



Maximizing benefits from 'biodiscovery': a Coastal State resource providers perspective

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Some definitions ...

Research State (user of the marine genetic resources
(MGRs) for biodiscovery purposes)

Coastal State (provider of MGRs to a Research State)

Biodiscovery (= bioprospecting, and in this instance, refers
only to marine natural products discovery)



An Australian perspective from a Queensland experience

- **Enabling environment**: How does a Coastal State attract a Research State to use their MGRs ?
 - o the 'stick': regulatory protocols, policy & legislation
 - o the 'carrot': access to MGRs in Australia & Queensland
- **Experiences in major biodiscovery collections**
- **Research State benefits**: an example of a successful biodiscovery partnership
- **Coastal State benefits**: 'environmental data' from collections for bioregional planning, new biological, genetic and chemical data, taxonomic capacity building, etc



'Biodiscovery' regulatory framework pre-2004

The (dis)enabling biodiscovery environment:

- **Myriad of Laws governing biodiscovery: E.g.**
 - o Forestry Act
 - o Land Act
 - o Nature Conservation Act
 - o Fisheries Act
 - o (State) Marine Parks Act
 - o Great Barrier Reef Marine Park Act
 - o Native Title Act
 - o Wet Tropics World Heritage Protection and Management Act
 - o Etc.



'Biodiscovery' regulatory framework pre-2004

The (dis)enabling biodiscovery environment:

Myriad of Laws:

• **Many access permits from many agencies: E.g.**

- o Marine Parks collections Permit, The Great Barrier Reef Marine Park Authority Regulations 1983 (Commonwealth)
- o EPA Collections Permit, Environmental Protection Agency, Queensland Parks & Wildlife Service, Marine Parks Regulations 1990 (Queensland)
- o DPI General Fisheries collections Permit, Department of Primary Industries and Fisheries, Queensland Fisheries Act, 1994
- o Museum Licence, Environmental Protection Agency, Queensland Parks & Wildlife Service, s170f Nature Conservation Regulation 1994.
- o Permit to 'Take, Use, Keep or Interfere with Cultural or Natural Resources (Scientific Purpose)', Environmental Protection Agency, Queensland Parks & Wildlife Service, S9(1)(A) Nature Conservation (Administration) Regulation 2006.
- o Commercial wildlife harvest licence under the Nature Conservation Act 1992
- o DNR Sales permit under the Forestry Act 1959 to remove material
- o Commercial wildlife licence under the Nature Conservation Act 1992 to use the material.



'Biodiscovery' regulatory framework pre-2004

The (dis)enabling biodiscovery environment:

Myriad of Laws:

• **Many access permits from many agencies:**

• **Lack of clarity:**

- o ownership of MGRs
- o right of access
- o rights to commercialisation, IP, etc from use of MGRs



'Biodiscovery' regulatory framework pre-2004

The (dis)enabling biodiscovery environment:

Myriad of Laws:

- Many access permits from many agencies:
- Lack of clarity:
- **Potentially ecologically unsound and unsustainable collection activities:**

- o few, if any, environmental benefits
- o research effort uncoordinated
- o new knowledge not in public domain



'Biodiscovery' regulatory framework pre-2004

The (dis)enabling biodiscovery environment:

Myriad of Laws:

- Many access permits from many agencies:
- Lack of clarity:
- **Potentially ecologically unsound and unsustainable collection activities:**

- **Little or no investment in Coastal State R&D:**

- o mostly offshore commercialisation & value-adding
- o little or no investment in infrastructure, capacity building, compound libraries
- o no contribution to Coastal State voucher specimen collections (environmental knowledge)



'Biodiscovery' regulatory framework pre-2004

- 2002:** Bonn Guidelines adopted by the CBD to provide extra guidance on ABS
- 2002:** Nationally Consistent Approach agreed by all states, territories and Commonwealth of Australia
- 2004:** Queensland 1st state to implement nationally consistent approach (CBD + Bonn Guidelines) = 'Queensland Biodiscovery Act 2004'
- Post 2004:** 2 other Australian jurisdictions have new legislation; 4 others currently developing policy



The 'stick': Queensland Biodiscovery Act 2004

- (<http://www.legislation.qld.gov.au/LEGISLTN/ACTS/2004/04AC019.pdf>)

The enabling environment: Purpose of the Act:

- 1. Regulatory:** provide certainty for all stakeholders by establishing a streamlined and clear legislative framework to regulate collection and use of all Queensland's native biological materials from lands and waters;

Tools:

Biological Collection Authority (BCA):

- single permit issued minimising duplication of regulation;
- regulated by a set of *Codes* (ethics, collection standards, minimising environmental damage etc)



BIODISCOVERY BILL 2004



The 'stick': Queensland Biodiscovery Act 2004

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The enabling environment: Purpose of the Act:

2. **Co-investment:** encourage investment in the Queensland's biodiscovery research and development sector;
3. **Commercialisation:** ensure fair and equitable benefit sharing from biodiscovery to Queensland;

Tools:

Benefit Sharing Agreement (BSA):

i.e. royalties, investment into Queensland's biotechnology industry, collaboration with researchers, development of new or improved products, obligation to lodge voucher samples in museums/ herbaria



BIODISCOVERY BILL 2004



The 'stick': Queensland Biodiscovery Act 2004

- (<http://www.legislation.qld.gov.au/LEGISLTN/ACTS/2004/04AC019.pdf>)

The enabling environment: Purpose of the Act:

4. **Environmental:** enhance knowledge of Queensland's biodiversity, promoting conservation and ecologically sustainable use of native biological resources.

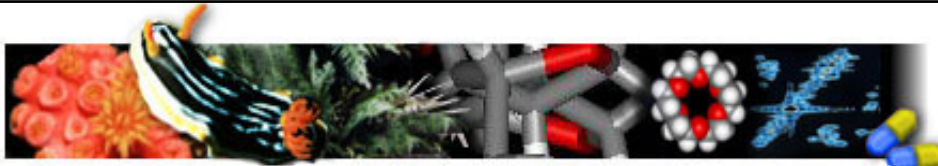
Tools:

Biodiscovery Plan:

developed by Research State in line with the Codes (e.g. source and scope of biological material, collection access, timetable & localities, proposed commercial outcomes, environmental data and other non-monetary benefits etc.)



BIODISCOVERY BILL 2004



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The enabling environment: Purpose of the Act:

- 4. **Environmental:** enhance knowledge of Queensland's biodiversity, promoting conservation and ecologically sustainable use of native biological resources.

Non-monetary benefits:

'environmental data' arguably as valuable as any potential monetary benefits from commercialisation.

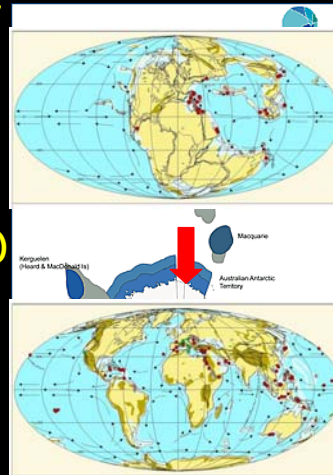


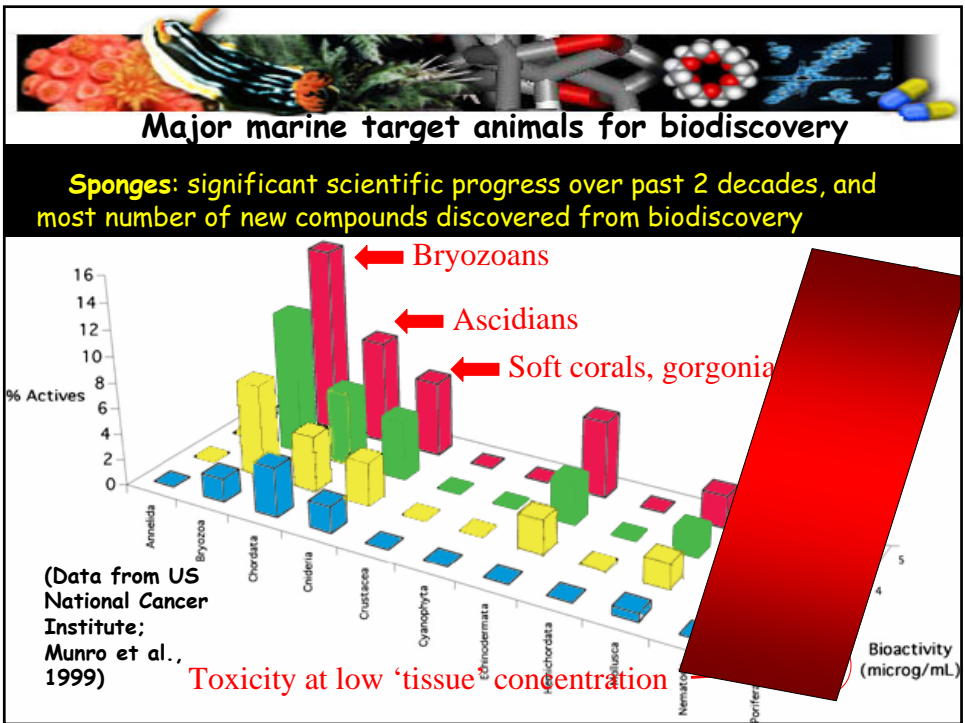
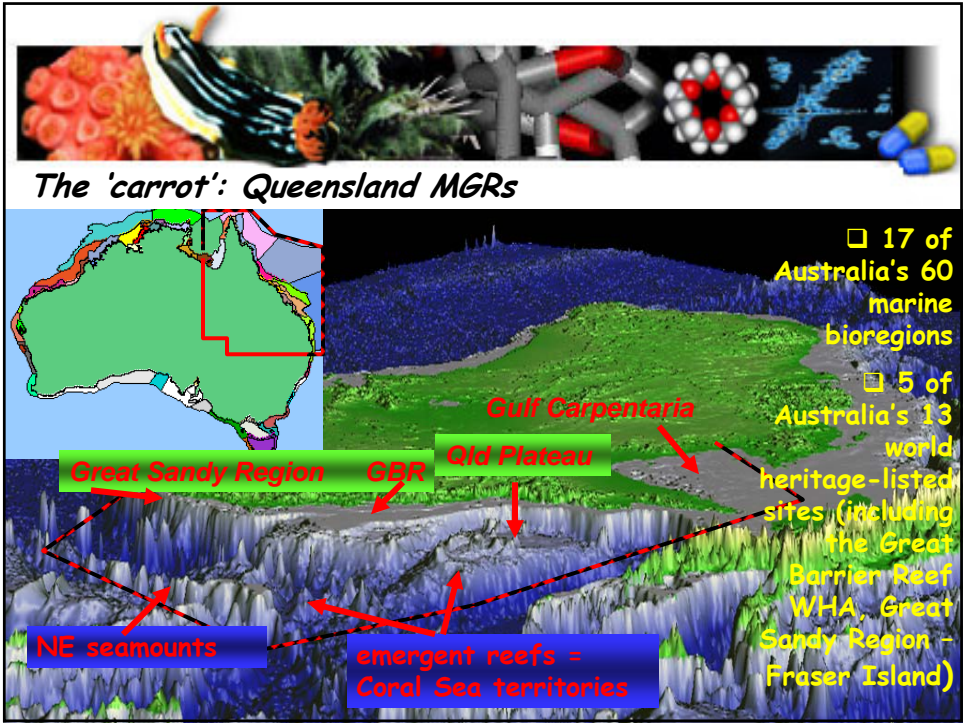
BIODISCOVERY BILL 2004



The 'carrot': Australian Marine Genetic Resources (MGRs)

- **Big** (70,000km continental coastline, 8.6 million km² continental marine territory; 16.1 million km² oceanic jurisdiction);
- **Diverse** (60 marine bioregions, all 5 oceanic climatic zones, tropics to polar, intertidal to the abyssal plains)
- **Highly Unique** (1 of the 19 'megadiverse' countries, huge proportion of endemic biota, Gondwanan origins & subsequent mixing with the Tethyan biota)







Experiences in major 'Biodiscovery' collections (PPP)

- 1974-1981: Roche Research Institute of Marine Pharmacology & Roche Pharmaceuticals
- 1987-1992; 2003-present: Australian Institute of Marine Science (AIMS) & US National Cancer Institute (NCI)

- 10kg biomass samples collected
- 6 extracts screened/week
- ~2,100 extracts screened over 7 years



Model example

- 100g biomass samples collected (200mg extract for screening)
- 180,000 extracts screened per day

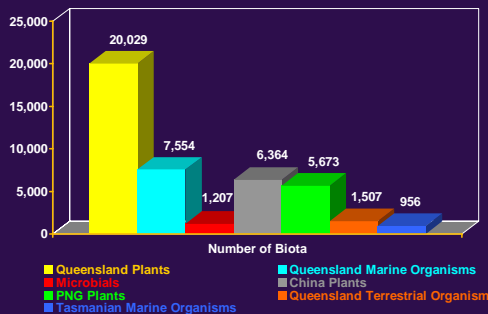


NPD/AZ partnership: Research State 'commercial' benefits



Specimen library

(>30,000 plants, animals, microorganisms)





NPD/AZ partnership: Research State 'commercial' benefits



Extract Library

(2D dot matrix coded microtube; 5 year shelf life;
384-well - 50 mL assay volume; 200 mg of sample
gives > 800 assays)



NPD/AZ partnership: Research State 'commercial' benefits



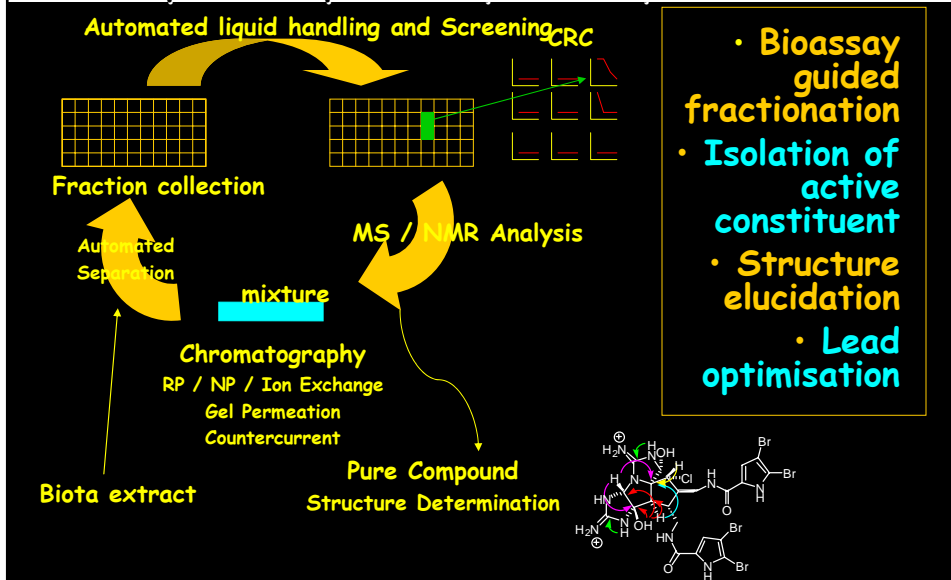
High throughput screening:

**focussing on: Receptors, Enzymes, Mechanism based
cellular assays**

(Cardiovascular, Respiratory, Inflammation, Gastrointestinal, Pain
Control, Oncology, Infection, CNS)

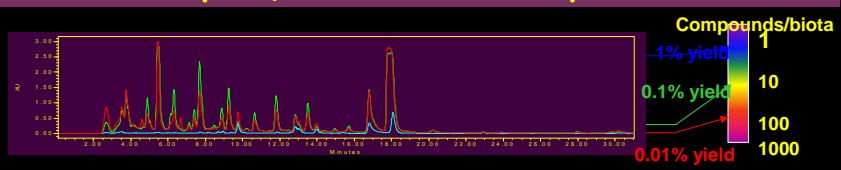


NPD/AZ partnership: Research State 'commercial' benefits

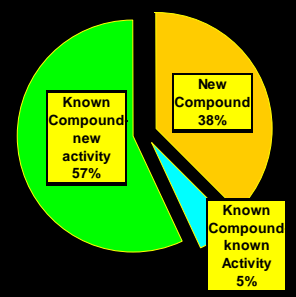


NPD/AZ partnership: Research State 'commercial' benefits

• Potential accessible chemical diversity (compounds with >0.001% yield) = 5-7 million compounds



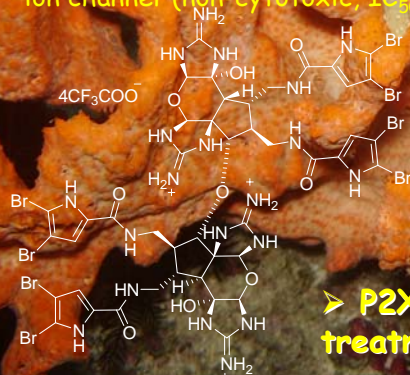
~1500 bioactive compounds isolated to date, 23 new structure classes discovered, 38% are novel structures, majority with novel biological activity





NPD/AZ partnership: Research State 'commercial' benefits

New compound '**Stylyssadines A**' *Stylyssa flabellata* from the GBR
and B' specific antagonist for P2X₇ (pain) receptor - purinergic ligand-gated ion channel (non-cytotoxic, IC₅₀ 1.8 mM)



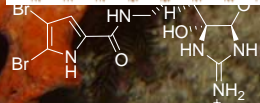
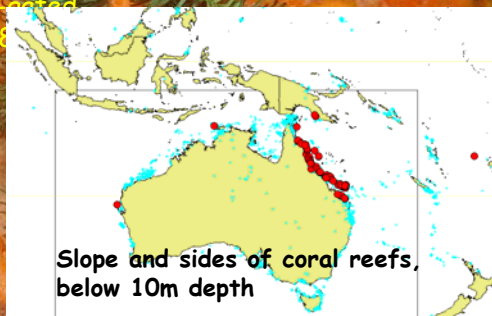
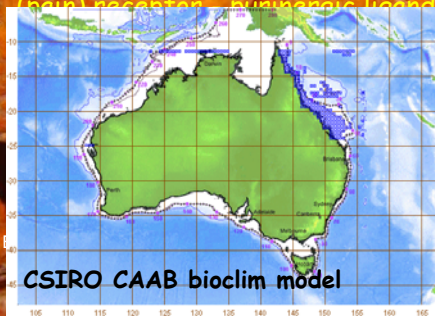
> P2X₇ antagonists may provide new treatment for inflammatory diseases

(Buchanan et al. *J. Org. Chem.*, 2007, 72, 2309-2317)




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NPD/AZ partnership: Research State 'commercial' benefits

Adenosine A_1 antagonists **Psammaplin A** and **Bisaprasin 11'-sulfate** [3H]DPCPX binding to brain adenosine A_1 receptors IC_{50}

Aplysinella rhax from the GBR

Modulates cAMP via adenylate cyclase effective for controlling blood flow, cardiovascular system and metabolism

(Pham et al, *J. Nat. Prod.* 2000, 63, 393 - 395)



NPD/AZ partnership: Research State 'commercial' benefits

Adenosine A_1 antagonists **Psammaplin A** and **Bisaprasin 11'-sulfate** [3H]DPCPX binding to brain adenosine A_1 receptors IC_{50}

Aplysinella rhax from the GBR

Coral rubble, rock, shallow water

Modulates cAMP via adenylate cyclase effective for controlling blood flow, cardiovascular system and metabolism

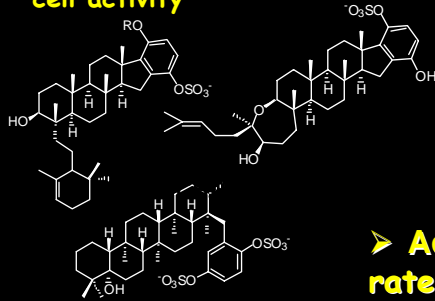
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NPD/AZ partnership: Research State 'commercial' benefits

Adociasulfate 1,7,8,9
inhibits H⁺-ATPase proton pump IC₅₀ essential to osteoclast bone resorption cell activity

Adocia (=Haliclona) aculeata from the GBR



(Kalaitzis et al, *J. Org. Chem.* 1999, 64, 5571 - 5574)

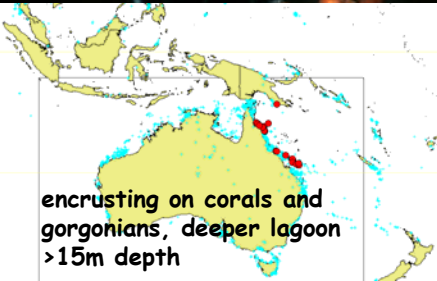
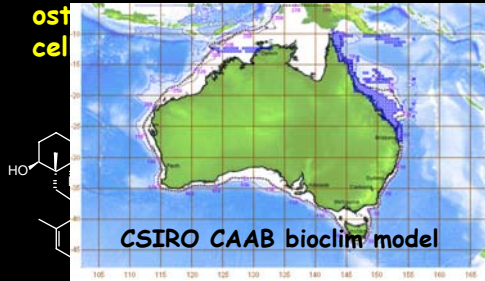
➤ Adociasulfate may reduce the rate of bone resorption and offer therapeutic value in osteoporosis



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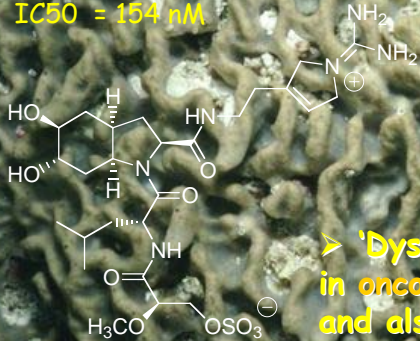
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NPD/AZ partnership: Research State 'commercial' benefits

New compound **'Dysinosin A'** found to inhibit the binding of [IL25] interleukin-8 [IL-8] to the human recombinant IL-8 receptor type A at IC50 = 154 nM

New species of marine sponge *Citronia astra* from outer GBR



> **'Dysinosin A'** found to be effective in oncology, awaiting Phase I trials, and also another compound effective against human α -thrombin

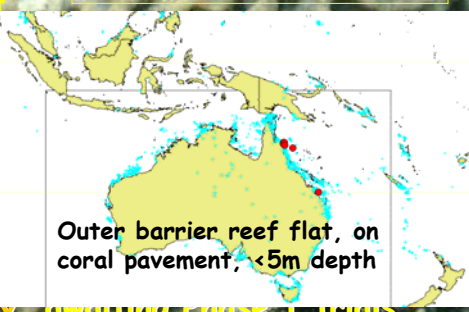
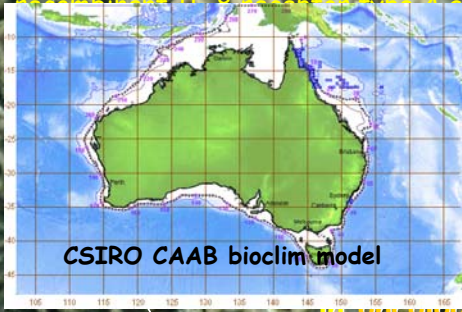
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NPD/AZ partnership: Research State 'commercial' benefits

Axinellamines B, C and D:
minimum bactericidal concentration for inhibition of *H. pylori* of 1000 mM

New species of *Axinella*
sp.1333 from Sydney



➤ Gastric bactericide potentially effective for treatment and prevention of gastric and duodenal ulcer and gastric cancer

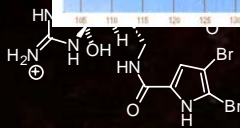
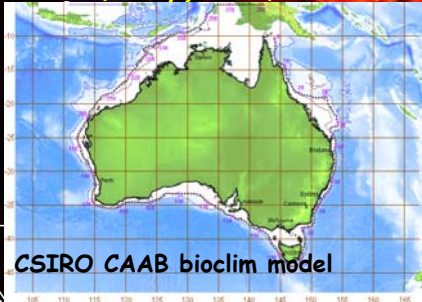
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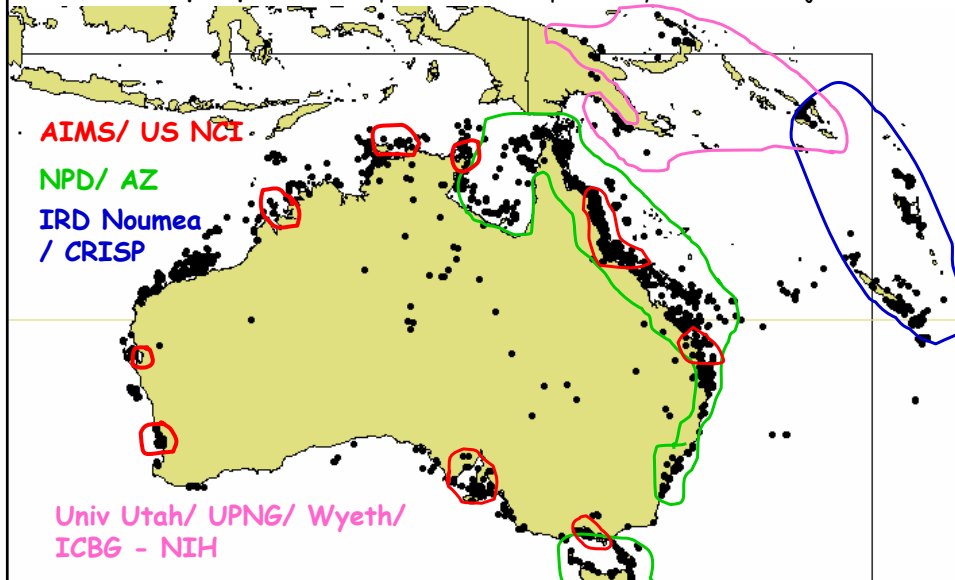


effective for treatment and prevention of gastric and duodenal ulcer and gastric cancer

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Coastal State benefits: environmental data (collections)

QM sponge collections: ~4,000 collection sites, ~30,000 specimen records, ~5,000 morphospecies; datapoints all underpinned by verifiable objects



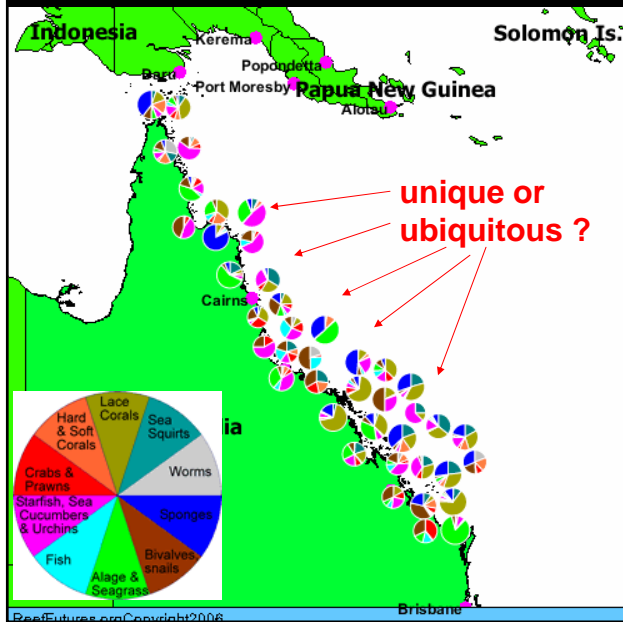
Capacity building: Taxonomy (theory and practice of classifying organisms; systematics, biogeography)

Collections: verifiable objects that underpin biodiversity and biodiscovery research

Taxonomy: enabling science underpinning most other biological sciences; essential to reliably differentiate MGRs in an international context (not to be confused with 'sorting' or 'identification')

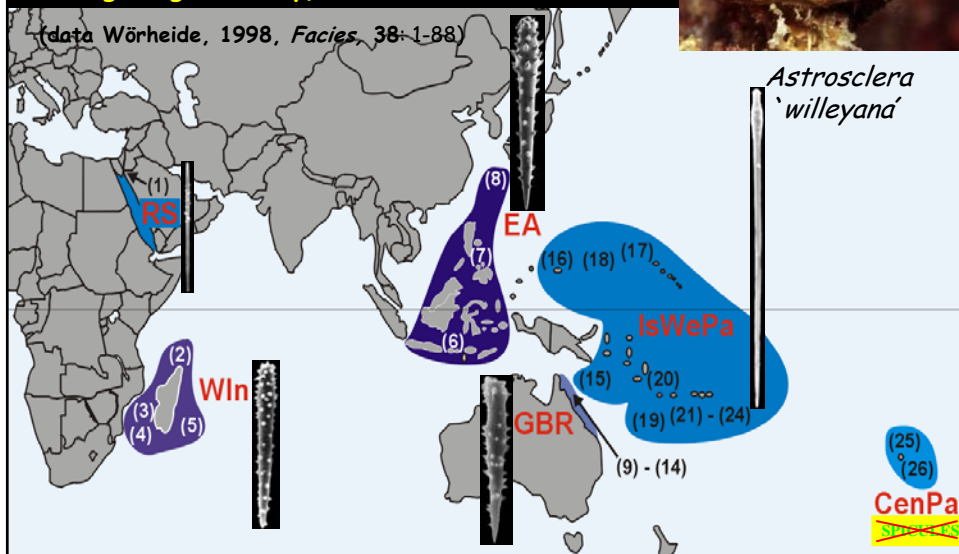
Taxonomic capability: in crisis (Australia)
1980s: ~ 190 full-time (long-term employed) taxonomists
2006: ~ 75 full-time taxonomists in museums, herbaria, universities, other government agencies

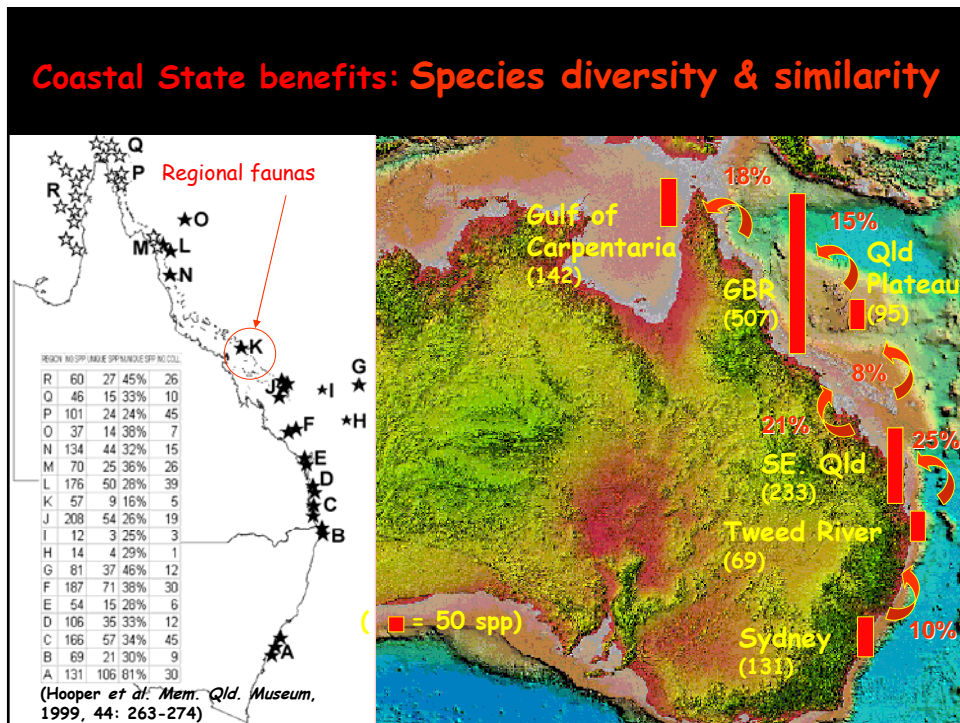
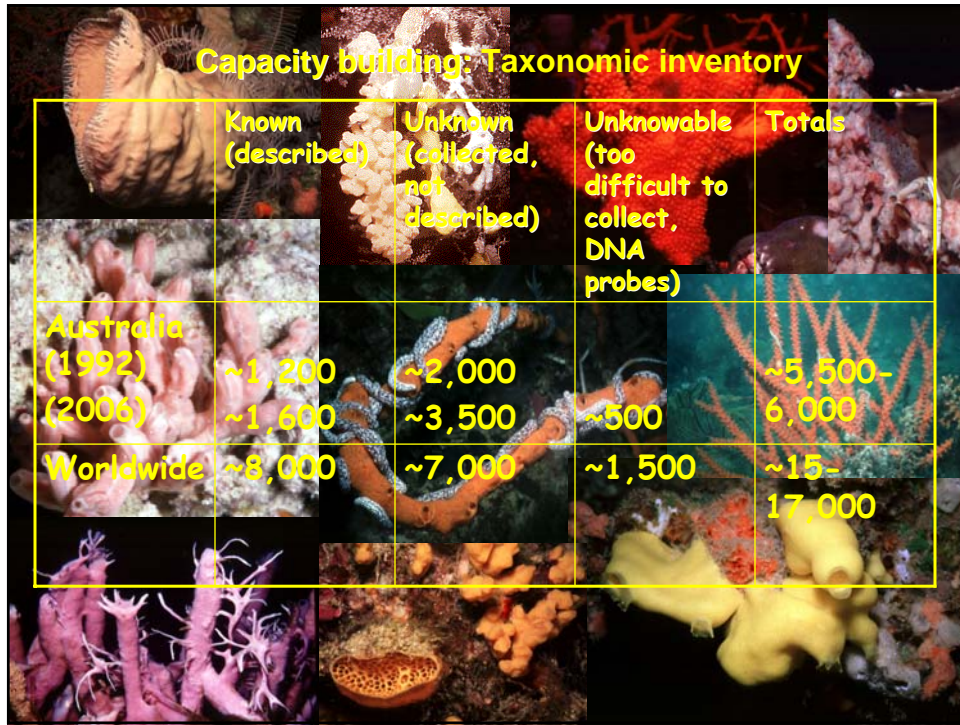
Capacity building: Taxonomy (GBR Seabed biodiversity)



- 150,000 specimens collected over 3 years throughout GBR inter-reef
- most identified to OTU level (i.e. same vs. different)
- but few yet identified to species (many new?)
- Without true taxonomy, how can we determine if species are unique to the GBR or found in other Coastal States?

Morphological (phenotype) versus genotype species concept problem (ultraconservative sponge morphologies, deeply divergent genetically)

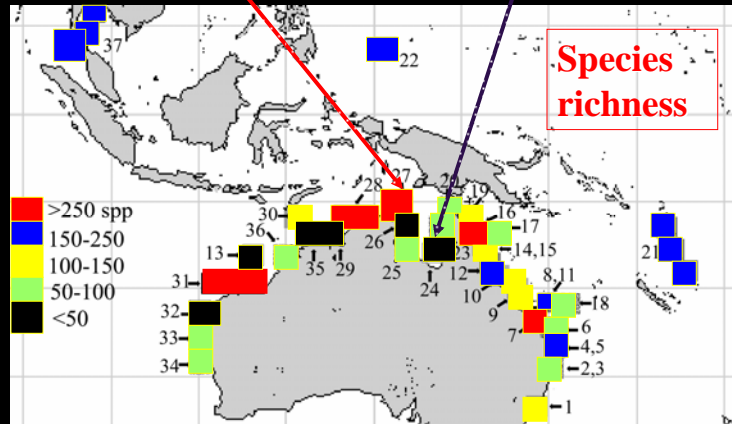




Coastal State benefits: 'Hotspots' of species richness

Biodiversity 'hotspots' (species rich, >250 spp/ region)

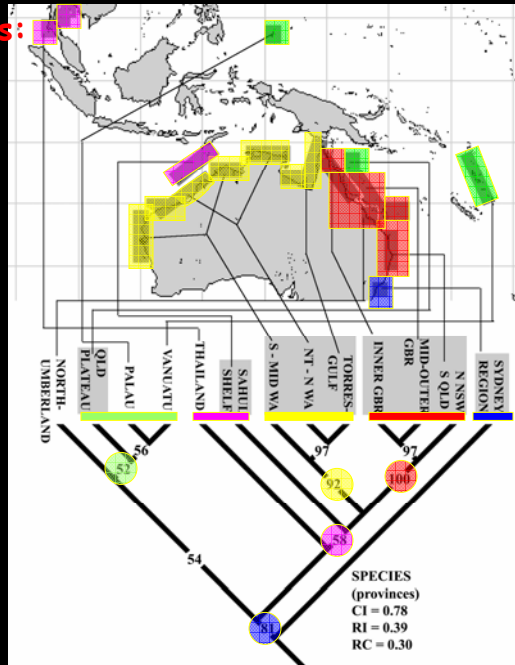
Species poor regions (<50 spp/ region)



(Hooper, Kennedy & Quinn, *Biodiv. & Conserv.*, 2002, 11(5): 851-885)

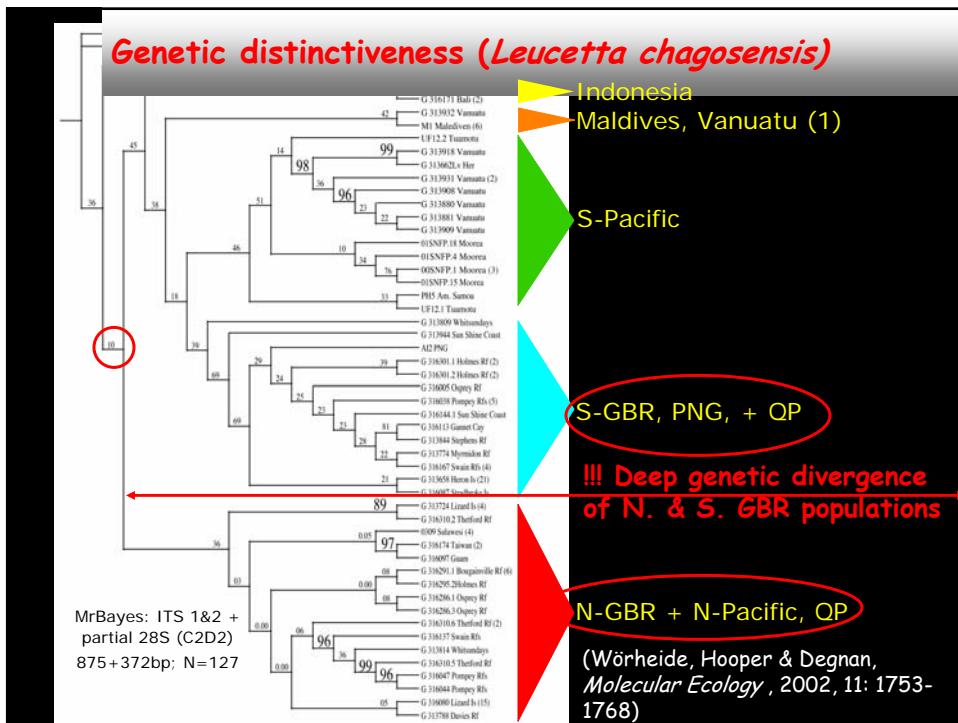
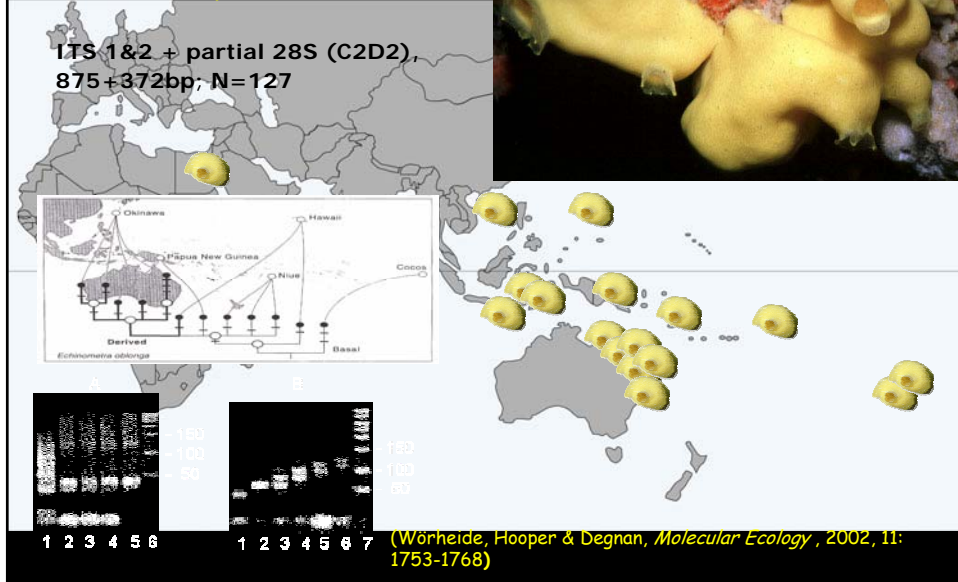
Coastal State benefits: Phylogenetic relationships

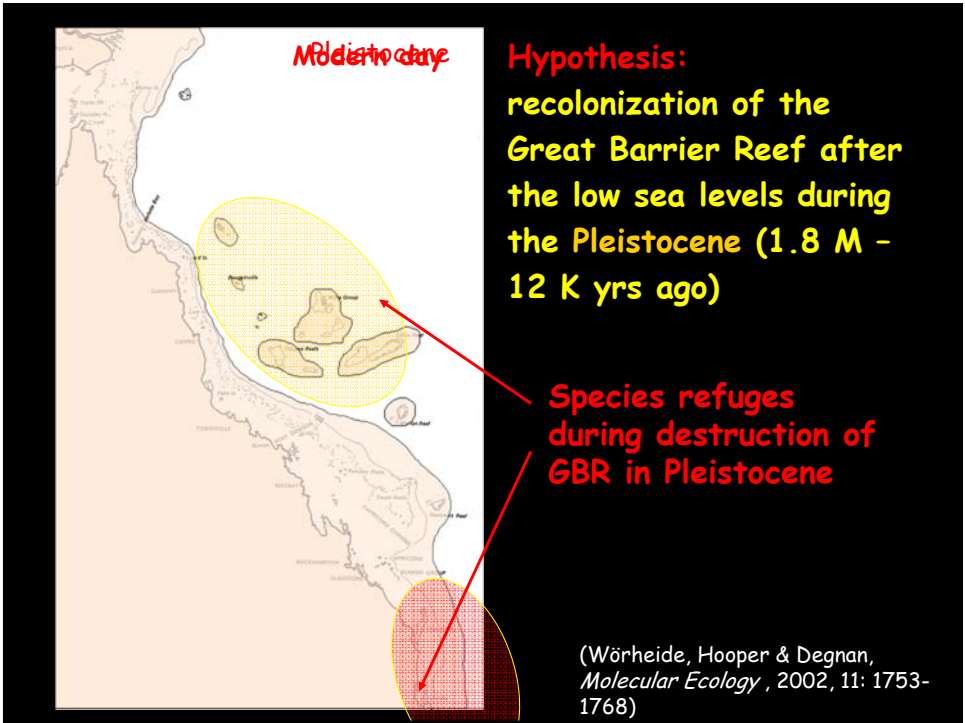
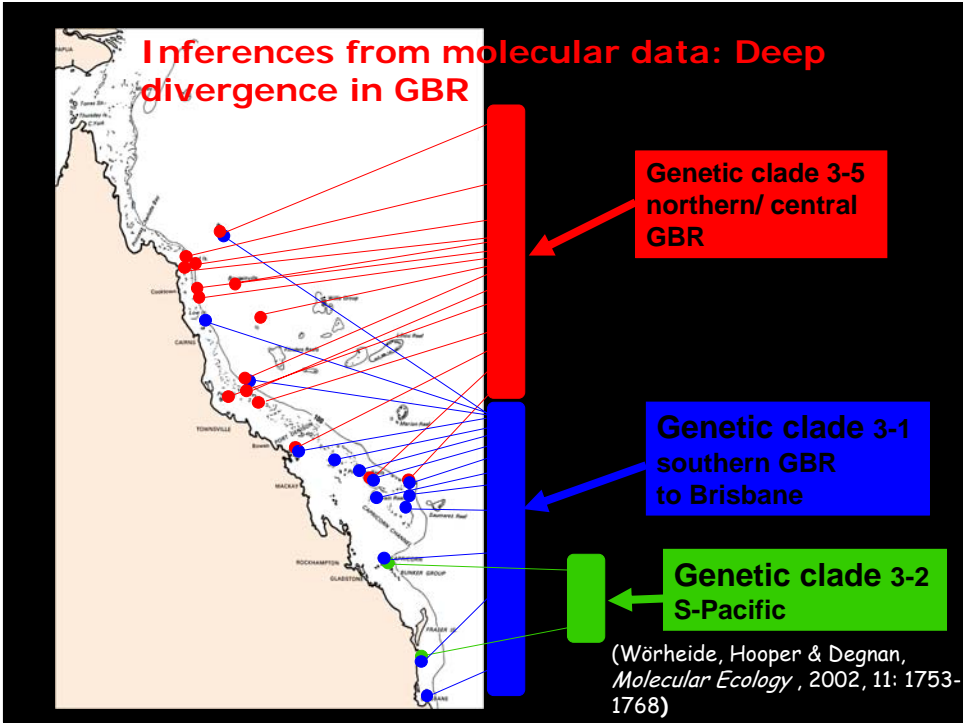
- Taxonomic relationships
- Evolutionary/ biogeographic history
- Artefacts of ancient connectivity
- Influenced by modern physical attributes (currents, sediments, etc)

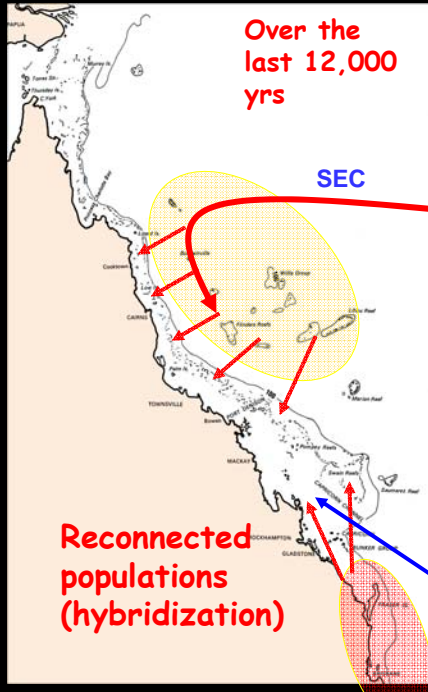


(Hooper, Kennedy & Quinn, *Biodiv. & Conserv.*, 2002, 11(5): 851-885)

Coastal State benefits: molecular studies, genetic diversity versus morphological diversity (connectivity, isolation, hybridization: *Leucetta chagosensis*)



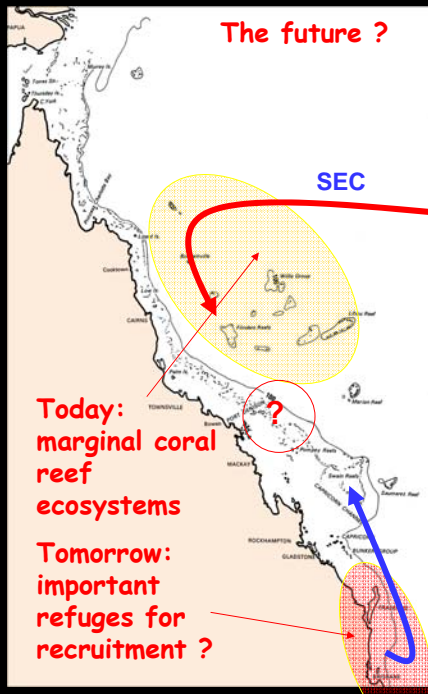




Hypothesis:
 recolonization of the Great Barrier Reef after the low sea levels during the Pleistocene (1.8m - 12k yrs ago)



(Wörheide, Hooper & Degnan, *Molecular Ecology*, 2002, 11: 1753-1768)



Climate change response ?
 Change of sea currents, new patterns of connectivity, increased severe storm events ? = loss of native faunas, increased invasive species via storm events ('blowins') ?



SPONGE BARCODING PROJECT

Primers

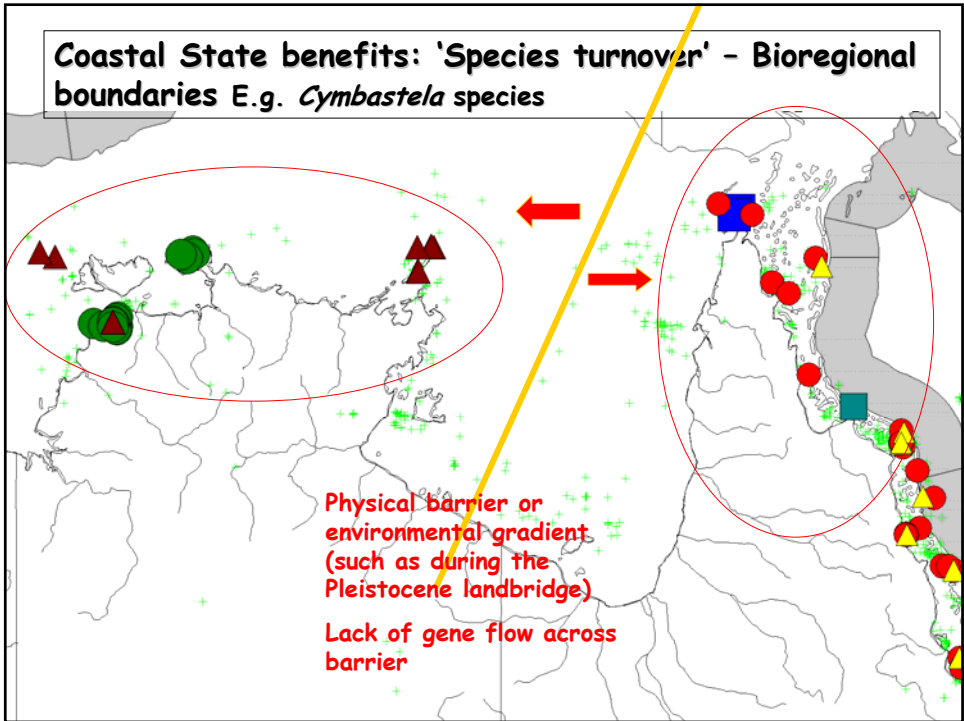
The standard barcoding fragment for the Barcoding of Life initiative is a ~ 640 bp long fragment located at the 5' site of the mitochondrial cytochrome oxidase subunit 1 (CO1). However, as this fragment might not display sufficient variability in sponges [1][2], we suggest sequencing an additional downstream region, which exhibits a higher substitution rate [3] in order to obtain a fragment of about 1,100 bp with a higher number of variable sites. A submission ITS-1 and 2 sequences, which could be added to the CO1-sequence tag, is also encouraged.

Primers in respect to *Amphimedon queenslandica* CO1 (1,593 bp)

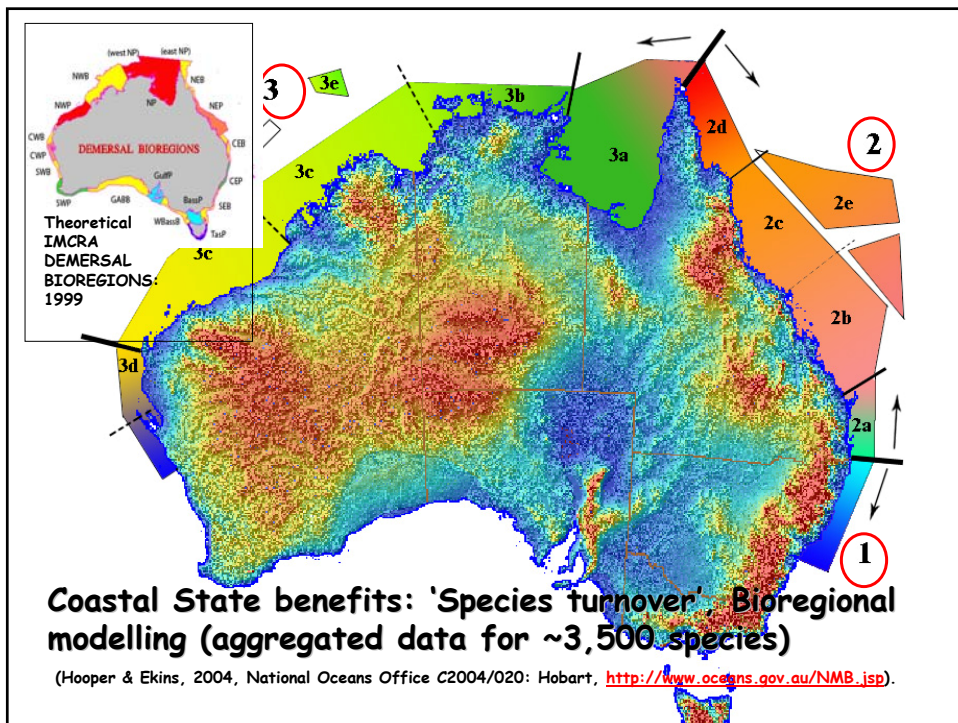
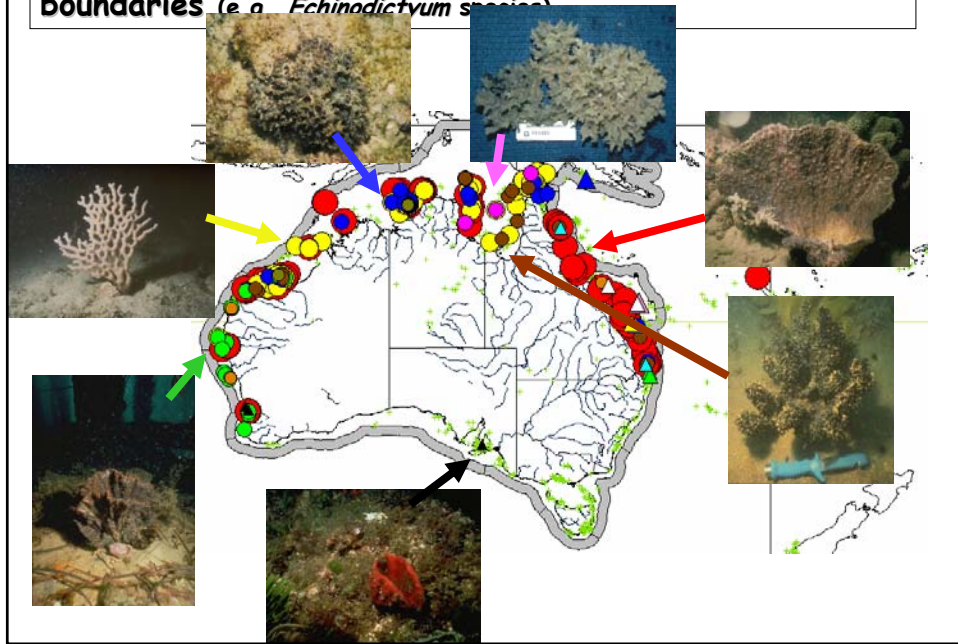
Qld species from biodiscovery used for sponge genome project

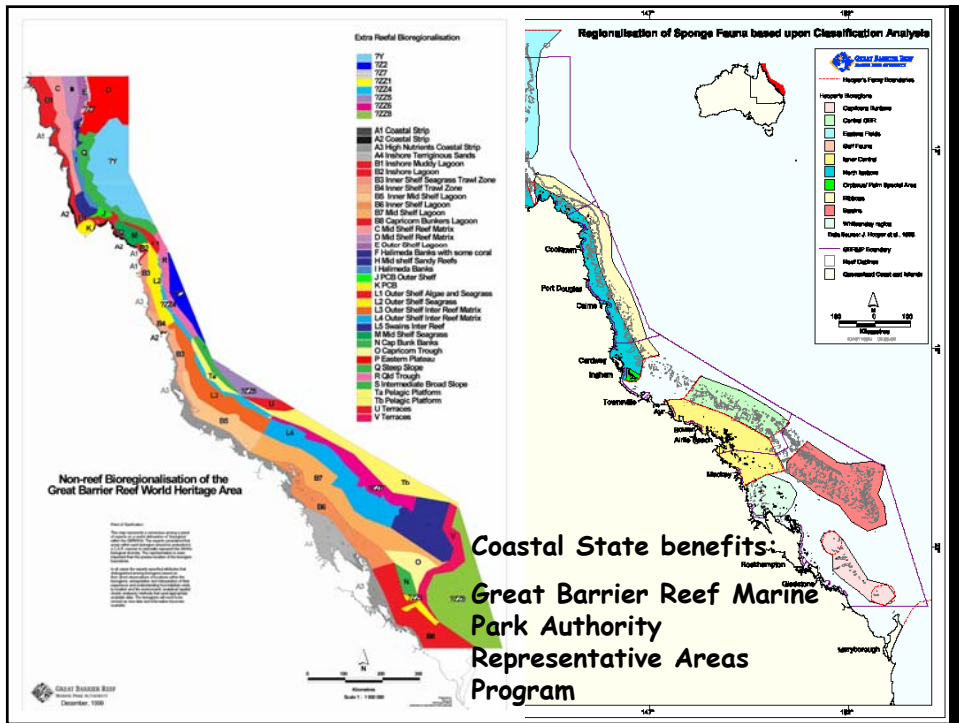
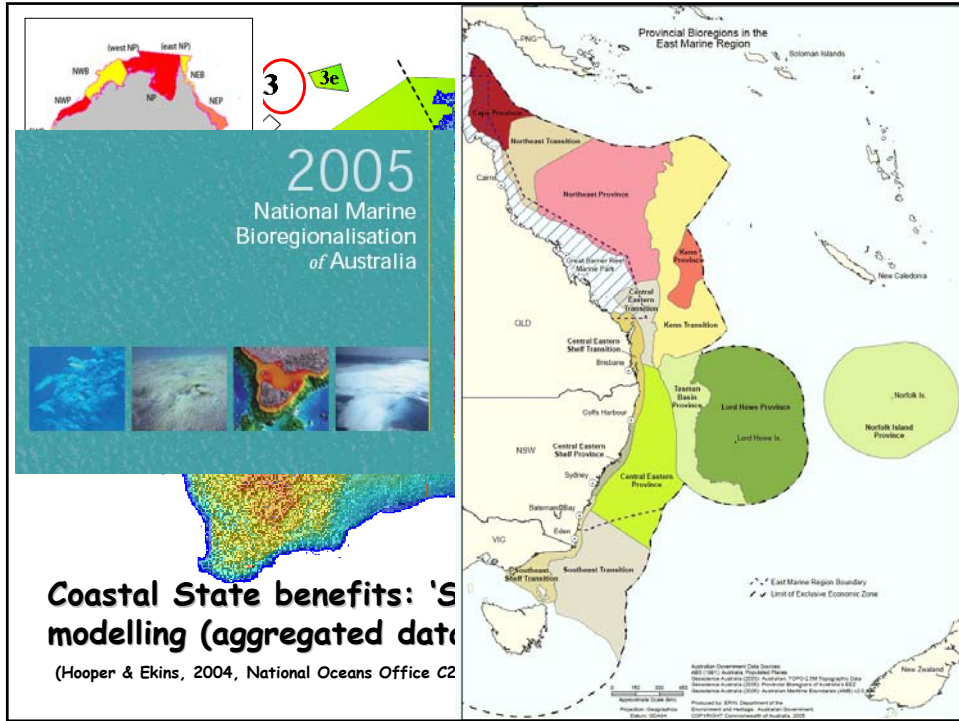
<http://www.spongebarcoding.org/>

~600 sequences contributed to sponge barcoding project (CO1, ITS-1 and 2) from samples collected from NPD/AZ bio-discovery



Coastal State benefits: 'Species turnover' - Bioregional boundaries (e.g. *Echinodictyum* species)







Summary:

Research State benefits: legislative certainty for access, IP, benefit sharing etc.; partnerships with Coastal State researchers infrastructure; biodiscovery products including building extract and compound libraries; discovery of new compounds and bioactive leads; potential commercialization = \$...

Coastal State benefits: environmental data' from biological collections, genetic and biochemical research; taxonomic and other capacity building support; contribution to barcoding projects; new knowledge pivotal to bioregional marine planning, management and ultimately conservation of MGRs; potential royalties ...