Implications of access and benefit-sharing (ABS) frameworks for collection and utilisation of marine biological samples

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Why Use Marine Bioresources?

Offers advantage over comparable terrestrial resource:

- Superior performance
- Better economics

Unprecedented activity in particular application:

- Enzymes: new reactivity/new biotransformation
- Small molecules: novel chemical structures & new mechanism of action
- Materials: new properties

Marine Biotechnology Products on the Market

Vent Polymerase
Origin: Vent bacterium
Production: Recombinant

ω-3 polyunsaturated fatty acids for heart disease Source: Fish
Production: Fish

Prialt for pain
Origin: Phillippino cone snail
Production: Recombinant

Halaven for cancer
Origin: Japanese deep water sponge
Production: Chemical synthesis

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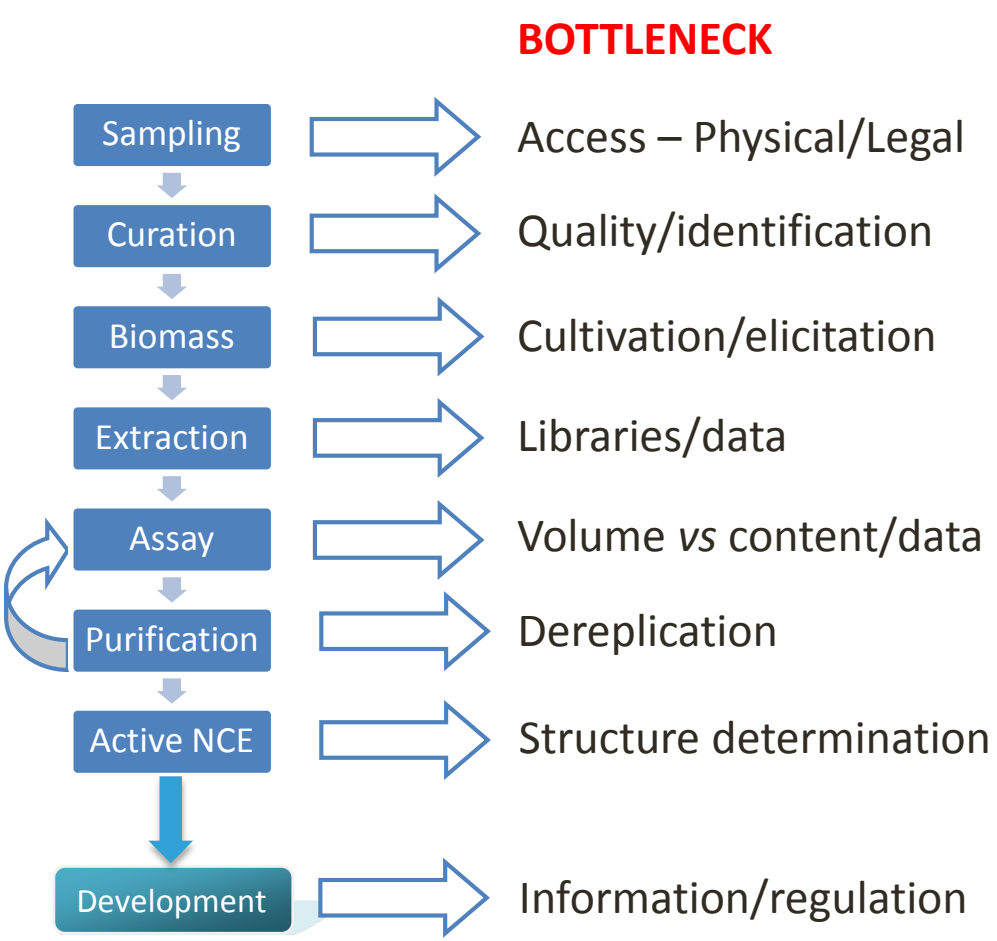
The Marine Biodiscovery Process

Biodiscovery is the discovery of compounds and associated ideas from natural sources to develop novel biomedicines.

Biodiscovery generates chemical diversity that is used to find initial biological activity in disease focused screens

Biodiscovery also includes the development of biomedical research tools, antifoulants, catalysts, nutraceuticals and cosmeceuticals.



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Applying ABS Nagoya-Style to BBNJ

- ABNJ does not refer to any ecological habitat or environment
- MGR has no real meaning to scientists
- May inhibit research due to difficulties in gaining access
  - Where stringent agreements exist few commercial deals have been done (Australia)
- Will it require an equivalent to access with prior informed consent?
- How will it be monitored/policed?
- Who will collect monetary benefits (ISA?) and who will distribute funds and how? How will terms be agreed (no MAT)?
- Becomes multilateral relationship not bilateral as in NP.
- Traceability becomes an issue as benefits may take a long time to be realised (& who will do this?).
- Expectations of financial returns may be very unrealistic.

Real Benefit Scenario

- Cost in 2014 to bring drug to market US$2,558 M* - >70% Clinical trials
- Typical industry royalties on natural products developed into drugs is 1-3%
- Halaven (Eisai), derived from a Japanese sponge makes US$200 M per year – in principle yielding US$ 2-6 M pa.
- Currently 7 approved marine drugs – total royalties would be US$ 10-50 M.
- Blockbuster drug (> US$ 1 Bn pa income) would yield US$10-30 M pa
- Currently 7 approved marine drugs come from ~28,000 discovered marine compounds (1 in 4000 chance) – none are 'blockbusters'
- All examples were discovered pre-CBD – not clear if actual royalties are being paid

*Tufts Study http://csdd.tufts.edu/news/complete_story/cost_study_press_event_webcast

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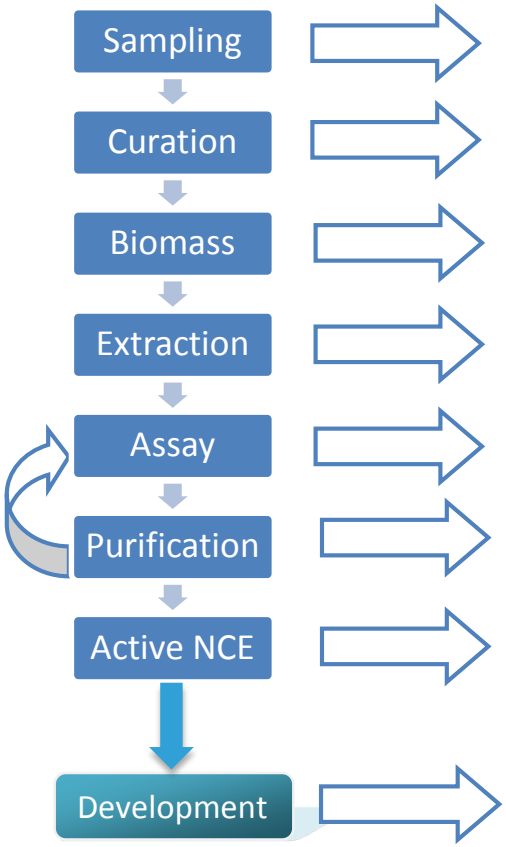
The Major Benefits are Non-Monetary

- In many cases most important benefits from use of bioresources
- In many cases these are the only benefits
- Non-monetary benefits may include:
  - Scientific exchanges/training
  - Technology transfer
  - Capacity building (infrastructure)
  - Enhanced reputation
  - Increased number/quality of scientific publications
  - Biodiversity conservation
  - Valuable regional resources developed (knowledge, samples, data)
- Non-monetary benefits still cost money – however they are upfront compared to royalties
- Is a Nagoya-like regime necessary or desirable? Will good practice suffice?

The Marine Biodiscovery Process
Elements of Good Practice



Current Good Practice

Sharing resources/samples, data infrastructure

Biobanks, trusted providers, metadata formats

Development of platform technologies for expression

Extract and fraction libraries – eg ESFRI OPENSCREEN

Screening platforms, databasing/datamining

Pure compound libraries to maximise usage

Use of prioritisation tools, efficient preclinical evaluation

Advent of personalised medicine, better industry awareness

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Current Good Practice in Cruise Planning

Application

- Cruise path/stations/equipment.

Award

- Clarification for feasibility/equipment availability.
- Check MPAs not entered.

After Cruise

- Data is logged with central agency – cruise report
- Sample list/locations collected/location stored
- Environmental data/images and video

Currently no requirement for post cruise data (eg genetic data) to be deposited. Species may not be identified until later, if at all
Responsible sampling protocols developed (eg Interridge)

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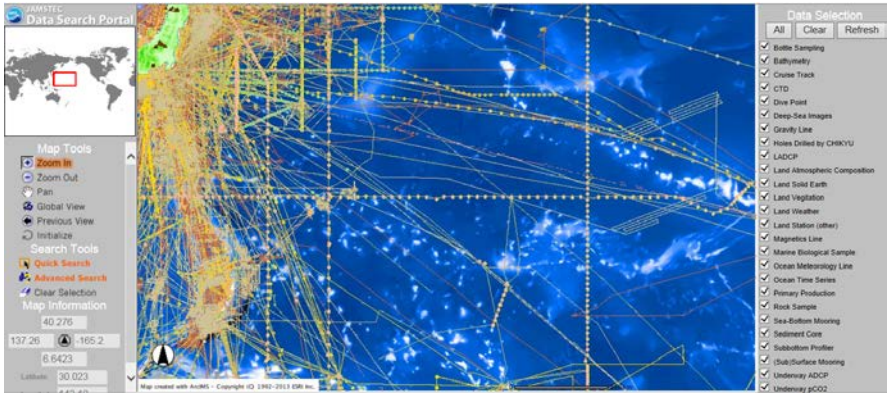
Good Practice for Cruise Data and Samples

Metadata may include

- Location
- Depth
- Temperature
- Salinity
- pH
- Oxygen content
- Seafloor conditions



Sample storage

- Ambient temperature
- Cooler (4°C)
- Freezer (-20°C)
- -80°C Freezer
- Liquid nitrogen (-196°C)
- Formaldehyde
- Ethanol
- DNA/RNA preservation liquids

ADD:
Use/Change of use

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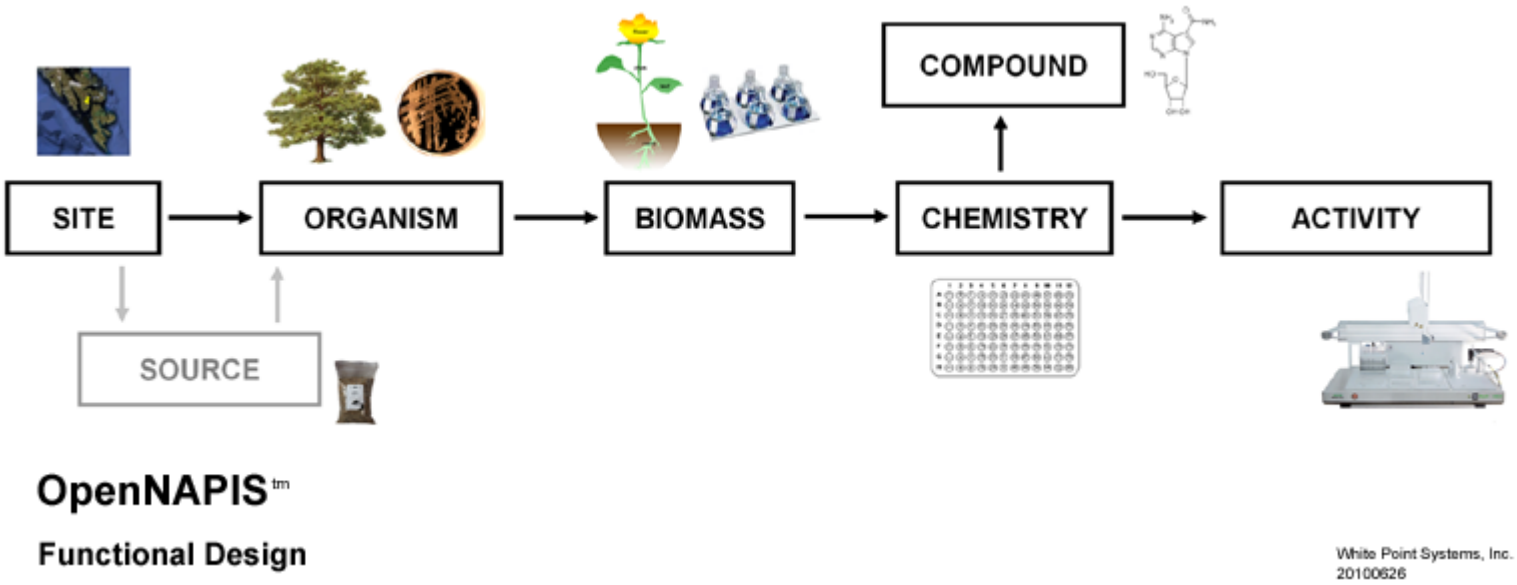
Extract/Pure Compound and Assay Data Management

Possible to track sample from origin to exploitation
(but better databases are needed)



Example of open access system: www.pangaea.de

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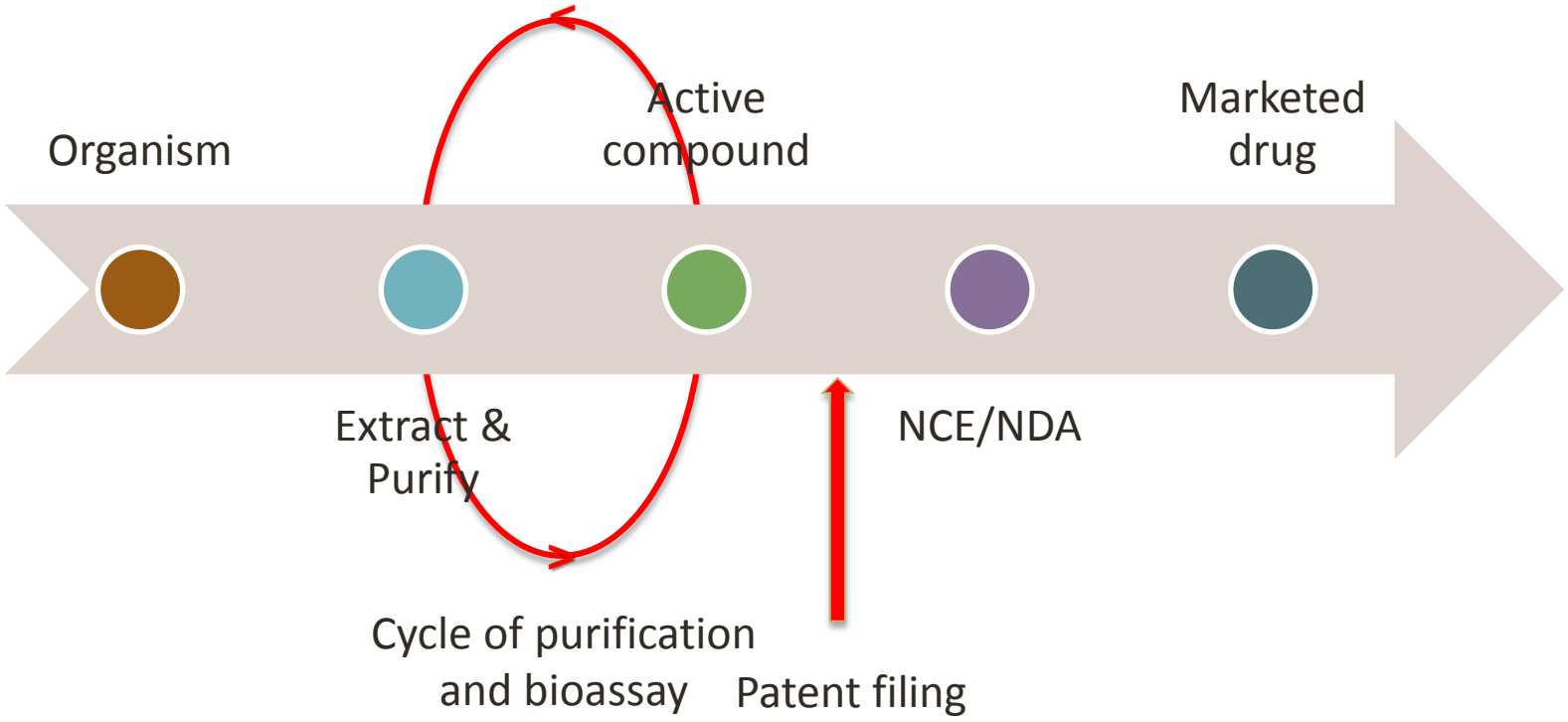
Value Inflection Point Model



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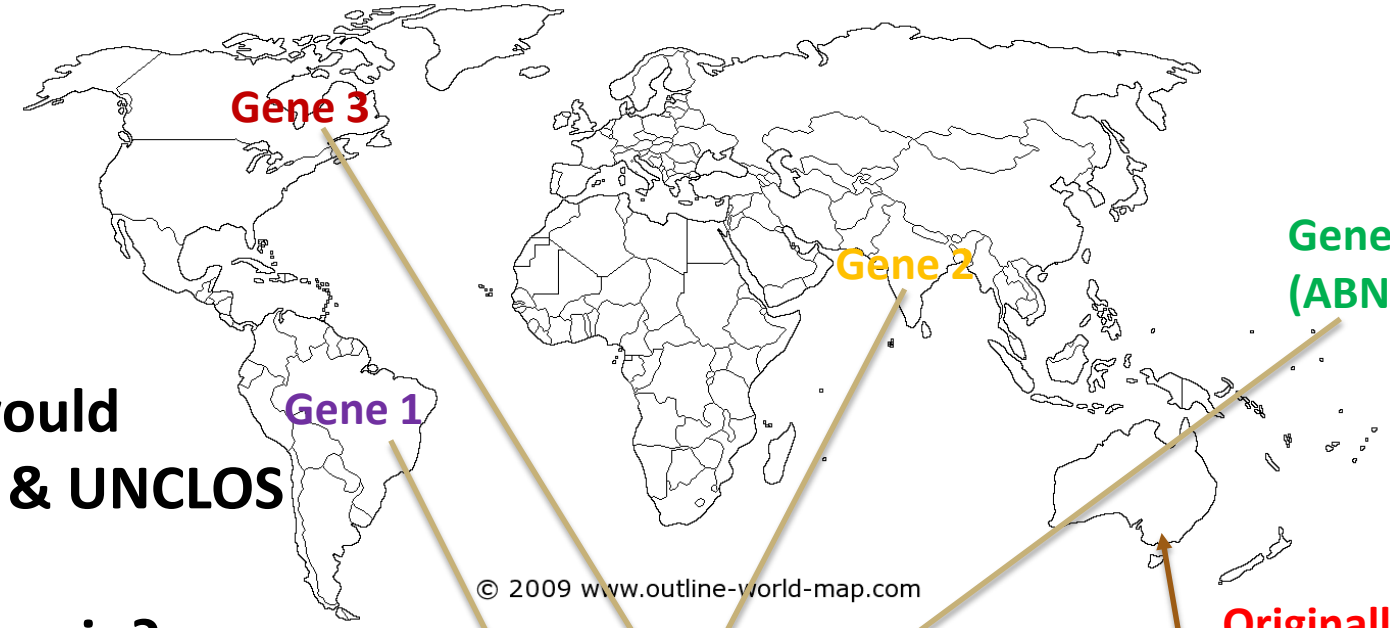
Value Inflection Point Model

- Where is the transition from basic research to research with commercial intent? (when does actual value become apparent?)
  - When research is initiated (statement in grant application?)
  - When organism is found to be active against disease based screen?
  - When pure compound with activity is identified?
  - When patent is filed?
  - When NCE is found and NDA is filed?
  - When commercial involvement begins? (ie industry funding/licencing of NCE to pharma)
- Not all patents commercialised. Some industries don't patent.
- Collection permits required?
- Who maintains data & how is use monitored?
- How is environmental impact assessed?

Science is Moving Very Quickly

- Gene sequencing is now inexpensive and extremely rapid
  - Sequence whole genomes quickly
  - Sequence metagenomes
- Bioinformatics is making huge advances
  - Genome mining to find enzymes/compounds
  - Understanding of how to express these compounds in alternative hosts
- Low cost gene synthesis is a game-changer
  - No longer need genetic resource, only sequence
  - Sequences can be optimised to express in alternative host
  - Genes can be easily combined
- **But:** open databases don't always indicate origin of materials.
- **Any UNCLOS implementing agreement developed over the next few years may not be flexible enough to deal with rapid scientific progress.**

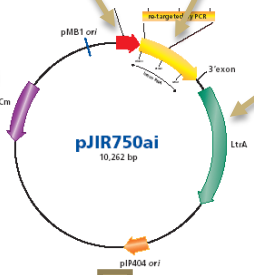
Possible Scenario



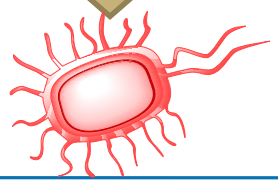
What would Nagoya & UNCLOS do with this scenario?

Vector and host may have associated IP rights

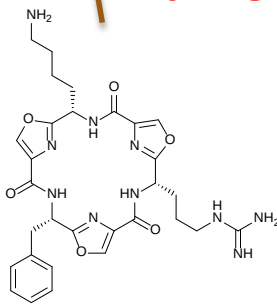
Vector



Host



Originally found in Australian EEZ Marine organism



Known bioactive compound

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Possible Scenario

- This is based on the use of synthetic biology in which genes from a number of different organisms are combined to make a product.
- The genes are combined in a ‘vector’ which allows them to work together. Vectors are artificial DNA constructs which are often owned by companies or have associated IP.
- The vector is incorporated into a ‘host’ organism, a modified easy-to-grow microorganism that can express the genes in the vector. The hosts are often owned by companies or have associated IP.
- Whilst in the host, the genes placed within the vector produce the proteins that biosynthesise the small molecules of interest.
- In this scenario the molecule generated was initially isolated from an Australian Great Barrier Reef seasquirt (marine invertebrate).

Origin of the Genes

- Gene from Brazilian reef organism – cloned without further modifications (actual gene taken from the organism unmodified and inserted into the vector).
- Gene from Indian marine cyanobacterium (blue-green alga). Organism collected by Indian scientist, sequenced, and whole genome deposited online in public database. Gene synthesised without modifications and incorporated in vector.
- Gene from Canadian marine sponge. Genome sequenced and deposited in online public database. Gene synthesised *with major modifications* and incorporated in vector.
- Gene from marine microorganism isolated from sediment obtained from deep sea trench. Trench is in ABNJ. (Gene can be native, synthetic or modified synthetic as in 1-3 above)

Open Access Model

- Current problems
  - Access is difficult to control and monitor
  - Nagoya requires researcher to prove samples are not from national jurisdiction
  - Synthetic biology will change everything – genes used may be heavily modified and bear no similarity to original genes
- Solution: share samples and data
- Open Access to Biodiversity Beyond National Jurisdiction?
- Open access typically used when:
  - There is no desire/need to control access
  - There is more than enough of a resource (samples/data) for all to utilise

Open Access Model

- Open Access Precedents
  - Biology - open data resources (also BioBricks)
  - Software – open source software can be used to make profit making products
  - Semiconductor industry – eg all contributors to chip design get right to exploit in their markets.
- Low cost – commensurate with size of problem
- Benefits will accrue locally on exploitation (jobs, knowledge, service industries etc)
- Is current good practice sufficient?
  - Access monitoring
  - Environmental impact
  - Data logging policy (time to deposition?)
  - Need for policing?

How Can We Ensure All Can Benefit?

- All should be able to benefit from discoveries
- Open access/open source typically leads to greater innovation, transparency and openness
- Requires capacity building to ensure fairness
- Access for landlocked & developing countries
  - Participate in cruises?
  - Access to actual samples (direct sampling strategy)
  - Access to open data - sample metadata, (meta)genomic, proteomic etc (make sure location/organism is clearly stated)
- Make sure all can benefit and can exploit
  - Develop scientific expertise
  - Build scientific infrastructure
  - Help identify/build local markets

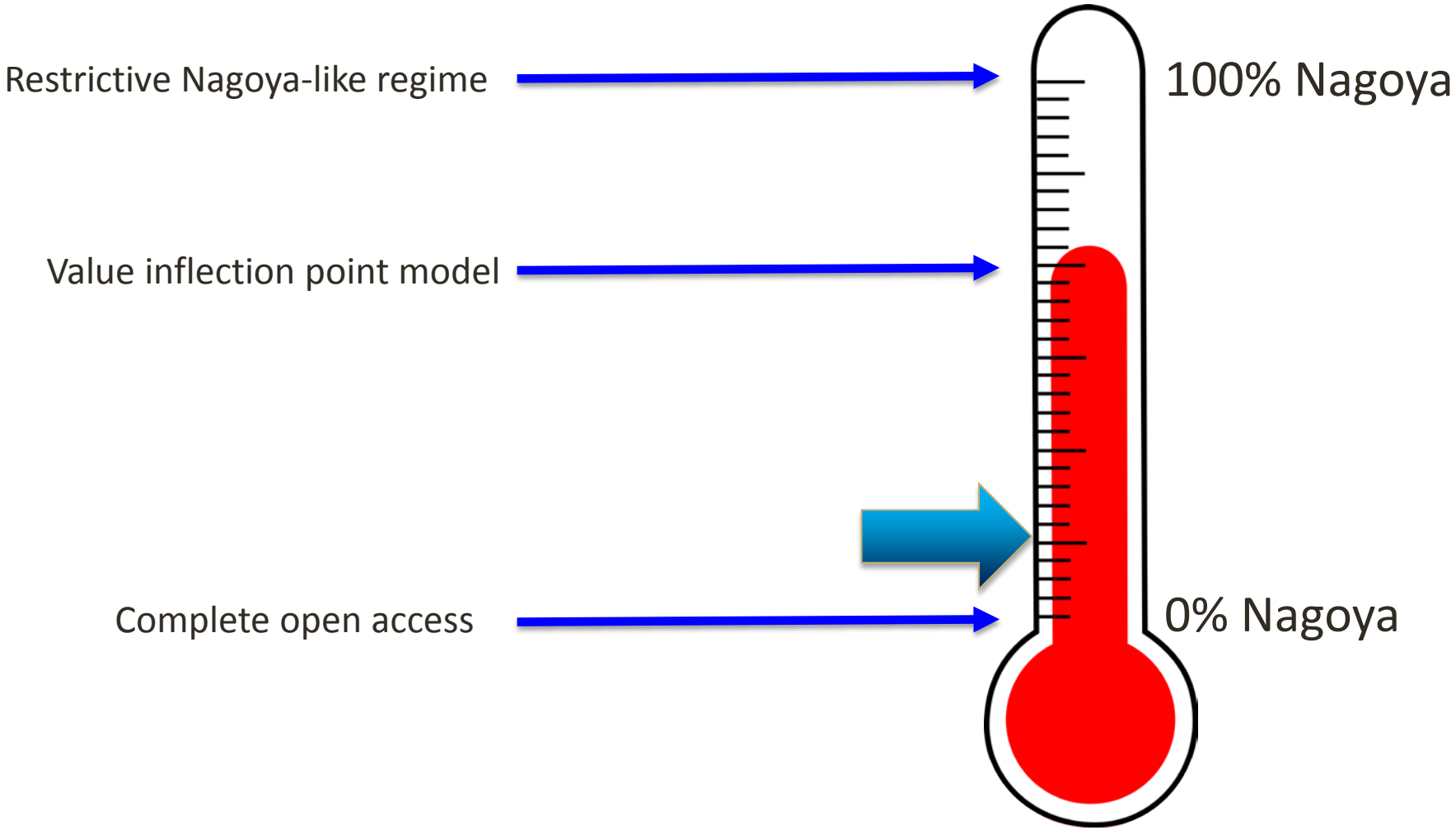
Aspects of UNCLOS Compatible with Open Access

- Rights of MSR include international cooperation and dissemination/knowledge transfer
- Apply Bermuda principles (rapid deposition of genomic data)
- Main goal of UNCLOS implementing agreement is to protect and conserve biodiversity
- Most MSR is basic research and benefits biodiversity conservation

BUT

- Environmental impact assessment difficult as no baseline data

Nagoya-O-Meter



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Conclusions

- Nagoya style ABS regime not workable for multiple reasons.
- Value inflection ABS model difficult to implement as there is no defined point where 'commercial intent' is declared in all cases.
- Any new UNCLOS implementing agreement will struggle to be flexible enough to accommodate pace of scientific progress
- Pragmatic solution is one that builds on idea of open access:
  - Collection of BBNJ not large scale (gauge importance of BBNJ)
  - Current good practice with minor changes may be sufficient as monitoring tool – much infrastructure already in place
  - Much data already open access and new data likely to be open access too
  - All can utilise/all can benefit
  - Requires capacity building so all can truly benefit
- What kind of legal regime is necessary to make open access workable?

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