for

treatment of parasitic disease in an individual, such as an animal or human being. Vitamin K3 has been found to be effective in the treatment of fish suffering from parasite infestation.

Lens collection

6.2 *Lates calcarifer*

Species name: *Lates calcarifer* **Kingdom:** Animalia **Phylum:** Chordata GBIF

Brief Description of the Species:
The barramundi or Asian seabass (*Lates calcarifer*) is a widely distributed species of salt and freshwater sportfish, with large, silver scales, which can change shade, depending on their environments. *L. calcarifer* bodies can reach up to 1.8 m (6 ft) long, and the maximum weight is about 60 kg (130 lb). The average length is about 0.6-1.2 m (2–4 ft). It is very popular in Thai cuisine (http://eol.org/pages/204766/overview).

Lates calcarifer are demersal, inhabiting coastal waters, estuaries, lagoons, and rivers; they are found in clear to turbid water, usually within a temperature range of 26−30 °C. This species does not undertake extensive migrations within or between river systems, which has presumably influenced establishment of genetically distinct stocks in Northern Australia.

Known Distribution of the Species
Lates calcarifer are a widely distributed species - from the Persian Gulf, through Southeast Asia to Papua New Guinea and Northern Australia (http://eol.org/pages/204766/overview).

First description
Lates calcarifer first descibed by German scientist Bloch, in 1790, and orginally named *Holocentrus calcarifer* .

6.2.1 Scientific Research on the Species

Research categories
Much of the research on *Lates calcarifer* is categorised as Fisheries (53), Marine and Freshwater Biology (45), Veterinary Sciences (13), Biotechnology & Applied Microbiology (9), Genetics & Heredity (8).

Research summary
Much of the research effort regarding *L. calcarifer* is concerned with optimising conditions for successful aquaculture of this valuable fish species. Some studies have investigated the natural history of the fish, particularly spawning and juveniles, as was the case in a study using controlled incubation of wildstock from the inland waters of Vietnam(10.1134/S1062359015040123).

Others have focused on optimising feed for this species – noting the success of live food in a study in the South China Sea(10.1016/S0044-8486(96)01490-1). Others noted physiological aspects of nutrition – essential fatty acid metabolism in *L. calcarifer*(10.1007/s10695-010-9409-4). Some studies have trialled the use of local seaweed species - K. alvarezii, E. denticulatum and S. polycystum – to replace commercial feed binder in the feed of *L.calcarifer* juveniles(10.1080/09712119.2015.1021805).

The genetics of *Lates calcarifer* have been the subject of some investigation by scientists with one study looking at the chromosomes of male and female fish (10.1508/cytologia.80.167). Prevalent diseases which effect successful aquaculture wee also given attention inn the literature with one study noting the pathological effects of SDS in *L.calcarifer* indicating it to be a viral infection (10.1111/j.1365-2761.2011.01319.x).

Fish aquaculture has an effect on the environment; this was the subject of a study examining pelagic carbon flow and water chemistry in mangrove estuaries with fish cage aquaculture of *L.calcarifer*(10.1016/S0141-1136(02)00276-3).

Aquatic or marine? *Lates calcarifer* live close to the sea floor, inhabiting coastal waters, estuaries, lagoons, and rivers; they are found in clear to turbid water - within a temperature range of 26—30 °C (http://eol.org/pages/204766/overview).

This species is able to adapt to a range of salinities and thus are found in freshwater, estuarine, lagoons, brackish, rivers and coastal areas (Davis, T.L.O. 1986). It has been shown that some of the fish move between salt and freshwater environments whilst others remain only in the marine environment.

Adults in freshwater usually migrate to spawn in water with higher salinity as eggs need saltwater to develop. Spawning most often occurs in brackish water like the river mouth and is seasonal (Moore, R. 1982).

Is there a description of any research locations that you can identify?

Marine fisheries in the Gulf of Thailand were the subject of a study looking at changes in 35 marine species including *Lates calcarifer* over a 26 year period (Tuantong, J.et al 2015).

Mangrove inlets and creeks in Selangor, Malaysia are the habitat for 119 species of fish (the majority of which are juveniles)- the common fish species included *Lates calcarifer* (10.1007/BF00008219). The tidally dominated mangrove estuaries of peninsualr Malaysia were the location of a study examining the

environmental effects of fish cage aquaculture of *L.calcarifer*(10.1016/S0141-1136(02)00276-3).

6.2.2 Patent activity

The majority of patent activity centres around aquaculture, specifically, feed, products and methods.

Patent activity includes the novel use of fish skin including lates calcarifer as an industrial source of collagen, (US 2012/0114570 A1).

Medical and cosmetic skin treatments have also been derived from the hatching fluid of fish including lates calcarifer.

Lens collection

6.3 *Litopenaeus vannamei*

- **Species name:** *Litopenaeus vannamei*
- **Kingdom:** Animalia
- **Phylum:** Arthropoda GBIF

Brief Description of the Species:
The dominant shrimp culture species in the world, they are benthic - occurring in waters of depth between 0-72m in marine habitats as adults, and estuarine environments as juveniles in subtropical to tropical climates(http://www.sealifebase.org/summary/Litopenaeus-vannamei.html). Asia has seen a phenomenal increase in the production of *L. vannamei*, no production was reported to FAO in 1999, but by 2004 it was nearly 1 116 000 tonnes having overtaken the production of *P. monodon* in China, Taiwan Province of China and Thailand. However, due to fears of importing exotic diseases it is only experimentally farmed in Cambodia, India, Malaysia, Myanmar and the Philippines. Thailand and Indonesia both freely permit its commercial culture but have official restrictions, so that only SPF/SPR broodstock may be imported(http://www.fao.org/fishery/culturedspecies/Penaeus_vannamei/en).

Known Distribution of the Species
Litopenaeus vannamei is native to the Eastern Pacific coast from Sonora, Mexico in the North, through Central and South America as far South as Tumbes in Peru ((http://www.fao.org/fishery/culturedspecies/Penaeus_vannamei/en)).

The main producer countries of Penaeus vannamei are: China, Thailand, Indonesia, Brazil, Ecuador, Mexico, Venezuela, Honduras, Guatemala, Nicaragua, Belize, Viet Nam, Malaysia, Tawian P.C., Pacific Islands, Peru, Colombia, Costa Rica, Panama, El Salvador, the United States of America, India, Philippines, Cambodia, Suriname, Saint Kitts, Jamaica, Cuba, Dominican Republic, Bahamas (http://www.fao.org/fishery/culturedspecies/Penaeus_vannamei/en).

Figure 6.2: By Xufanc (Own work)

First description
Litopenaeus vannamei was first described in 1931 as *Penaeus vannamei* by Boone.(https://www.gbif.org/species/2223871)

6.3.1 Scientific Research on the Species in the ASEAN Region

Research categories
Much of the research on *Litopenaeus vannamei* is categorised as Fisheries (54), Marine and Freshwater Biology (32), Veterinary Sciences (26), Biotechnology & Applied Microbiology (10), Immunology (10), Biochemistry and Molecular Biology (6).

Research summary
Much of the research on *Litopenaeus vannamei* as the worlds dominant cultured shrimp species was with regard to maximising yield, through selecting robust broodstock as well as via disease treatment and prevention.

Researchers found that cold storage of spermatophores from broodstock was effective is dones[?] so with antibiotic within the mineral oil surrounding the sperm (10.1016/j.aquaculture.2006.08.018). Another study focussed on reproduction of *Litopenaeus vannamei* looked at the success of crosses with limited

numbers of males and females, and noted that male broodstock could be selected with desirable traits (10.2306/scienceasia1513-1874.2008.34.115).

Diseases of *Litopenaeus vannamei* and other commercially farmed shrimps blight production and so much of the research literature is focussed on how to overcome some of these diseases: via longer rearing and less dense stocking to protect against infectious myonecrosis (10.1016/j.jip.2010.03.001), or introduction of immune stimulating agents PAP-phMGFP (10.1016/j.fsi.2011.06.010)and CHH (10.1016/j.fsi.2011.01.014). Another study found the use of dsRNA injected into prawns to be effective as both a preventative, and treatment for Penaeus stylirostris densovirus (PstDNV) infection(10.1016/j.virusres.2010.09.009). Similarly galangal extract and trans-p-coumaryl diacetate stimulated the immune system response, thereby promoting resistance to V. harveyi infection in *Litopenaeus vannamei*(10.1007/s10499-014-9822-2). Detecting Taura Syndrome Virus in Shrimps via diagnostic test kits was the subject of another study (10.3354/dao069249)

Antibiotic resistance is a growing problem worldwide in the aquaculture industry and for human health. As such much of the literature was focussed on looking at alternatives to antibiotic use, such as probiotics. One study found the use of bacteria, yeasts, and algae in water additives or artemia enriched enhanced survival and growth rate of *Litopenaeus vannamei* (10.1016/j.anifeedsci.2011.07.003). The probiotic Bacillus subtilis BS11 supplement was found to benefit *Litopenaeus vannamei* growth and survival after infection with Vibrio harveyi, conferring disease resistance (10.1111/anu.12040).

The food safety of cultured seafood is paid some attention amongst the research literature, -minimal sequential ozone treatment and ice storage for *Litopenaeus vannamei* has been shown to have an antioxidant like action and could promise further safety for shrimp consumption (10.1016/j.lwt.2014.02.007).

Astaxanthin extract from *Litopenaeus vannamei* has been demonstrated in one study to act as anti-inflammatory alternative against carrageenan-induced paw oedema and pain behaviour in mice (10.3390/molecules21030382).

Genetics were the subject of several studies in the literature including the correlation between genetics and body weight in *Litopenaeus vannamei* (10.1111/j.1365-2052.2005.01274.x). Genetic variation and population structure of wild *Litopenaeus vannamei* from 4 geographic locations from Mexico to Panama were investigated using 5 microsatellite DNA and it was found that subpopulations exist (10.1007/s10126-004-3138-6).

Aquatic or marine? *Litopenaeus vannamei* live in marine habitats as adults, and estuarine environments (brackish water) as juveniles in subtropical to tropical climates(http://www.sealifebase.org/summary/Litopenaeus-vannamei.html

Is there a description of any research locations that you can identify? Brazil and Indonesia are mentioned in a study on infectious myonecrosis of Brazilian farmed *Litopenaeus vannamei* (10.1016/j.jip.2010.03.001).

China, Thailand, Peru to Mexico on the Pacific coast, and Taiwan are referenced in a paper about the most widely cultured alien crustacean in the world *Litopenaeus vannamei* (10.1007/978-94-007-0591-3_17). Genetic variation among 4 populations of *L.vannamei* from locations along the coast between Mexico and Panama were the subject of one investigation which noted subpopulations were present (10.1007/s10126-004-3138-6).

Enterocytozoon hepatopenaei has been found in *L.vannamei* farms across India - within the states of: Tamil nadu, Andhra Pradesh and Odisha. *E.hepatopenaei* has also been detected in shrimp cultured in China, Vietnam and Thailand and is suspected to have occurred in Malaysia and Indonesia and to be linked with severely retarded growth (10.3354/dao03036).

6.3.2 Patent activity

There are 309 patent documents for *Litopenaeus vannamei*, the most commonly cited patent being for a commercial aquaculture system using algae and artemia as food stuffs for juveniles. Many other patent documents relate to differing forms of aquaculture system for growing *Litopenaeus vannamei*. Other *L. vannamei* patent documents relate to feed compositions, such as one without fish meal.

Some patent documents for *L. vannamei* relate to inducing immune responses, for example using dsRNA to modulate gene expression and responses to pathogens.

Lens collection

6.4 *Macrobachium rosenbergii*

- **Species name:** *Macrobachium rosenbergii*
- **Kingdom:** Animalia
- **Phylum:** Arthropoda GBIF

Brief Description of the Species:
Macrobachium rosenbergii known as the Giant River Prawn and the Giant Freshwater Prawn - it is widely fished and also is the main freshwater shrimp cultivated within the commercial aquaculture industry, IUCN. The body length of this large prawn species is 320 mm for males; and 250 mm for females, as it is a sexually dimporphic species. FAO.org.

Global production of the Giant River Prawn has grown since its inception in the 1970's and by 2002 was 200 000 tonnes/yr FAO.org.

Known Distribution of the Species
M. rosenbergii is native to Bangladesh; Brunei Darussalam; Cambodia; China; India; Indonesia (Java); Malaysia (Peninsular Malaysia, Sabah, Sarawak); Myanmar (Myanmar (mainland)); Pakistan; Philippines; Singapore; Sri Lanka; Thailand IUCN. The geographic distribution is now much wider than this as it has been introduced to all continents for aquaculture and is now found in Brazil, Venezuela, Australia, United States, Iceland, Japan, Germany, Iran, Taiwan,GBIF.

First description
M. rosenbergii was first described by Johannes De Man in 1879 as *Palaemon rosenbergii* in the publication: De Man, 1879, Notes Leyden Mus., 1:167, however in 1966 Johnson renamed it to its current nomenclature of *Macrobachium rosenbergii* (Holthuis,L.B. 1980).

Figure 6.3: © Citron / CC BY-SA 3.0

6.4.1 Scientific Research on the Species in the ASEAN Region

Research categories
Much of the research on *M. Rosenbergii* in the region is categorised as fisheries (77), followed by Marine and Freshwater Biology (46), Biochemistry & Molecular Biology (21), Veterinary Sciences (20), Zoology (13), Immunology (12) amongst others.

Research summary
The majority of the research effort on *Macrobachium rosenbergii* is directed

towards maximising aquaculture yield to increase economic gain of shrimp farmers. So the research is broadly concerned with disease prevention/treatment, nutrition, stocking densities, reproductive success, and genetic make up of broodstock. Understanding the diseases of *M.rosenbergii* - such as *L. garvieae* a bacteria that infects shrimps (Dangwetngam, M. and Suanyuk, N. 2014), and White Tail Disease virus (10.1016/j.jip.2010.09.007) which causes large scale mortality in aquaculture populations- can enable treatments and preventative strategies to be adopted. Improving yield of shrimp farmers has led many to look to the genetic quality of broodstock - analysing the parentage of existing broodstock (10.1016/j.aquaculture.2011.10.045), as well as comparing this with wild samples (10.1016/j.bse.2014.12.023).This genetic analysis can then help develop a more successful breeding strategy (10.1016/j.aquaculture.2009.12.011). The nutritional composition of feed given to farmed *M.rosenbergii* is another common theme of research in the literature, as well fed shrimps grow bigger and reproduction is increased (10.7717/peerj.2735). However for shrimp farmers in the Mekong Delta region of Vietnam, identifying non commercial feed options - due to affordability issues- is key (10.1111/j.1444-2906.2005.00961.x). Understanding how eye stalks inhibit reproduction in female *M.rosenbergii* (10.2306/scienceasia1513-1874.2014.40.157), as well as understanding how sex differentiation occurs (10.3390/ijms17050690) and when to intervene to create all male stock (10.1016/j.aquaculture.2012.03.015) are some of the reproductive focussed areas of research covered in the literature.

Aquatic or marine? Although *M. rosenbergii* is predominantly a tropical freshwater species, the larval stage of the species is found within adjacent brackish water, as females migrate to estuaries to lay their eggs FAO.org.Most of the *M. rosenbergii* farms are in freshwater inland locations, however some are in estuarine and coastal locations where salinity in the ponds can fluctuate and effect breeding success of females (10.1016/j.aquaculture.2008.04.035).

Is there a description of any research locations that you can identify?
Much of the research involves laboratory bred cultures of *M.rosenbergii*, although some studies do include wild samples as is the case in a genetic study by Schneider et al 2013 910.1111/j.1365-2109.2012.03147.x). Schneiders' study used cultured prawn samples from: Andhra Pradesh, India; Kaneohe, Hawaii, USA; Tamashiro Market, Honolulu, Hawaii, USA; University of Negev, Beer Sheva, Israel;Frankfort, Kentucky, USA; Leland, Mississippi, USA; Weatherford, Texas, USA as well as wild prawn samples from Hmaw River, Hlaing River and the Pan Hlaing River - tributaries of the Yangon River, Yangon, Myanmar; and Mahanadi River, Orissa, India. There are some references to more specific locations for wild samples within the literature - such as research into a breeding strategy for genetic improvement using wild strains Vietnam (Dong Nai and Mekong) (10.1016/j.aquaculture.2009.12.011)(10.1111/jwas.12148).*L. garvieae* was isolated from *M.rosenbergii* samples taken from cultures and wild prawns from the Phatthalung and Songkhla, provinces of southern Thailand (Dangwetngam, M. and Suanyuk, N., 2014). Some research doesn't specify anything more than the country such as in a study detailing culture technology in Thailand (10.1111/j.1365-2109.2011.03037.x). Genetic diversity analysis was undertaken on cultured samples from farms in Zhejiang, Guangdong and Guangxi provinces, China, as well as wild samples from Dong Nai River and Mekong River, Vietnam (10.1016/j.bse.2014.12.023).

6.4.2 Patent activity

The top cited patent involving *M.Rosenbergii* is regarding feed composition for shrimps in aquaculture settings. The invention specifies a range of percentage compositions of lipid:carbohydrate:protein, differing nutritional sources, particle size and types - as an alternative to live feed for shrimp larvae.

The largest family number of a patent associated with *M.Rosenbergii* is for another type of feed, this time for [preparation and use of methionylmethionine as a feed additive for fish And crustaceans] (https://www.lens.org/lens/patent/US_2010_0098801_A1).

Lens collection

6.5 *Nypa fruticans*

- **Species name:** *Nypa fruticans*
- **Kingdom:** Plantae
- **Phylum:** Tracheophyta GBIF

Brief Description of the Species:
Nypa fruticans is a palm found in the upstream estuarine zone in all intertidal regions. It forms extensive belts along brackish to tidal freshwater creeks and

rivers. It is very fast growing, especially in fresh water, and is a competitive species (http://eol.org/pages/1137487/details). It is the only palm adapted to the mangrove biome and grows in terrestrial, marine and freshwater habitats.

The trunk of *Nypa fruticans* grows underground with the leaves, female flower inflorences and male flowers visible above the ground (http://www.efloras.org/florataxon.aspx?flora_id=2&taxon_id=220009317).

Nypa fruticans is used for a wide range of commercial goods and services including- thatching and for making alcoholic drinks through a fermentation process(http://www.iucnredlist.org/details/178800/0). It is an important emerging source of biofuel, capable of producing ethanol ranging from 6,480 to 20,000 L/ha, a higher yield than sugarcane(http://agris.fao.org/agris-search/search.do?recordID=MY2015000742). It is considered to be of 'Least concern as it is widespread and locally common (http://www.iucnredlist.org/details/178800/0).

Figure 6.4: By Qaalvin Own work

Known Distribution of the Species

Nypa fruticans ranges from Sri Lanka and the Ganges Delta through to the west Pacific. In South and South-East Asia it is found in Bangladesh, Brunei Darussalam, Cambodia, China, India, Indonesia, Japan, Malaysia, Myanmar, Singapore, Sri Lanka, Thailand, and Viet Nam . In much of its native range it

has been planted and exists in large or small-scale plantations (http://eol.org/pages/1137487/overview).

Nypa fruticans has been introduced to Cameroon and Nigeria in West Africa and to Panama in Central America and Trinidad and Tobago in the Caribbean. (http://eol.org/pages/1137487/overview).

First description
Nypa fruticans was first described by a German botanist called Christoph Carl Friedrich von Wurmb in 1781.

6.5.1 Scientific Research on the Species

Research categories
Much of the research on *Nypa fruticans* is categorised as Environmental Sciences (8), Biology (6), Marine and Freshwater Biology (6), and Plant Sciences (6).

Research summary
Much of the research on *Nypa fruticans* is studying its role within mangrove biomes, an important ecological and economic habitat type. In the Segara Anakan lagoon, Java, mangrove tree density and diversity was examined at the eastern part of the lake - *Nypa fruticans* was present and characterised a mature undisturbed forest (10.1007/s10113-008-0074-4). Within Malaysia - on Carey Island - a similar demographic study was conducted looking at the percentage of *Nypa fruticans* seedling, juvenile, adult and mature present the population showed a majority of adults with 67.9% (Aslezaeim, N. and Rozainah, MZ. 2010). Also in Malaysia a study of forest structure, diversity index and above-ground biomass was conducted on *N.fruticans* at Tok Bali mangrove forest, Kelantan (Kamaruzaman, J et al 2007).

Low genetic diversity for *N.fruticans* was found amongst six natural populations from China, Vietnam, and Thailand across a total of 183 individuals (10.1016/j.aquabot.2009.09.003). Creating *N.fruticans* seedlings was the focus of some research due to the economic benefits of the plant - mass clonal propagation of disease free planting materials was successfully trialled in one study (Abad, R G et al 2015). In another propagation study in Vietnam, a participatory action research methodology was used to successfully establish an *N.fruticans* (and other mangrove species) nursery on unused acid sulphate soil -normally considered unsuitable for mangrove growth (Nguyen, T P 2016).

Species living on *N.fruticans* or within the mangrove biome it creates were the focus some of the literature with several studies examining the fungi present on samples from different populations. One study tested the fungi growing on *N.fruticans* for heavy metal tolerance and found that one that was able to successfully grow deposit heavy metal pollution - meaning it could potentially be used as a type of absorbent material (10.1007/s12601-015-0040-2). Species diversity of marine fungi on *Nypa fruticans* in Samut Songkhram Province, Thailand were investigated, with 81 fungal taxa recorded

(10.1515/BOT.2005.049). Taxonomy of fungus found on *Nypa fruticans* in the intertidal regions in Trang and Trat provinces, Thailand was examined in another study (10.7872/crym/v36.iss3.2015.319). Biodiversity and ecology of higher filamentous fungi on *Nypa fruticans* along the Tutong River, Brunei were examined during 1999, with Forty-six taxa recorded (Hyde, K.D.and Sarma, V.V. 2006).

Both mudskippers and fireflies were found to inhabit populations of *Nypa fruticans* within the literature. Mudskippers, *Periophthalmodon septemradiatus* were recorded for the first time in Peninsular Malaysia, from the small tributaries of the rivers Selangor and Muar (Khaironizam, MZ and Norma-Rashid, Y. 2003). Whereas *Pteroptyx* fireflies are commonly reported to congregate in large numbers in mangroves, but researchers found they preferred vegetation consisting mainly of *S. caseolaris* and *N.fruticans* (10.1007/s11273-009-9172-4). A study of the root-associating bacteria of *N.fruticans* found in brackish-water mud in Sarawak, Malaysia, discovered that *Burkholderia vietnamiensis* to be its main nitrogen-fixing bacterium (10.1271/bbb.100397). Another important type of organism examined in the literature was that of the pollinators inhabiting *N.fruticans* mangroves in an Oxford University study, within the submerged Melaleuca forests of Vietnam (Nguyen, Q. 2008).

The economic exploitation of *N.fruticans* was examined by some researchers, one Malaysian paper looked at the ripe and unripe fruit content to see if can be used as a food source (10.1051/fruits/2013089). Whilst another scientist examined the potential of *N.fruticans* in the Philippines for alcohol production (Rasco, E.T., 2010).

Aquatic or marine?
N.fruticans grows in mangrove forests in upwater estuarine locations, so it is aquatic, and terrestrial - as it is exposed at low tide, and marine as the salt water from the ocean meets the freshwater of the rivers (http://eol.org/pages/1137487/details).

Is there a description of any research locations that you can identify?
A demographic study of *Nypa fruticans* was undertaken on Carey Island Malaysia (Aslezaeim, N.and Rozainah, M.Z., 2010). Forest structure was also examined at Tok Bali mangrove forest, Kelantan, Malaysia Kamaruzaman (Kamaruzaman, J. et al. 2007).A study looking at tree density and diversity of mangroves in different areas of Segara Anakan lagoon, Java, noted the presence of *N.fruticans* as an indicator of a mature forest(10.1007/s10113-008-0074-4).

In the Vam Ray area Kien Giang Province, Vietnam, a participatory research methodology was used to establish a mangrove nursery on soil considered previously to be unsuitable - 5 types of mangrove species were successfully grown grown including *Nypa fruticans* seedlings (Nguyen, T.P., 2016); providing a potential source of income for local people.

Genetic diversity of populations from six natural populations of *Nypa fruticans* from China, Vietnam, and Thailand was assessed, and showed an extremely low

level of genetic diversity (10.1016/j.aquabot.2009.09.003).

Selangor and Muar rivers of Malaysia were discovered to contain mudskipper populations, whilst a 2010 study of alcohol production potential took place in Vinzons, Camarines Norte, Philippines(Rasco, E.T., 2010). Pollinators of *Nypa fruticans* were examined in the submerged meleuca forests of South Vietnam (Nguyen, Q. 2008) and the bacteria inhabiting the rhizomes of *Nypa fruticans* in Sarawak Malaysia were identified (10.1271/bbb.100397).

6.5.2 Patent activity

There are 10 patent documents for *Nypa fruticans* , the most commonly cited patent document is for a [tnf-alpha and nitric oxide production inhibitor using an extract from the plant body of the palm] (https://www.lens.org/lens/patent/JP_2007008817_A).

Lens collection

6.6 *Oreochromis niloticus*

- **Species name:** *Oreochromis niloticus*
- **Kingdom:** Animalia

- **Phylum:** Chordata GBIF

Brief Description of the Species:
Oreochromis niloticus is a species of Tilapia, a cichlid fish native to the nile basin in Africa and coastal rivers of Israel, however it's an economically important species of fish which has been introduced widely outside of its natural range.

O. niloticus adults grow to 60cm and live up to 9 years weighing up to 4.3kg. It lives in freshwater and can tolerate brackish water, wit a temperature range of 8-42°C.It's an omnivore feeding on plankton as well as mosquito larvae.Groups of cichlids establish social hierarchies in which dominant males have priority for access to mate and food.

Commercial aquaculture of *O. niloticus* dates back to ancient Egypt, as they are fast growing and produce good fillets. The wild type of *O. niloticus* is less popular today as the meat is dark so a lighter meat variety is used in aquaculture.

Known Distribution of the Species
O. niloticus has been taken from its native African and Israeli habitats to tropical and subtropical waters all over the world for aquaculture. Nile tilapia from Japan were introduced to Thailand in 1965, and from Thailand they were sent to the Philippines. Nile tilapia from Cote d'Ivoire were introduced to Brazil in 1971, and from Brazil they were sent to the United States in 1974. In 1978, Nile tilapia was introduced to China, which leads the world in tilapia production

and consistently produced more than half of the global production in every year from 1992 to 2003 (FAO).

First description
Oreochromis niloticus was first described by [Linnaeus in 1758 who named it Perca nilotica, this was changed to the current name by Greenwood, P. H. 1960] in his publication which revised the Lake Victoria Haplochromis species (https://www.gbif.org/species/4285694).

6.6.1 Scientific Research on the Species in the ASEAN Region

Research categories
Much of the research on *Oreochromis niloticus* is categorised as Fisheries (78), Marine and Freshwater Biology (61), Veterinary Sciences (14), Agriculture, Dairy and Animal Science (11).
Research summary
The research literature on *Oreochromis niloticus* is largely concerned with improving productivity of the aquaculture industry that grows tilapia commercially. Methods of aquaculture are investigated: such as factors effecting rice polyculture, brackish water aquaculture and cage aquaculture. Rice polyculture involving the farming of *Oreochromis niloticus* amongst other fish species in paddy fields (10.1016/S0044-8486(02)00005-4) has several elements for investigation including rice seeding rate (10.1016/S0044-8486(98)00396-2), nitrogen cycling (10.1007/s10705-007-9106-6) and the ecological/economic benefits of this form of polyculture.

Brackish water aquaculture requires salinity tolerance, which is not a feature of *Oreochromis niloticus* - it is the least salt tolerant tilapia, but has a quick

growth rate. *O.niloticus* is increasingly being cultured in coastal ponds (especially in the Philippines, Indonesia and Vietnam) - sometimes with shrimps - so it would be beneficial if a more salt tolerant hybrid could be produced (10.1016/j.aquaculture.2005.02.008).

Stocking density of *O.niloticus* in cages was investigated by the Asian Institute of Technology in Thailand (10.1016/S0044-8486(96)01377-4). The combined net yield of both caged and open-pond tilapia was found to be highest in the treatment with 50 fish m(-3).

The feed used in the aquaculture of *O.niloticus* is the focus of much research effort, including the replacement of fish oil with vegetable oil (10.1007/s11745-007-3057-1) - which gave worse yields, however using cheap farm waste -mushroom stalks -to replace rice bran in feeds gave a greater yield for less money (Bahari, I. te al 2014). Scientists supplementing *O.niloticus* feed with antimicrobial herbal extracts found no mortality in S. agalactiae infected Nile tilapia for fish receiving dried matter of A. paniculata aqueous extract supplemented feeds at ratios (w/w) of 4:36 and 5:35 ((10.1016/j.jbiosc.2009.01.024). Probiotic supplemented feeds were found to increase survival in *O.niloticus* infected with *Aeromonas hydrophila* (Areechon, N. et al 2016).

Infections of fish with pathogens in intensively farmed aquaculture environments can lead to mass mortality and economic loss, hence much of the literature is concerned with understanding pathogens, and methods of combating losses. Intensive *O.niloticus* egg incubation creates conditions favourable for microbe growth leading to mass mortalities of fish larvae (Jantrakajorn, S. and Wongtavatchai, J. 2015). Scientists studied the immune response of *O.niloticus* to better understand how to develop vaccines (Bunyatratchata, W. et al 2015). Occurrence of infections in cultured populations of *O.niloticus* are studied to better understand the disease as was the case with a population infected with Neoechinorhynchus in the Philippines (Paller, V and de la Cruz C 2012).

Heavy metal contamination of watercourses containing farmed *O.niloticus* is a concern in the literature due to heavy industry waste being released, an and the potential resultant build up in the flesh of farmed fish eaten by local people (10.1016/j.proenv.2015.10.057 selangor)(10.1111/j.1365-3156.2007.01939.x). Reduction of copper-induced tissue changes in *O.niloticus* by calcium exposure is beneficial in reducing effects in marine species(10.1080/15376510903173674).

Many *O.niloticus* farmers produce all-male populations because of the superior growth rate of males compared to females. The literature discussed different methods for achieving this such as hormonal sex reversal(Guerrero, R.D. 2008), as well as genetic manipulation to create YY male broodstock achieving a 95.6% male sex ratio in the population(10.1139/cjfas-54-2-396).

Understanding the genetic make up of different breeds of *O.niloticus* (10.1508/cytologia.78.9), and selective breeding using different strains to genetically improve broodstock - is the focus of some researchers (10.1016/S0044-8486(97)00230-5).Red Tilapia a strain of *O.niloticus* bred for its white flesh is

a popular strain for culture.

Aquatic or marine?

Native to the Nile basin rivers and lakes in Africa and coastal rivers of Israel] *O.niloticus* is primarily a freshwater fish(http://eol.org/pages/356343/data?toc_id=4#1448). However brackish water aquaculture is on the rise in Philippines, Indonesia and Vietnam which culture *O.niloticus* - which requires salinity tolerance - not a strength of *Oreochromis niloticus*, as it is the least salt tolerant cichlid fish, but has a quick growth rate; research is being conducted to breed a more salt tolerant hybrid of *Oreochromis niloticus* (10.1016/j.aquaculture.2005.02.008).

Is there a description of any research locations that you can identify? *O.niloticus* is farmed in its native African countries, and Israel but has also been exported for aquaculture in fresh and brackish water locations across the world including: Egypt, Thailand, Philippines, Indonesia, Malaysia, Vietnam, and Bangladesh.

Some more specific locations are mentioned in the literature such as a study sampling the fish pathogen *Aeromonas hydrophila* occurrence in the *O.niloticus* population in West Bay of Laguna de Bay, Barangay Bayanan, Muntinlupa City, Malaysia in three months during 2005 (Cabrera E. et al. 2006), similarly another study sampled a population in Sampaloc Lake, Philippines for the occurrence of a fish pathogen called 'Neoechinorhynchus'(Paller, V. and De la Cruz, C. 2012). Polyculture of *O.niloticus* with 'bleeker' was the focus of a study in the Mekong delta Vietnam. Heavy metal incidence was investigated in two separate studies in Indonesia one sampling the Galas River & Beranang mining pool, Selangor(10.1016/j.proenv.2015.10.057); and another sampling Lake Cirata, West Java(10.1196/annals.1454.037). Nitrogen cycling in rice fish culture in Bangladesh, was the subject of a study (10.1007/s10705-007-9106-6).Spawning season was studied in two lakes in the Cote d'Ivoire (10.1023/A:100758801082). The spatio-temporal dynamics of fish larvae in Sirindhron Reservoir, Lower Mekong Basin, north-east Thailand (10.21077/ijf.2016.63.3.54491-02).

6.6.2 Patent activity

A partitioned aquaculture system for *O.niloticus* and other marine organisms, with an algal channel to control flow rate in the system is the invention associated with *O.niloticus* that has been cited most often.

The preparation and use of methionylmethionine as feed additive for fish and crustaceans is the patent document associated with *O.niloticus* with the largest patent family.

Lens collection

6.7 *Penaeus mondon*

- **Species name:** *Penaeus monodon*
- **Kingdom:** Animalia
- **Phylum:** Arthropoda

Brief Description of the Species:
Penaeus monodon, the Giant Tiger Prawn, is one example of a group of giant prawn species with economical importance to the commercial fisheries industry (L.B.Holthius (1949)). The total catch reported for this species for 1999 was 144 042 t with the largest catches from India (93 830t) and Indonesia (31 510 t) FAO.org. *P. monodon* lives in marine (adults) and estuarine (juveniles) environments, between 0-110 metres in depth and grow to a maximum of 336mm in length, weighing 60-130g FAO.org. There are two specimens of *P. monodon* recorded on vertnet, both are held at the University Museum of Zoology Cambridge and were collected in India - one specifies the Madras region.

Known Distribution of the Species
"Indo-West Pacific: E. and S.E. Africa and Pakistan to Japan, the Malay Archipelago and northern Australia" (L.B.Holthius (1980)).

First description
Penaeus monodon was first described by Johan Christian Fabricus in 1798, but clarification of which species this name referred to came later in 1949, when Lipke Holthuis showed it to be the type species of the genus *Penaeus* (L.B.Holthius (1949)).

6.7.1 Scientific Research on the Species in the ASEAN Region

Research categories
Much of the research on *P.monodon* is categorised as fisheries (288), followed by Marine and Freshwater Biology (179), Veterinary Sciences (123), Immunology (81), Zoology (60), Biochemistry & Molecular Biology (58), Biotechnology and Applied Microbiology (45), Virology (32) and so on.

Research summary
The majority of the research effort on *P.monodon* is directed towards maximising fisheries yield and increasing economic gain. As such a lot of the *P.monodon* literature is concerned with understanding the immune response of the shrimp populations to the main viral and bacterial pathogens which cause large scale mortality in the population, such as White Spot Syndrome Virus (WSSV), Yellow Head Virus (YHV) and *Vibrio harveyi*(10.1016/j.fsi.2011.10.013) (10.1016/j.dci.2012.09.001). Whilst others are focussed on improving shrimp reproduction for example injecting female broodstock with a hormone that

Figure 6.5: CSIRO

stimulates the ovaries (10.1016/j.aquaculture.2015.04.027 shrimp repro). Some work is concerned with identifying sub-populations of P. monodon where there is significant genetic differentiation between samples collected from different geographic areas ((Jarayabhand, P et al 2000).

Aquatic or marine?

P. monodon is fished from wild populations in offshore marine waters, however there is reference to inshore and pond fishing in some countries: Singapore, Malaya, Philippines, Thailand and Vietnam (L.B.Holthius (1980)) (10.1111/jwas.12423). In addition juveniles live in river mouth and estuarine mangrove environments predominantly - which act as a nursery with adults living in deeper offshore environments. Wild marine populations are commonly used to establish disease free broodstock for commercial pond fisheries inland (10.1016/j.aquaculture.2010.08.015). Thus some of the research is solely focussed on captive inland populations from commercial farms (10.1007/s11259-010-9434-x) whilst others are comparative studies between wild and captive specimens.

Is there a description of any research locations that you can identify? Much of the research involves laboratory bred broodstock of *P. monodon*, but from different geographical populations, where often only the country is cited: Australia, China, Taiwan, Malaysia, Vietnam, Thailand, Papua New Guinea, New Caledonia, India, Singapore, Philippines, Tanzania, Japan, Sulawesi, Sumatra, and Brazil. There are some references to more specific locations within the literature such as research in the Mekong Delta Region of Southern Vietnam looking at different pond farming methods - including mangrove ponds (10.1080/13657305.2013.747224).Similarly another study investigated *P.monodon* overfishing by artisanal fishermen in the Saadan Estuary in Tanzania, again an area with mangroves (10.1016/j.ocecoaman.2013.05.003). The Brunei waters of the South China Sea are the location mentioned in a study seeking disease free broodstock for inland shrimp farms (10.1016/j.aquaculture.2010.08.015). A study investigating genetic variation amongst *P.monodon* from 5 geographic locations within Thai waters lists: Chumphon and Trad within the Gulf of Thailand, as well as Phangnga, Satun, and Trang within the Andaman Sea (Jarayabhand, P et al 2000).Another genetic diversity study on P. monodon cites samples taken from the coastal waters of Qinglan (Hainan Province of China) and Malaysia (Li Shaojing et al 2008). Joseph Bonaparte Gulf in northern Australia was cited in a study on a new 7th genotype of YHV to infect shrimp ponds in Australia (10.3354/dao02894).South western and south eastern Indian coastal

populations of farmed shrimps are used in a disease study of P.monodon (10.3354/dao01835).

6.7.2 Patent activity

The top cited patent document involving *P. monodon* is for a dual purpose installation - whereby a system converts ocean thermal energy into electrical energy, at the same time the system benefits a lagoon population of *P.monodon* which are reared for the food industry. The system involves pumping cold deep sea water - which is nutrient rich to cool the working fluid and condense it, the surface water warms the working fluid and evaporates it. The closed cycle converts heat energy to electricity and the shrimps benefit from the nutrient rich deep seawater.

The cited example of a suitable location in the patent document is the Lime Island chain 1000 miles south of Hawaii, with the Philippine Tiger Prawn *P.monodon* being used. It doesn't specify utilising samples of *P.monodon* when inventing the system which is included in this document.

The second most cited patent document involving P.monodon is for a non metallic bioreactor, suitable for unicellular or multicellular culture - with *P.monodon* being one of the listed species that could be farmed within it. There is no location specified for this patent as it is a bioreactor design.

Specialised Feed composition for aquatic organisms including larvae of *P. monodon*. Similarly to above there is no location specified for this patent document.

This patent is for methods of delivering dsRNA into invertebrate marine organisms such as shrimps, to illicit an immune response. This includes methods of delivery of the dsRNA i.e. whether it is injected, ingested in a feed medium, or placed within an algae that is ingested.In addition methods of identifying genes in invertebrates that are involved in immune responses are also included.

Lens Collection

6.8 *Pomacea canaliculata*

- **Species name:** *Pomacea canaliculata*
- **Kingdom:** Animalia
- **Phylum:** Mollusca GBIF

Brief Description of the Species:
Pomacea canaliculata is a freshwater snail with a voracious appetite for water plants including lotus, water chestnut, taro and rice. Introduced widely from its native South America by the aquarium trade and as a source of human food, it is now a major crop pest in south east Asia (primarily in rice) and Hawaii (taro) and poses a serious threat to many wetlands around the world through

potential habitat modification and competition with native species. A highly generalist and voracious macrophytophagous herbivore. Most plants are eaten (http://www.iucngisd.org/gisd/species.php?sc=135).

The activity rate of *Pomacea canaliculata* varies highly with the water temperature. At 18°C they hardly move around, whilst the opposite is true at higher temperatures e.g. 25°C (The (http://www.iucngisd.org/gisd/species.php?sc=135).

Females lay clusters of bright pink eggs attached to solid surfaces and reproductive output can be enormous with clutch sizes of up to 1000, but averages are probably 200-300. Clutches are laid every few weeks (http://www.iucngisd.org/gisd/species.php?sc=135).

Figure 6.6: By H. Zell (Own work)

Known Distribution of the Species

P. canaliculata is native from Argentina to the Amazon basin, as well as being introduced to most of southern, eastern, and southeast Asia and the southern part of the United States (http://eol.org/pages/467346/overview). *P. canaliculata* is widely distributed in lakes, ponds and swamps throughout its native range of the Amazon Inferior Basin and the Plata Basin (http://www.iucngisd.org/gisd/species.php?sc=135).

Biogeographic Regions: nearctic (Introduced); oriental (Introduced); neotropical (Native); oceanic islands (Introduced)(http://eol.org/pages/467346/overview).

First description

The French Biologist Jean Baptiste Lamarck first described *P. canaliculata* in the natural history of invertebrates in 1822 (https://www.gbif.org/species/2292582).

6.8.1 Scientific Research on the Species in the ASEAN Region

Research categories
Much of the research on *Pomacea canaliculata* is categorised as Agronomy (7), Biotechnology and Applied Microbiology (4), Entomology (4), Environmental Sciences (4), Toxicology (4), Agriculture, Multidisciplinary (3).

Research summary

Much of the research on *Pomacea canaliculata* is concerned with ways to effectively control the invasive pest in agricultural settings, including the use of fish predators in rice fields (10.1016/j.cropro.2006.01.012), as well as molluscicides (De la Cruz, M.S. and Joshi, R.C.2001). Quinoa saponins a natural molluscicide were found to be an effective environmentally friendly alternative to synthetic molluscicides at eradicating *Pomacea canaliculata*, especially in direct seeded cultures of rice (10.1016/j.cropro.2007.08.010). In a study in Thailand natural pathogens of *Pomacea canaliculata* were isolated from the soil - strains of *Pseudomonas aeruginosa* and *P. fluoescens* (10.1023/B:WIBI.0000007312.97058.48).

The human health risk posed by *Pomacea canaliculata* with regard to its transmission of parasites was the focus of several studies which monitored snail populations in aquatic bodies near populated areas. One study examined the effect of the building of a dam in central Laos PDR on numbers of all snails including *Pomacea canaliculata* - the intermediate host of *A.cantonensis*- it was the snail species found in the greatest numbers during 2010 and 2011; numbers increased greatly from 1.3% in 2010 to 53.3% in 2011 (Brey, P.T. 2015).

In 2006/7 tsunami and non-tsunami affected areas of Takua Pa District, Phang-Nga Province were examined for snails that transmit human parasitic diseases - 16 species were identified including *Pomacea canaliculata*. Knowledge of these medically important snails and their parasitic diseases, and prevention were given to Takua Pa people (Butraporn, P. 2010).

Another public health focus of the literature regarding *Pomacea canaliculata* concerned their potential use as biomonitors in waterways which could be subject to heavy metal pollution. This was shown to effect the tissues of the snails in an observable manner at levels below the safety limit, at a lake in Thailand (10.1016/j.ecoenv.2012.09.018). Similarly another study focussed on the effect of copper sulphate exposure on the tissue of *Pomacea canaliculata*, they also found the snail to be an effective potential bioindicator of copper contamination in aquatic environments (10.1016/j.ecoenv.2015.08.010).

A better understanding of the general biology of *Pomacea canaliculata* led some

researchers to look at its life cycle (Arfan, A. et al 2015), whilst others examined genetic diversity (Bai, Xu et al 2011) and some specifically looked at tolerance of different climatic populations to dessication and cold (10.1093/mollus/eyq049).

Differing cultivation methods were examined to note any effect on the mortality rate of rice due to *Pomacea canaliculata* infested ponds. One study noted that planting out 21 days after sowing gave a greater chance of survival for the rice seedlings (10.1016/j.cropro.2014.06.022).

Aquatic or marine? Although *Pomacea canaliculata* is largely a freshwater snail, reference is made to them occupying, marsh, swamp and marine habitats (http://eol.org/pages/467346/overview).

Is there a description of any research locations that you can identify?

Snails in Beung Boraphet reservoir, Nakhon Sawan Province, central Thailand were examined in a study of metal pollution (10.1016/j.ecoenv.2012.09.018). Areas of Takua Pa District, Phang-Nga Province were investigated for fresh- and brackish-water snails that transmit human parasitic diseases during 2006 and 2007 (Butraporn, P. 2010). Another study in Thailand looked at natural microbe pathogens in the soil (10.1023/B:WIBI.0000007312.97058.48).

The Philippines is the location of a couple of studies including one on rice cultivation methods to reduce mortality (10.1016/j.cropro.2014.06.022), and a molluscicide study in Munoz, Nueva Ecija (De la Cruz, MS. and Joshi, RC 2001), as well as a genetic diversity analysis using a population from Los Banos (Bai, X. et al 2011).

The effect of building a dam on the snail population was investigated at Khammouane Province, central Laos (Brey, P.T. 2015).

China (Yuyao, Taizhou, Fuzhou, Guangzhou, Nanning, Kunming) (Bai, Xu et al 2011), Japan (Kyushu and Luzon Mindanao) (10.1093/mollus/eyq049) and Taiwan are also mentioned within the research literature (Baker, GH. 1998).

6.8.2 Patent activity

There are 114 patent documents for *Pomacea canaliculata*, the most commonly cited patent document is for a modified plant chemical called 'saponin' that can be used to kill these molluscs in areas where they are considered a pest US20070196517A1.

Lens collection

6.9 *Vibrio harveyi*

- **Species name:** *Vibrio harveyi*

- **Kingdom:** Bacteria
- **Phylum:** Proteobacteria GBIF

Brief Description of the Species:
Vibrio harveyi, is a Gram-negative, bioluminescent, common marine bacterium in the same genus as *Vibrio parahaemolyticus*. *V. harveyi* is rod-shaped and can be found free-swimming in tropical marine waters, living commensally in the gut microflora of marine animals, a minority of *V.harveyi* strains are pathogenic to marine animals, including Gorgonian corals, oysters, prawns, lobsters, the common snook, barramundi, turbot, milkfish, and seahorses. It is responsible for luminous vibriosis, a disease that affects commercially farmed penaeid prawns such as *P.monodon*. Additionally, based on samples taken by ocean-going ships, V. harveyi is thought to be the cause of the [milky seas effect] (https://www.nrl.navy.mil/media/news-releases/2005/nrl-scientists-detect-milky-sea-phenomena), in which, during the night, a uniform blue glow is emitted from the seawater. Some glows can cover nearly 6,000 sq mi (16,000 km2) (http://eol.org/pages/973242/details).

V. harveyi related strains have been isolated from the deep sea >1000m2, these may be ecologically differentiated strains, adapted to a different ecological niche or be distributed across the oceans (Thompson and Austin 2006).

Although normally a benign bacteria in marine cultured environments, the prevalence of the pathogenic strains of *V. harveyi* - that differ by a few pathogenic determinant genes - can cause a problem in high nutrient, high density conditions leading to a rapid spread of virulent strains (Ben-Haim et al., 2003).

Although closely related to the human pathogen *V. parahaemolyticus*, *V. harveyi* is not known as a human pathogen. This is one of the first organisms in which [quorum sensing] (https://www.ncbi.nlm.nih.gov/genome?term=txid669%5Borgn%5D) was described, whereby communities of bacteria communicate with each other via secreted signalling molecules synchronising community behaviour by regulating gene expression - both within and between bacteria species.

Known Distribution of the Species
Vibrio harveyi is a common bacteria inhabiting largely tropical marine waters - as it requires sodium chloride (10.1111/j.1472-765X.2006.01989.x), and prefers warmer water temperatures.

First description
Vibrio harveyi was named by Baumann et al. in 1981, further to the work of Johnson & Shunk, 1936 who originally named the species *Achromobacter herveyi*. GBIF

6.9.1 Scientific Research on the Species in the ASEAN Region

Research categories
Much of the research on *Vibrio harveyi* is categorised as Fisheries (72), Marine and Freshwater Biology (44), Veterinary Sciences (37), Immunology (30), Microbiology (24), Biotechnology and Applied Microbiology (23) and Biochemistry and Molecular Biology (19).

Research summary
The research effort on *Vibrio harveyi* is largely concerned with infection of fish, molluscs and crustaceans within the aquaculture industry. As such a lot of the *V. harveyi* literature is concerned with understanding the pathogenic strains of the bacteria that infects commercially farmed marine organisms, particularly shrimps: methods of rapidly detecting V.harveyi infections (2672.2003.02020.x), antimicrobial peptides produced by marine organisms that could combat *V.harveyi* (10.1016/j.aquaculture.2009.01.026) and naturally occurring compounds that have antimicrobial properties against *V.harveyi* whilst being safe to cultured marine organisms(10.1111/are.13043). Shrimps infected with *V. harveyi* produce an antimicrobial peptide that has been shown to be effective in combating the bacteria when administered into a culture or injected into shrimps(10.1016/j.aquaculture.2009.01.026).

Overuse of antibiotics in aquaculture is blamed for an increase in antibiotic resistant strains of bacteria (10.1016/j.fm.2016.02.008), so *V.harveyi* researchers are looking at alternative methods of combating the bacteria, including the use of novel natural compounds found in cyanobacteria(10.1111/are.13043) and extracts from *Sargassum oligocystum* (Apines-Amar, MJS. et al., 2011).

Aquatic or marine?
Vibrio harveyi is found in marine and estuarine waters, however its presence has also been noted in Giant Freshwater Prawn larvae which inhabit brackish water as juveniles and freshwater as adults(10.1016/j.aquaculture.2013.05.015).

Is there a description of any research locations that you can identify?
Much of the research referencing specific locations for *V.harveyi* is from investigations into the cause of aquaculture shrimp mortalities as was the case in pond-cultured Penaeus monodon in the provinces of Bohol, Misamis Occidental, Lanao del Norte and Zamboanga del Sur, Philippines (Inui, Y. et al., 2003). Similarly dead shrimp larvae from hatcheries in Jepara, Indonesia(10.1016/0044-8486(94)00374-W), Southern Thailand (10.3354/dao035195), and Iran (Afsharnasab, M. et al., 2014) were found to contain *V.harveyi*. Seasonal changes in the composition of a variety of vibrio species including *V.harveyi* were investigated in samples taken from Yoshimi Bay, Hibiki-nada Sea, Japan.

6.9.2 Patent activity

Nucleic acid and amino acid sequences relating to pseudomonas aeruginosa for methods for the detection, prevention and treatment of pathological conditions resulting from bacterial infection including *V.harveyi*.

Microorganisms for therapy wherein the microorganisms gather in inflamed or cancerous tissues and cause cells to become leaky, resulting in production of antibodies, one such type of microorganism is attentuated Vibrio

Lens collection

6.10 *Vibrio parahaemolyticus*

- **Species name:** *Vibrio parahaemolyticus*
- **Kingdom:** Bacteria

- **Phylum:** Proteobacteria GBIF

Brief Description of the Species:
Vibrio parahaemolyticus, is a gram negative bacteria that is found in estuarine, coastal and marine waters Letchumanan et al 2014 and is present in higher concentrations between May and October when temperatures are warmer CDC. *V. parahaemolyticus* responsible for the disease vibriosis in humans, contracted through eating raw contaminated shellfish such as oysters, or exposure of a wound to infected salt or brackish water CDC. *V. parahaemolyticus* is found in a free swimming state, using a single flagellum to attach to zooplankton, fish, shellfish or suspended matter in the water Letchumanan et al 2014(10.3389/fmicb.2014.00705). The prevalence of the pathogenic strains of *V. parahaemolyticus* isolated from seafood, and clinical samples shows it to have a worldwide distribution across South East Asia, Europe, and US posing an ongoing health threat to the population. Within Asia, samples have been found in seafood in markets in China, Malaysia, India, Bangladesh, Taiwan, Laos, hong Kong and Japan Letchumanan et al 2014(10.3389/fmicb.2014.00705).

Known Distribution of the Species
"Present in the Gulf of Mexico" GBIF.

First description
Vibrio parahaemolyticus was named by Sazaki et al.in 1963, further to the work of Fujino et al. in 1951 who originally named the species *Pasteurella parahaemolytica* (GBIF).

Figure 6.7: Janice Carr/CDC

6.10.1 Scientific Research on the Species in the ASEAN Region

Research categories
Much of the research on *Vibrio parahaemolyticus* is categorised as Microbiology (60), Food Science and Technology (30), Biotechnology and Applied Microbiology (29), Fisheries (29), Veterinary Sciences (21), Infectious diseases (19), Marine and Freshwater Biology (17), Immunology (11) and so on.

Research summary
The research effort on *Vibrio parahaemolyticus* is largely concerned with infection of fish, molluscs and crustaceans within the aquaculture industry, as well as infection of humans that eat infected seafood. As such a lot of the *V. parahaemolyticus* literature is concerned with understanding the pathogenic strains of the bacteria that infects humans and commercially reared seafood including: methods of rapidly detecting strains causing an infection (10.1017/S0950268806006017), vaccines offering protection (10.1016/j.vaccine.2011.04.021) and ways of treating the infection. Shrimps infected with *Vibrio parahaemolyticus* can develop acute hepatopancreatic necrosis disease causing severe mortalities in SE Asia and Mexico, some research has been directed to noting any genetic difference between bacterial infections from different geographical areas.

Overuse of antibiotics in aquaculture is blamed for an increase in antibiotic resistant strains of *Vibrio parahaemolyticus* (10.1016/j.fm.2016.02.008), so researchers are also looking at alternative methods of combatting the bacteria: including the use of bacteria phage - such as one discovered in Laos (Higa, N. et al 1999). In ensuring people don't become sick from eating seafood, some research has been focussed on food preservatives that extend the life of seafood because of their inhibitory effect on *Vibrio parahaemolyticus*such as botanical extracts from *Terminalia chebula* (Kaewmanee,P et al 2012) and *Zingiber spectabile*(10.1016/j.foodcont.2012.09.012), and best practice for safe processing of seafood (10.1016/j.foodcont.2012.02.009). There are many studies noting the range of strains present in certain geographic areas, in Taiwan and 14 other countries 535 strains were identified of *Vibrio parahaemolyticus* (10.1016/j.ijfoodmicro.2006.09.024) - either by testing samples of infected faeces of people from clinical settings, (10.1099/jmm.0.47439-0) or sampling water and noting the strains of *Vibrio parahaemolyticus* present. Certain strains are given more attention, as they are more virulent, pathogenic and novel - so there is little resistance in the local human population - it is these strains, such as the pandemic strain, that are of more concern in the literature.

Aquatic or marine?
Vibrio parahaemolyticus is found in marine and brackish waters, however its presence has also been noted in a tropical coastal lagoon from 2 samples collected in the estuary near Yor Island, Songkhla Lake, Thailand (10.1139/W11-084).

Is there a description of any research locations that you can identify?
Much of the research involving samples taken from humans infected with *Vibrio parahaemolyticus* reference a country for example:US, Italy, Brazil, Philippines, Malaysia, China, India, Thailand, Iran, South Africa and Australia, (10.1016/j.fm.2016.02.008). Some clinical studies are more specific in noting a hospital or region: a study conducted at Hat Yai Hospital in southern Thai-

land (10.1099/jmm.0.47439-0) for example, and a similar stool sample study in the infectious Diseases Hospital in Kolkata, India examining strains present in infected samples using the PFGE analysis technique to identify the strains (10.1371/journal.pntd.0002815). Food poisoning cases in Kangawa Prefecture, Japan were the source of 18 strains of *V. parahaemolyticus* studied in laboratories in Thailand to note the specific genes present (10.1007/s002849900188).

Forty two strains of *Vibrio parahaemolyticus* were isolated form samples of water taken form the estuaries around Bangladesh in the Bay of Bengal, with some being of the virulent and ptahogenic strains posing a risk to inhabitants of coastal villeages in the area(42 10.1128/AEM.00266-09). A study on patients with diarrhoea in North Jakarta, Indonesia, found *Vibrio parahaemolyticus* was responsible for a substantial number of cases, with incidence being highest in the dry season (June and July), many of the samples showed antibiotic resistance to some antibiotics (10.1016/S0732-8893(00)00232-7).

Samples of seafood were analysed from Hong Kong, Indonesia, Thailand and Vietnam - of the samples taken 45.9% contained *Vibrio parahaemolyticus*, with more of teh samples from Hong Kong and Thailand containing teh bacteria (10.1016/S0168-1605(99)00143-9).

170 strains of *V. parahaemolyticus* were isolated from water samples collected along the Georgian coast of the Black Sea, water temperature was shown to be a factor in its presence especially in the Green cape samples(10.3389/fmicb.2014.00045).

###Patent activity

The top cited patent document involving *V. parahaemolyticus* is for identification of essential genes used to help *V. parahaemolyticus* multiply - a sequence of nucleic acids is used to undertsand which are the key important proteins in the bacteria and then drugs, or antibodies can be produced to prevent replication of the bacteria.

The patent document with the largest family is for the use of a peptide as a therapeutic agent when someone has a *V. parahaemolyticus* infection.

Lens collection

Chapter 7

Annex 2: Methodology

In this section we describe the basic methodology and data sources used for the Scientific and Patent Landscape for Marine Genetic Resources in South East Asia. Methods can be divided into the following categories.

1. Searching the Scientific Literature
2. Searching the Patent Literature
3. Identifying Species Names

7.1 The Scientific Literature

Web of Science from Clarivate Analytics (formerly Thomson Reuters) is a leading commercial database of scientific literature and is widely available in Universities. Web of Science covers thousands of journals across multiple subjects and is made up of a number of databases available under a range of subscription models. We used the Web of Science (WOS) Core Collection consisting of data from over 18,000 journals along with conference proceedings. This database is common to all subscription models for Web of Science (with the others being optional). Use of the Core Collection therefore assists with the reproducibility of research. The Core Collection also contains more detailed fields, for example on author affiliations, than other databases in the family and is therefore a preferred choice for bibliometric research.

7.1.1 Searching Web of Science

We focused on obtaining scientific literature about the ten ASEAN countries in two categories:

1. Scientific literature listing an author from the country in the Address field of scientific publications.

2. Scientific Literature that referenced the country in the Topic Field (Titles, Abstracts, Author Keywords and Keywords Plus (titles of cited literature))

We searched across all years beginning in 1900 to the period between late May 2017 and mid-June 2017.

Downloads of Web of Science records were formerly limited to 500 records per set. Where the number of records exceeded 100,000 we sought to limit the datasets by Web of Science Subject Categories. Web of Science Subject Categories describe the *subject areas* of journals in Web of Science rather than the articles themselves. In selecting the Subject Categories we focused on those areas with a biological connection and for traditional knowledge we looked at the social sciences. The Analyze function in Web of Science permits the ranking of records based on the subject category and aided in the selection process.

In cases where we refined the data by subject area we typically started the research by using the Analyze function on subject categories ordered alphabetically to make the selection. This was limited to the top 100 categories. In a second step we then used the full list to download a smaller set containing other relevant subject categories. Typically these were smaller subject areas (such as Entomology or Marine Engineering) that did not appear in the top 100. To capture data potentially relevant to traditional knowledge we included social science subject areas while recognising that the majority of records would not be relevant.

In cases where datasets were refined by subject category we sought to cast the net as widely as possible while keeping the results below 100,000.

7.1.2 Overall Trends

We obtained an overview of research trends for each category using the `Analyze` function in Web of Science to identify the top 500 authors, the top 600 organizations (organizations enhanced), data on publication years, and the ranked Web of Science Subject Categories.

We then downloaded the results, tidied up the data titles and imported the files into RStudio. Individual country data was joined using the dplyr function `full_join` for an SQL join. Because the data for each country varies in length, this joins the tables together on the subject categories and introduces an NA for Not Available where a category is missing for an individual field. These files were compiled in the data folder of the repository as `asean_authors`, `asean_categiries`, `asean_organizations` and `asean_year`.

7.2 Patent Data

Patent Data for the research consisted of three components.

1. PATSTAT

The EPO World Patent Statistical Database (PATSTAT) is a statistical database developed by the European Patent Office in collaboration with OECD and other partners. It contains the basic content of the core DOCDB database and has been augmented with additional data tables such as cleaned assignee names and economic sector tables. As a statistical database PATSTAT is not suitable for text mining and requires knowledge of SQL.

We used the Intelligent Information Services Corporation (IISC) portal to access the EPO World Patent Statistical Database (PATSTAT) Autumn 2016 edition. PATSTAT is a SQL based database and IISC has the advantage of providing a simplified interface and directly compiling datasets for use in VantagePoint from Search Technology Inc. This considerably simplified the requirements for using PATSTAT and processing the data but is limited to VantagePoint users.

Query construction in IISC PATSTAT is straightforward. We constructed two queries for the ASEAN data. The first query involves searching for records where an ASEAN country code appears in the person country field of the person PATSTAT tls206_person table.

Dataset 1 Query:

"(**?** (BN | KH | ID | LA | MY | MM | PH | SG | TH | VN))""

Dataset 1 file: asean_person_country_patstat.vpt

This 6 gigabyte dataset in VantagePoint format contains 109,744 application records where the person_country in PATSTAT table tls206_person country contained a two letter country code that was either xxxxxx.

Dataset 2 Query:

"(**?** (BN | KH | ID | LA | MY | MM | PH | SG | TH | VN))"

Dataset 2: asean_publn_auth_patstat.

This 4.8 Gigabyte file contains 173,461 application records filed within the 10 ASEAN countries.

2. ABSPAT

ABSPAT is an in house research dataset that is based on text mining 11 million full text patent documents from the European Patent Office, the United States Patent and Trademark Office and the Patent Cooperation Treaty in the period to 2013. The index consists of references to species names that appear in the title, abstract, description or claims of patent documents using the Global Names Index (see below). The index was improved in 2014 by adding an additional index using the World Register of Marine Species (WoRMS) and additional data from the Ocean Biogeographic Information System database. The index covers patent documents back to 1976 but terminates in 2013 when the research on which it is based was completed (in 2014).

3. Clarivate Analytics Derwent Innovation

Clarivate Analytics provides access to the commercial Derwent Innovation (formerly Thomson Innovation). Derwent Innovation has the advantage of possessing copies of the National Collections for ASEAN countries. In addition Derwent Innovation provides ready access to whole texts exports for text mining and additional supplementary Abstract fields prepared by specialists on the use, advantage and novelty of a claimed invention. This information can be very useful in understanding the focus of an invention.

We downloaded the relevant records from Derwent Innovation for text mining using Vantage Point. In a subsequent step described in greater detail in the section on the patent landscape we used a modified search to capture additional references to species and an ASEAN country. This data was text mined to identify marine species in the title, abstract, description and claims.

7.3 Species Data

The raw data from Web of Science was imported in to the Academic version of VantagePoint text mining and analytics software from Search Technology Inc. Vantage Point provides easy access to the words and phrases that appear in the titles, abstracts, author keywords and keywords plus of Web of Science data.

Building on previous work we used a version of the Global Names Index that had been edited from the original 19 million to a list of 6 million binomial names. This list was used to identify species names in the combined titles, abstracts, author keywords and keywords plus.

Marine species in the species data were identified using a text version of the World Register of Marine Species.

The species names and species like names in the Global Names Index are raw names and include many spelling variations and synonyms for the same species. To resolve these issues we used the Global Biodiversity Information Facility (GBIF) API or web service through the ROpenSci rgbif and taxize.

In an additional step the Lifewatch Belgium data service was used for bulk retrieval of information on Aphia accepted names and available environment information from the WoRMS online database.

Species occurrence data was downloaded from GBIF for each ASEAN country and an additional bounding box dataset was downloaded to capture additional marine records as described in section 1 on Biodiversity in the ASEAN region.

7.4 Mapping

The geographic locations of research organisations involved in marine research were converted from abbreviated form in Web of Science to longer forms suitable for georeferencing.

We used the R `placement` package to access the Google Maps API to geocode organisation names in Web of Science data. The data was visualized in Tableau

7.5 Data Processing

Name cleaning for person and organisation names was performed in VantagePoint from Search Technology Inc.

The majority of data processing was performed in the R programming language (R Core Team, 2013). Primary data processing was performed using the tidyverse packages developed by Hadley Wickham and colleagues. The refinr package by Chris Muir was used for additional name cleaning. The geofacet package by Ryan Hafen was used in the creation of faceted plots.

ROpenSci packages were used extensively during the research, notably rgbif, taxize and rcrossref developed and maintained by Scott Chamberlain and colleagues.

Text mining was performed in Vantage Point and in R using the tidytext package from Julia Silge and Daniel Robinson (Fay, 2018)

7.6 Visualisation

Visualisation of the data outside the mapping using leaflet was carried out as follows

1. Exploratory graphs were created in R with ggplot2 and later with geofacet. The main graphing was conducted in Tableau
2. Networks were visualised in Gephi
3. Sankey diagrams were created in R using the networkD3 package
4. An online interactive workbook was created in Tableau Public

Bibliography

(2015). Rhizophora apiculata: Duke, n., kathiresan, k., salmo III, s.g., fernando, e.s., peras, j.r., sukardjo, s. & miyagi, t.

Allaire, J., Xie, Y., McPherson, J., Luraschi, J., Ushey, K., Atkins, A., Wickham, H., Cheng, J., and Chang, W. (2018). *rmarkdown: Dynamic Documents for R*. R package version 1.10.

Arnaud-Haond, S., Teixeira, S., Massa, S. I., Billot, C., Saenger, P., Coupland, G., Duarte, C. M., and Serrão, E. A. (2006). Genetic structure at range edge: low diversity and high inbreeding in southeast asian mangrove (avicennia marina) populations. *Molecular Ecology*, 15(12):3515–3525.

Aung, T. T., Than, M. M., Katsuhiro, O., and Yukira, M. (2011). Assessing the status of three mangrove species restored by the local community in the cyclone-affected area of the ayeyarwady delta, myanmar. *Wetlands Ecology and Management*, 19(2):195–208.

Ayuningrum, D., Kristiana, R., Asagabaldan, M., Sabdono, A., Radjasa, O., Nuryadi, H., and Trianto, A. (2017). Isolation, characterisation and antagonistic activity of bacteria symbionts hardcoral pavona sp. isolated from panjang island, jepara against infectious multi-drug resistant (MDR) bacteria. *IOP Conference Series: Earth and Environmental Science*, 55:012029.

Baie, S. H. and Sheikh, K. (2000). The wound healing properties of channa striatus-cetrimide cream — tensile strength measurement. *Journal of Ethnopharmacology*, 71(1-2):93–100.

Barghi, N., Concepcion, G. P., Olivera, B. M., and Lluisma, A. O. (2015). Characterization of the complete mitochondrial genome of conus tribblei walls, 1977. *Mitochondrial DNA Part A*, 27(6):4451–4452.

Bentsen, H. B., Eknath, A. E., de Vera, M. S. P., Danting, J. C., Bolivar, H. L., Reyes, R. A., Dionisio, E. E., Longalong, F. M., Circa, A. V., Tayamen, M. M., and Gjerde, B. (1998). Genetic improvement of farmed tilapias: growth performance in a complete diallel cross experiment with eight strains of oreochromis niloticus. *Aquaculture*, 160(1-2):145–173.

Blondel, V. D., Guillaume, J.-L., Lambiotte, R., and Lefebvre, E. (2008). Fast

unfolding of communities in large networks. *Journal of Statistical Mechanics: Theory and Experiment*, 2008(10):P10008.

Bonami, J.-R. and Widada, J. S. (2011). Viral diseases of the giant fresh water prawn macrobrachium rosenbergii: A review. *Journal of Invertebrate Pathology*, 106(1):131–142.

Boonsri, N., Rudtanatip, T., Withyachumnarnkul, B., and Wongprasert, K. (2016). Protein extract from red seaweed gracilaria fisheri prevents acute hepatopancreatic necrosis disease (AHPND) infection in shrimp. *Journal of Applied Phycology*, 29(3):1597–1608.

Brenner, S., Elgar, G., Sanford, R., Macrae, A., Venkatesh, B., and Aparicio, S. (1993). Characterization of the pufferfish (fugu) genome as a compact model vertebrate genome. *Nature*, 366(6452):265–268.

Cai, Y. and Ng, P. K. L. (2002). The freshwater palaemonid prawns (crustacea: Decapoda: Caridea) of myanmar. *Hydrobiologia*, 487(1):59–83.

Callow, J. A. and Callow, M. E. (2011). Trends in the development of environmentally friendly fouling-resistant marine coatings. *Nature Communications*, 2:244.

Chamberlain, S. (2018). *rgbif: Interface to the Global 'Biodiversity' Information Facility API*. https://github.com/ropensci/rgbif (devel) https://ropenscilabs.github.io/occurrence-manual/ (manual).

Chamberlain, S., Szoecs, E., Foster, Z., and Arendsee, Z. (2018). *taxize: Taxonomic Information from Around the Web*. R package version 0.9.4.

Chang, Y., Liu, W., Chen, T., Chan, T., Liu, K., Chuang, J., Kou, G., Lo, C., and Wang, H. (2012). Feeding hermit crabs to shrimp broodstock increases their risk of WSSV infection. *Diseases of Aquatic Organisms*, 98(3):193–199.

da Silva, V. A., dos Santos, F. L., Bezerra, S. S., Pedrosa, V. F., de P. Mendes, P., and Mendes, E. S. (2010). A multi-season survey for infectious myonecrosis in farmed shrimp, litopenaeus vannamei, in pernambuco, brazil. *Journal of Invertebrate Pathology*, 104(3):161–165.

De Grave, S., Shy, J., and Wowor, D. & Page, T. (2012). Macrobrachium rosenbergii.

de Groof, A., Guelen, L., Deijs, M., van der Wal, Y., Miyata, M., Ng, K. S., van Grinsven, L., Simmelink, B., Biermann, Y., Grisez, L., van Lent, J., de Ronde, A., Chang, S. F., Schrier, C., and van der Hoek, L. (2015). A novel virus causes scale drop disease in lates calcarifer. *PLOS Pathogens*, 11(8):e1005074.

Doi, M., Toledo, J. D., Golez, M. S. N., de los Santos, M., and Ohno, A. (1997). *Hydrobiologia*, 358(1/3):259–263.

Duangprom, S., Kornthong, N., Suwansa-ard, S., Srikawnawan, W., Chotwiwatthanakun, C., and Sobhon, P. (2017). Distribution of crustacean hyper-

glycemic hormones (CHH) in the mud crab (scylla olivacea) and their differential expression following serotonin stimulation. *Aquaculture*, 468:481–488.

Duke, N., Kathiresan, K., Salmo III, S., Fernando, E.S. andPeras, J., Sukardjo, S., Miyagi, T., Ellison, J., Koedam, N., Wang, Y., Primavera, J., Jin Eong, O., and Wan-Hong Yong, J. & Ngoc Nam, V. (2008). Avicennia marina.

Eusebio, P. S., Coloso, R. M., and Mamauag, R. E. P. (2004). Apparent digestibility of selected ingredients in diets for juvenile grouper, epinephelus coioides (hamilton). *Aquaculture Research*, 35(13):1261–1269.

Fay, C. (2018). Text mining with r: A tidy approach. *Journal of Statistical Software*, 83(Book Review 1).

Floerl, O., Sunde, L., and Bloecher, N. (2016). Potential environmental risks associated with biofouling management in salmon aquaculture. *Aquaculture Environment Interactions*, 8:407–417.

Gamage, R. N. (2016). Blue economy in southeast asia: Oceans as the new frontier of economic development. *Maritime Affairs: Journal of the National Maritime Foundation of India*, 12(2):1–15.

Giang, L. H., Hong, P. N., Tuan, M. S., and Harada, K. (2003). Genetic variation of avicennia marina (forsk.) vierh. (avicenniaceae) in vietnam revealed by microsatellite and AFLP markers. *Genes & Genetic Systems*, 78(6):399–407.

Gonnet, F., Bouazza, B., Millot, G. A., Ziaei, S., Garcia, L., Butler-Browne, G. S., Mouly, V., Tortajada, J., Danos, O., and Svinartchouk, F. (2008). Proteome analysis of differentiating human myoblasts by dialysis-assisted two-dimensional gel electrophoresis (DAGE). *PROTEOMICS*, 8(2):264–278.

Guo, M., Wei, J., Huang, X., Huang, Y., and Qin, Q. (2012). Antiviral effects of beta-defensin derived from orange-spotted grouper (epinephelus coioides). *Fish & Shellfish Immunology*, 32(5):828–838.

Guo, S. F., Lee, H. P., Chaw, K. C., Miklas, J., Teo, S. L. M., Dickinson, G. H., Birch, W. R., and Khoo, B. C. (2011). Effect of ultrasound on cyprids and juvenile barnacles. *Biofouling*, 27(2):185–192.

Hai, T. N. and Yakupitiyage, A. (2005). The effects of the decomposition of mangrove leaf litter on water quality, growth and survival of black tiger shrimp (penaeus monodon fabricius, 1798). *Aquaculture*, 250(3-4):700–712.

Hawkins, A., Smith, R., Tan, S., and Yasin, Z. (1998). Suspension-feeding behaviour in tropical bivalve molluscs:perna viridis, crassostrea belcheri, crassostrea iradelei, saccostrea cucculata and pinctada margarifera. *Marine Ecology Progress Series*, 166:173–185.

Hishamunda, N., Ridler, N. B., Bueno, P., and Yap, W. G. (2009). Commercial aquaculture in southeast asia: Some policy lessons. *Food Policy*, 34(1):102–107.

hua Hu, Y. and Sun, L. (2011). A bivalent vibrio harveyi DNA vaccine induces strong protection in japanese flounder (paralichthys olivaceus). *Vaccine*, 29(26):4328–4333.

Isa, I. I. M., Bakar, S. A., Tohid, S. F. M., and Jais, A. M. M. (2016). Channa striatus cream down-regulates tumour necrosis factor (TNF)-alpha gene expression and alleviates chronic-like dermatitis in mouse model. *Journal of Ethnopharmacology*, 194:469–474.

JACOBSEN, R., JIMENEZ, E. C., GRILLEY, M., WATKINS, M., HILLYARD, D., CRUZ, L. J., and OLIVERA, B. M. (2009). The contryphans, a d-trvptophan-containing family of conus peptides: interconversion between conformers. *The Journal of Peptide Research*, 51(3):173–179.

Jain, R., Monthakantirat, O., Tengamnuay, P., and De-Eknamkul, W. (2014). Avicequinone c isolated from avicennia marina exhibits 5a-reductase-type 1 inhibitory activity using an androgenic alopecia relevant cell-based assay system. *Molecules*, 19(5):6809–6821.

Jain, R., Monthakantirat, O., Tengamnuay, P., and De-Eknamkul, W. (2015). Identification of a new plant extract for androgenic alopecia treatment using a non-radioactive human hair dermal papilla cell-based assay. *BMC Complementary and Alternative Medicine*, 16(1).

Jaree, P., Tassanakajon, A., and Somboonwiwat, K. (2012). Effect of the anti-lipopolysaccharide factor isoform 3 (ALFPm3) from penaeus monodon on vibrio harveyi cells. *Developmental & Comparative Immunology*, 38(4):554–560.

Jyothi-Prakash, P. A., Mohanty, B., Wijaya, E., Lim, T.-M., Lin, Q., Loh, C.-S., and Kumar, P. P. (2014). Identification of salt gland-associated genes and characterization of a dehydrin from the salt secretor mangrove avicennia officinalis. *BMC Plant Biology*, 14(1).

Kaewkascholkul, N., Somboonviwat, K., Asakawa, S., Hirono, I., Tassanakajon, A., and Somboonwiwat, K. (2016). Shrimp miRNAs regulate innate immune response against white spot syndrome virus infection. *Developmental & Comparative Immunology*, 60:191–201.

Kamal, A. H. M. M. and Mair, G. C. (2005). Salinity tolerance in superior genotypes of tilapia, oreochromis niloticus, oreochromis mossambicus and their hybrids. *Aquaculture*, 247(1-4):189–201.

Kangpanich, C., Pratoomyot, J., Siranonthana, N., and Senanan, W. (2016). Effects of arachidonic acid supplementation in maturation diet on female reproductive performance and larval quality of giant river prawn (macrobrachium rosenbergii). *PeerJ*, 4:e2735.

Karaket, T. and Poompuang, S. (2012). CERVUS vs. COLONY for successful parentage and sibship determinations in freshwater prawn macrobrachium rosenbergii de man. *Aquaculture*, 324-325:307–311.

Khong, N. M., Yusoff, F. M., Jamilah, B., Basri, M., Maznah, I., Chan, K. W., and Nishikawa, J. (2016). Nutritional composition and total collagen content of three commercially important edible jellyfish. *Food Chemistry*, 196:953–960.

Kiem, P. V., Huyen, L. T., Hang, D. T., Nhiem, N. X., Tai, B. H., Anh, H. L. T., Cuong, P. V., Quang, T. H., Minh, C. V., Dau, N. V., Kim, Y.-A., Subedi, L., Kim, S. Y., and Kim, S. H. (2017). Sesquiterpene derivatives from marine sponge smenospongia cerebriformis and their anti-inflammatory activity. *Bioorganic & Medicinal Chemistry Letters*, 27(7):1525–1529.

Kim, S.-K. and Li, Y.-X. (2012). Biological activities and health effects of terpenoids from marine fungi. In *Marine Medicinal Foods - Implications and Applications - Animals and Microbes*, pages 409–413. Elsevier.

KRISHNAMURTHY, P., JYOTHI-PRAKASH, P. A., QIN, L., HE, J., LIN, Q., LOH, C.-S., and KUMAR, P. P. (2014). Role of root hydrophobic barriers in salt exclusion of a mangrove plantAvicennia officinalis. *Plant, Cell & Environment*, 37(7):1656–1671.

Krishnamurthy, P., Tan, X. F., Lim, T. K., Lim, T.-M., Kumar, P. P., Loh, C.-S., and Lin, Q. (2014). Proteomic analysis of plasma membrane and tonoplast from the leaves of mangrove plantAvicennia officinalis. *PROTEOMICS*, 14(21-22):2545–2557.

Leu, J.-H., Chang, C.-C., Wu, J.-L., Hsu, C.-W., Hirono, I., Aoki, T., Juan, H.-F., Lo, C.-F., Kou, G.-H., and Huang, H.-C. (2007). Comparative analysis of differentially expressed genes in normal and white spot syndrome virus infected penaeus monodon. *BMC Genomics*, 8(1):120.

Loy, J., Loy, D., Mogler, M., Janke, B., Kamrud, K., Harris, D., and Bartholomay, L. (2013). Sequence-optimized and targeted double-stranded RNA as a therapeutic antiviral treatment against infectious myonecrosis virus in litopenaeus vannamei. *Diseases of Aquatic Organisms*, 105(1):57–64.

Loy, J. D., Mogler, M. A., Loy, D. S., Janke, B., Kamrud, K., Scura, E. D., Harris, D. L. H., and Bartholomay, L. C. (2012). dsRNA provides sequence-dependent protection against infectious myonecrosis virus in litopenaeus vannamei. *Journal of General Virology*, 93(Pt_4):880–888.

Maneechote, N., ek Yingyongnarongkul, B., Suksamran, A., and Lumyong, S. (2016). Inhibition ofVibriospp. by 2-hydroxyethyl-11-hydroxyhexadec-9-enoate of marine CyanobacteriumLeptolyngbyasp. LT19. *Aquaculture Research*, 48(5):2088–2095.

Marasigan, A. N., Sato, S., Fukuyo, Y., and Kodama, M. (2001). Accumulation of a high level of diarrhetic shellfish toxins in the green mussel perna viridis during a bloom of dinophysis caudata and dinophysis miles in sapian bay, panay island, the philippines. *Fisheries Science*, 67(5):994–996.

Meeratana, P., Withyachumnarnkul, B., Damrongphol, P., Wongprasert, K.,

Suseangtham, A., and Sobhon, P. (2006). Serotonin induces ovarian maturation in giant freshwater prawn broodstock, macrobrachium rosenbergii de man. *Aquaculture*, 260(1-4):315–325.

Minh, C. V., Kiem, P. V., and Dang, N. H. (2017). Marine natural products and their potential application in the future. *ASEAN Journal on Science and Technology for Development*, 22(4):297.

Mohd-Yusof, N. Y., Monroig, O., Mohd-Adnan, A., Wan, K.-L., and Tocher, D. R. (2010). Investigation of highly unsaturated fatty acid metabolism in the asian sea bass, lates calcarifer. *Fish Physiology and Biochemistry*, 36(4):827–843.

Montresor, A., Cong, D. T., Anh, T. L., Ehrhardt, A., Mondadori, E., Thi, T. D., Khanh, T. L., Albonico, M., and Palmer, K. L. (2007). Cost containment in a school deworming programme targeting over 2.7 million children in vietnam. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 101(5):461–464.

Nair, G. B., Ramamurthy, T., Bhattacharya, S. K., Dutta, B., Takeda, Y., and Sack, D. A. (2007). Global dissemination of vibrio parahaemolyticus serotype o3:k6 and its serovariants. *Clinical Microbiology Reviews*, 20(1):39–48.

Ngoc, N. T., Huong, P. T. M., Thanh, N. V., Chi, N. T. P., Dang, N. H., Cuong, N. X., Nam, N. H., Thung, D. C., Kiem, P. V., and Minh, C. V. (2017). Cytotoxic steroids from the vietnamese soft coral sinularia conferta. *Chemical and Pharmaceutical Bulletin*, 65(3):300–305.

Nguyen, B., Caer, J.-P., Mourier, G., Thai, R., Lamthanh, H., Servent, D., Benoit, E., and Molgó, J. (2014a). Characterization of a novel conus bandanus conopeptide belonging to the m-superfamily containing bromotryptophan. *Marine Drugs*, 12(12):3449–3465.

Nguyen, B., Caer, J.-P. L., Aráoz, R., Thai, R., Lamthanh, H., Benoit, E., and Molgó, J. (2014b). Isolation, purification and functional characterization of alpha-BnIA from conus bandanus venom. *Toxicon*, 91:155–163.

Nguyen, B., Caer, J.-P. L., Lamthanh, H., Mourier, G., Servent, D., Aráoz, R., Benoit, E., and Molgó, J. (2014c). 41. a novel bromotryptophan gamma-carboxyglutamic acid-containing-conotoxin from the venom of conus bandanus. *Toxicon*, 91:181.

Nguyen, B., Molgó, J., Lamthanh, H., Benoit, E., Khuc, T. A., Ngo, D. N., Nguyen, N. T., Millares, P., and Caer, J.-P. L. (2013). High accuracy mass spectrometry comparison of conus bandanus and conus marmoreus venoms from the south central coast of vietnam. *Toxicon*, 75:148–159.

Nguyen, H., Caruso, D., Lebrun, M., Nguyen, N., Trinh, T., Meile, J.-C., Chu-Ky, S., and Sarter, S. (2016). Antibacterial activity ofLitsea cubeba(lauraceae, may chang) and its effects on the biological response of common carpCyprinus

carpiochallenged withAeromonas hydrophila. *Journal of Applied Microbiology*, 121(2):341–351.

Nimrat, S., Boonthai, T., and Vuthiphandchai, V. (2011). Effects of probiotic forms, compositions of and mode of probiotic administration on rearing of pacific white shrimp (litopenaeus vannamei) larvae and postlarvae. *Animal Feed Science and Technology*, 169(3-4):244–258.

Nimrat, S., Siriboonlamom, S., Zhang, S., Xu, Y., and Vuthiphandchai, V. (2006). Chilled storage of white shrimp (litopenaeus vannamei) spermatophores. *Aquaculture*, 261(3):944–951.

Olewiler, N., Francisco, H. A., and Ferrer, A. J. G., editors (2016). *Marine and Coastal Ecosystem Valuation, Institutions, and Policy in Southeast Asia*. Springer Singapore.

Pangestuti, R. and Kim, S.-K. (2015). Peptide-derived from seahorse exerts a protective effect against cholinergic neuronal death in in vitro model of alzheimer's disease. *Procedia Chemistry*, 14:343–352.

Petrone, L., Lee, S. S. C., Teo, S. L. M., and Birch, W. R. (2013). A novel geometry for a laboratory-based larval settlement assay. *Biofouling*, 29(2):213–221.

Phang, I. Y., Chaw, K. C., Choo, S. S. H., Kang, R. K. C., Lee, S. S. C., Birch, W. R., Teo, S. L. M., and Vancso, G. J. (2009). Marine biofouling field tests, settlement assay and footprint micromorphology of cyprid larvae ofBalanus amphitriteon model surfaces. *Biofouling*, 25(2):139–147.

Pongtippatee, P., Vanichviriyakit, R., Chavadej, J., Plodpai, P., Pratoomchart, B., Sobhon, P., and Withyachumnarnkul, B. (2007). Acrosome reaction in the sperm of the black tiger shrimp penaeus monodon (decapoda, penaeidae). *Aquaculture Research*, 38(15):1635–1644.

Ponprateep, S., Somboonwiwat, K., and Tassanakajon, A. (2009). Recombinant anti-lipopolysaccharide factor isoform 3 and the prevention of vibriosis in the black tiger shrimp, penaeus monodon. *Aquaculture*, 289(3-4):219–224.

Ponprateep, S., Tassanakajon, A., and Rimphanitchayakit, V. (2011). A kazal type serine proteinase SPIPm2 from the black tiger shrimp penaeus monodon is capable of neutralization and protection of hemocytes from the white spot syndrome virus. *Fish & Shellfish Immunology*, 31(6):1179–1185.

Preyavichyapugdee, N., Sahaphong, S., Riengrojpitak, S., Grams, R., Viyanant, V., and Sobhon, P. (2008). Fasciola gigantica and schistosoma mansoni: Vaccine potential of recombinant glutathione s-transferase (rFgGST26) against infections in mice. *Experimental Parasitology*, 119(2):229–237.

Qin, Q., Wu, T., Jia, T., Hegde, A., and Zhang, R. (2006). Development and characterization of a new tropical marine fish cell line from grouper, epinephelus coioides susceptible to iridovirus and nodavirus. *Journal of Virological Methods*, 131(1):58–64.

Quang, T. H., Ha, T. T., Minh, C. V., Kiem, P. V., Huong, H. T., Ngan, N. T. T., Nhiem, N. X., Tung, N. H., Tai, B. H., Thuy, D. T. T., Song, S. B., Kang, H.-K., and Kim, Y. H. (2011). Cytotoxic and anti-inflammatory cembranoids from the vietnamese soft coral lobophytum laevigatum. *Bioorganic & Medicinal Chemistry*, 19(8):2625–2632.

R Core Team (2013). *R: A Language and Environment for Statistical Computing*. R Foundation for Statistical Computing, Vienna, Austria.

R Core Team (2018). *R: A Language and Environment for Statistical Computing*. R Foundation for Statistical Computing, Vienna, Austria.

Rahman, M., Bhuiyan, N. A., Kuhn, I., Ramamurthy, T., Rahman, M., Mollby, R., and Nair, G. B. (2006). Biochemical fingerprinting of vibrio parahaemolyticus by the PhenePlate system: comparison between pandemic and non-pandemic serotypes. *Epidemiology and Infection*, 134(05):985.

Rahman, R., Leow, T., Salleh, A., and Basri, M. (2007). Geobacillus zalihae sp. nov., a thermophilic lipolytic bacterium isolated from palm oil mill effluent in malaysia. *BMC Microbiology*, 7(1):77.

Ramilo, C. A., Zafaralla, G. C., Nadasdi, L., Hammerland, L. G., Yoshikami, D., Gray, W. R., Kristipati, R., Ramachandran, J., and Miljanich, G. (1992). Novel .alpha.- and .omega.-conotoxins and conus striatus venom. *Biochemistry*, 31(41):9919–9926.

Rattanarojpong, T., Wang, H.-C., Lo, C.-F., and Flegel, T. W. (2007). Analysis of differently expressed proteins and transcripts in gills ofPenaeus vannameiafter yellow head virus infection. *PROTEOMICS*, 7(20):3809–3814.

Robinson, D. and Silge, J. (2018). *tidytext: Text Mining using 'dplyr', 'ggplot2', and Other Tidy Tools*. R package version 0.1.9.

Shadrin, A. M. and Pavlov, D. S. (2015). Embryonic and larval development of the asian seabass lates calcarifer (pisces: Perciformes: Latidae) under thermostatically controlled conditions. *Biology Bulletin*, 42(4):334–346.

Shansudin, L., Yusof, M., Azis, A., and Shukri, Y. (1997). The potential of certain indigenous copepod species as live food for commercial fish larval rearing. *Aquaculture*, 151(1-4):351–356.

Shapawi, R. and Zamry, A. A. (2015). Response of asian seabass,lates calcariferjuvenile fed with different seaweed-based diets. *Journal of Applied Animal Research*, 44(1):121–125.

Shih, H.-T., Ng, P. K. L., Schubart, C. D., and Chang, H.-W. (2007). Phylogeny and phylogeography of the genus geothelphusa (crustacea: Decapoda, brachyura, potamidae) in southwestern taiwan based on two mitochondrial genes. *Zoological Science*, 24(1):57–66.

Shon, K.-J., Hasson, A., Spira, M. E., Cruz, L. J., Gray, W. R., and Olivera, B. M. (1994). .delta.-conotoxin GmVIA, a novel peptide from the venom of conus gloriamaris. *Biochemistry*, 33(38):11420–11425.

Sivasothy, Y., Sulaiman, S. F., Ooi, K. L., Ibrahim, H., and Awang, K. (2013). Antioxidant and antibacterial activities of flavonoids and curcuminoids from zingiber spectabile griff. *Food Control*, 30(2):714–720.

SOMBOONWIWAT, K., MARCOS, M., TASSANAKAJON, A., KLINBUNGA, S., AUMELAS, A., ROMESTAND, B., GUEGUEN, Y., BOZE, H., MOULIN, G., and BACHERE, E. (2005). Recombinant expression and anti-microbial activity of anti-lipopolysaccharide factor (ALF) from the black tiger shrimp. *Developmental & Comparative Immunology*, 29(10):841–851.

Supungul, P., Klinbunga, S., Pichyangkura, R., Hirono, I., Aoki, T., and Tassanakajon, A. (2004). Antimicrobial peptides discovered in the black tiger shrimp penaeus monodon using the EST approach. *Diseases of Aquatic Organisms*, 61:123–135.

Suraprasit, S., Methatham, T., Jaree, P., Phiwsaiya, K., Senapin, S., Hirono, I., Lo, C. F., Tassanakajon, A., and Somboonwiwat, K. (2014). Anti-lipopolysaccharide factor isoform 3 from penaeus monodon (ALF pm 3) exhibits antiviral activity by interacting with WSSV structural proteins. *Antiviral Research*, 110:142–150.

Syafitri, E., Prayitno, S. B., Ma'ruf, W. F., and Radjasa, O. K. (2017). Genetic diversity of the causative agent of ice-ice disease of the seaweed kappaphycus alvarezii from karimunjawa island, indonesia. *IOP Conference Series: Earth and Environmental Science*, 55:012044.

Tan, J., Lim, P.-E., and Phang, S.-M. (2012). Phylogenetic relationship of kappaphycus doty and eucheuma j. agardh (solieriaceae, rhodophyta) in malaysia. *Journal of Applied Phycology*, 25(1):13–29.

Tan, K. S. and Ransangan, J. (2016). Feeding behaviour of green mussels,perna viridisfarmed in marudu bay, malaysia. *Aquaculture Research*, 48(3):1216–1231.

Thanh, H. N., Liu, Q., Zhao, L., Zhang, H., and Liu, J. (2015). Genetic diversity of the cultured giant freshwater prawn (macrobrachium rosenbergii) in china based on microsatellite markers. *Biochemical Systematics and Ecology*, 59:144–154.

Thanh, N. M., Nguyen, N. H., Ponzoni, R. W., Vu, N. T., Barnes, A. C., and Mather, P. B. (2010). Estimates of strain additive and non-additive genetic effects for growth traits in a diallel cross of three strains of giant freshwater prawn (macrobrachium rosenbergii) in vietnam. *Aquaculture*, 299(1-4):30–36.

Thao, N., Luyen, B., Koo, J., Kim, S., Koh, Y., Cuong, N., Nam, N., Kiem, P. V., Kim, Y., and Minh, C. V. (2015a). Anti-inflammatory components of the vietnamese starfish protoreaster nodosus. *Biological Research*, 48(1):12.

Thao, N. P., Luyen, B. T. T., Kim, E. J., Kang, J. I., Kang, H. K., Cuong, N. X., Nam, N. H., Kiem, P. V., Minh, C. V., and Kim, Y. H. (2015b). Steroidal constituents from the edible sea UrchinDiadema savignyiMichelin

induce apoptosis in human cancer cells. *Journal of Medicinal Food*, 18(1):45–53.

Tinh, T. H., Nuidate, T., Vuddhakul, V., and Rodkhum, C. (2016). Antibacterial activity of pyrogallol, a polyphenol compound against vibrio parahaemolyticus isolated from the central region of thailand. *Procedia Chemistry*, 18:162–168.

Trianto, A., Widyaningsih, S., Radjasa, O., and Pribadi, R. (2017). Symbiotic fungus of marine sponge axinella sp. producing antibacterial agent. *IOP Conference Series: Earth and Environmental Science*, 55:012005.

Tuyen, N., Verreth, J., Vlak, J., and de Jong, M. (2014). Horizontal transmission dynamics of white spot syndrome virus by cohabitation trials in juvenile penaeus monodon and p. vannamei. *Preventive Veterinary Medicine*, 117(1):286–294.

Vaiphasa, C., de Boer, W. F., Skidmore, A. K., Panitchart, S., Vaiphasa, T., Bamrongrugsa, N., and Santitamnont, P. (2007). Impact of solid shrimp pond waste materials on mangrove growth and mortality: a case study from pak phanang, thailand. *Hydrobiologia*, 591(1):47–57.

Vien, L. T., Ngoan, B. T., Hanh, T. T. H., Vinh, L. B., Thung, D. C., Thao, D. T., Thanh, N. V., Cuong, N. X., Nam, N. H., Kiem, P. V., and Minh, C. V. (2016). Steroid glycosides from the starfish pentaceraster gracilis. *Journal of Asian Natural Products Research*, 19(5):474–480.

Vromant, N., Nam, C. Q., and Ollevier, F. (2002). Growth performance of barbodes gonionotus (bleeker) in intensively cultivated rice fields. *Aquaculture*, 212(1-4):167–178.

Wickham, H. (2017). *tidyverse: Easily Install and Load the 'Tidyverse'*. R package version 1.2.1.

Wongteerasupaya, C., Tongcheua, W., Boonsaeng, V., Panyim, S., Tassanakajon, A., Withyachumnarnkul, B., and Flegel, T. (1997). Detection of yellowhead virus (YHV) of penaeus monodon by RT-PCR amplification. *Diseases of Aquatic Organisms*, 31:181–186.

Wongteerasupaya, C., Vickers, J., Sriurairatana, S., Nash, G., Akarajamorn, A., Boonsaeng, V., Panyim, S., Tassanakajon, A., Withyachumnarnkul, B., and Flegel, T. (1995). A non-occluded, systemic baculovirus that occurs in cells of ectodermal and mesodermal origin and causes high mortality in the black tiger prawn penaeus monodon. *Diseases of Aquatic Organisms*, 21:69–77.

Wuthisuthimethavee, S., Lumubol, P., Vanavichit, A., and Tragoonrung, S. (2003). Development of microsatellite markers in black tiger shrimp (penaeus monodon fabricius). *Aquaculture*, 224(1-4):39–50.

Xie, Y. (2018). *bookdown: Authoring Books and Technical Documents with R Markdown*. R package version 0.7.

Yap, C., Ismail, A., and Tan, S. (2004). Heavy metal (cd, cu, pb and zn) concentrations in the green-lipped mussel perna viridis (linnaeus) collected from some wild and aquacultural sites in the west coast of peninsular malaysia. *Food Chemistry*, 84(4):569–575.

Yap, C., Ismail, A., Tan, S., and Omar, H. (2002). Correlations between speciation of cd, cu, pb and zn in sediment and their concentrations in total soft tissue of green-lipped mussel perna viridis from the west coast of peninsular malaysia. *Environment International*, 28(1-2):117–126.

Yap, C., Ismail, A., Tan, S., and Rahim, I. A. (2003). Can the shell of the green-lipped mussel perna viridis from the west coast of peninsular malaysia be a potential biomonitoring material for cd, pb and zn? *Estuarine, Coastal and Shelf Science*, 57(4):623–630.

Ye, M., Khoo, K. K., Xu, S., Zhou, M., Boonyalai, N., Perugini, M. A., Shao, X., Chi, C., Galea, C. A., Wang, C., and Norton, R. S. (2012). A helical conotoxin fromConus imperialisHas a novel cysteine framework and defines a new superfamily. *Journal of Biological Chemistry*, 287(18):14973–14983.

Ye, Y., Li, J., and Wu, C. (2015). Genetic diversity and population connectivity of the asian green mussel perna viridis in south china sea, inferred from mitochondria DNA markers. *Biochemical Systematics and Ecology*, 61:470–476.

Zhila, H., Mahmood, H., and Rozainah, M. Z. (2013). Biodiversity and biomass of a natural and degraded mangrove forest of peninsular malaysia. *Environmental Earth Sciences*, 71(11):4629–4635.

Zhou, J.-G., Wei, J.-G., Xu, D., Cui, H.-C., Yan, Y., Ou-Yang, Z.-L., Huang, X.-H., Huang, Y.-H., and Qin, Q.-W. (2011). Molecular cloning and characterization of two novel hepcidins from orange-spotted grouper, epinephelus coioides. *Fish & Shellfish Immunology*, 30(2):559–568.

Zuraini, A., Somchit, M., Solihah, M., Goh, Y., Arifah, A., Zakaria, M., Somchit, N., Rajion, M., Zakaria, Z., and Jais, A. M. (2006). Fatty acid and amino acid composition of three local malaysian channa spp. fish. *Food Chemistry*, 97(4):674–678.