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Short Communication

MIRRI Recommendations for Exploiting the Full Potential of Micro-Organism Data

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Abstract

The Microbial Resource Research Infrastructure (MIRRI) stresses the importance of access to microbial data as well as to high quality microorganisms in the execution of sound science and innovative research and development. MIRRI's mission is to remove fragmentation in resource and service availability and focus on fundamental needs and challenges that face the microbial domain Biological Resource Centres (mBRCs) and the user of microorganisms. MIRRI aims to provide a single access entry point to state-of-the-art microbial biological services and to expert and technical platforms to enable researchers to carry out in-house research on mBRC holdings. This requires improvement in the interoperability between mBRCs and overarching, as well as complementary data offers, and the implementation of quality management including standardised procedures, best practices and appropriate tools to increase the quality of the resources collected and their associated data as well as performed services. The MIRRI consortium currently comprises 16 partner and 28 collaborating parties from 19 countries across Europe and brings together data on microorganism holdings from all these centres. MIRRI partners follow common protocols on data management for mBRC holdings that will enable users to access the microorganisms'yet unrecognised potential, deliver regulatory compliance and facilitate knowledge and technology transfer. One of the most fundamental problems of managing a collection of microorganisms is keeping pace with the taxonomy and resultant name changes being introduced for species. To overcome such problems MIRRI has produced a data policy and strategy in order to establish an integrated portal for mBRCs.

ABBREVIATIONS

mBRCs: microbial domain Biological Resource Centres; MIRRI: Microbial Resource Research Infrastructure; EMbaRC: European Consortium of Microbial Resources Centres; EMBRIC: European Marine Biological Research Infrastructure Cluster; CoL: Catalogue of Life; EoL: Encyclopedia of Life; ELIXIR: European Life Science Infrastructure for Biological Information; OECD: Organisation for Economic Co-operation and Development

INTRODUCTION

The Microbial Resource Research Infrastructure (MIRRI) stresses the importance of access to microbial data as well as to high quality microorganisms in the execution of sound science and innovative research and development. This is clearly outlined in the key deliverable D4.4 *Final Draft of Business Plan Content* and the third iteration business case from the MIRRI preparatory phase project which are summarised in the periodic and final MIRRI reports (see http://www.mirri.org/downloads.html for the 2nd periodic report and http://cordis.europa.eu/result/rcn/189282_en.html for the summary reports). MIRRI's mission is to remove fragmentation in resource and service availability and focus on fundamental needs and challenges that face the microbial domain Biological Resource Centres (mBRCs) and the user of microorganisms. The goal is to facilitate legally protected and regulative compliant access to resources in mBRCs and associated data to maintain a comprehensive supply of biological material and information keeping with the demands of the research community. In doing so it wishes to increase capacity and engender trust in order to facilitate access to materials from countries of mega diversity. All this requires the linkage of member mBRC holdings with contextual data and publicly available data generated on these microorganisms and to ensure that key reference strains from publications are available for the furtherance of science. MIRRI aims to provide a single access entry point to state-of-the-art microbial biological services and to expert and technical platforms to enable researchers to carry out in-house research on mBRC holdings. This requires

- improvement in the interoperability between mBRCs and overarching, as well as complementary data offers,
- implementation of quality management including standardised procedures, best practices and appropriate tools to increase the quality of the resources collected and their associated data as well as performed services.

The data management standards utilised are built on

previous work for example in the OECD Guidelines for best practice in BRCs where criteria are set and recommendations for minimum data sets are described for the microorganisms [1]. The European Consortium of Microbial Resources Centres (EMbaRC) project (http://www.embarc.eu/) brought together guidelines for optimal formatting/annotation of data related to the biological materials held by the European mBRCs [2]. The EMbaRC website provides numerous guidance documents relevant to the development of common standards, improving strain and DNA storage methods and exploring new approaches in species identification. MIRRI is building on these and sharing developed common practice whilst establishing relationships with other European research infrastructures and Pan-European organisations in related fields. MIRRI encourages mBRCs to conduct research to add value to strains, match and pool services for public and private institutions and launch joint activities and the provision of coordinated external user access to the research infrastructure. This requires sound data management strategy and implementation tools; MIRRI has laid the foundations to do this in its business case and implementation policies and strategies.

THE ORGANISATIONAL STRUCTURE OF MIRRI

The MIRRI consortium currently comprises 16 partner and 28 collaborating parties from 19 countries across Europe and brings together data on microorganism holdings from all these centres. MIRRI will set the framework for mBRCs to change their operations so that they can underpin and improve practises in the microbiological sciences more effectively and efficiently. This will include the provision of recommended data sets for mBRC holdings that will enable users to access the microorganisms' yet unrecognised potential, deliver regulatory compliance and facilitate knowledge and technology transfer. The mBRC commitments to this are defined more fully in the Partner Charter [3], signed upon joining MIRRI. MIRRI will work to counteract the declining basic taxonomic expertise. MIRRI provides coherence in the application of quality standards, homogeneity in data storage and management and sharing of the workload to help release the hidden potential of microorganisms. With its anticipated intense dialog with users and stakeholders, MIRRI has the potential to add value to research innovation, bring together and foster currently isolated research projects. MIRRI will integrate services and resources, bridging the void between the organisms and envisaged biotechnological solutions and products in order to enhance competitiveness of Europe's bio-industry, including the support of SME's business.

The goal can only be achieved by a distributed research infrastructure with operational units in most, if not all, European Member States. MIRRI will be implemented under an ERIC (European Research Infrastructure Consortium) which is under negotiation at the present time by nine interested European Member States. The MIRRI-ERIC will implement a work programme as adopted by the Assembly of Members and provide the common gateway to resources and expertise available in the individual mBRCs. It will operate on the basis of a central organisation, managed by the Central Coordinating Unit. The user services will be facilitated by the nodes via the collaboration of the respective national stakeholder community. The individual mBRCs maintain their own legal status. The nodes facilitate the respective national stakeholder community, universities, bio-industries, policy makers and scientists to access microbial knowledge. MIRRI invites stakeholders to participate in its further development to meet its objectives.

The idea of releasing the full value in microbial resources is pivotal to delivery of the bioeconomy. Simply put, such value is the potential for use of microbial resources, as well as the biological systems and components therein, in basic and applied science as well as in innovation (for example, the potential that may be inherent in some fungal metabolites to act as new generation antimicrobials). There is also a need to be able to focus the full volume of mBRC expertise and capacity together on providing the specific resources to facilitate discovery of solutions to some of our grand challenges such as antimicrobials for control of resistant diseases and accelerate discovery in healthcare. Greater rigour and greater cooperation is required to ensure that research matches industry and societal demand. The broader user community needs to be brought into a strategic discussion with MIRRI on addressing such gaps in the short, medium and longer terms.

ADRESSING THE GAPS IN KNOWLEDGE

mBRCs are both repositories of materials as well as of huge amounts of data on microbial system functioning but the integration of systems data with organism taxonomy, functionality and geographical origin (amongst other factors) is at best patchy. Furthermore, there are large gaps and overlaps in the knowledge pool of microbial resources that are described, with concomitant missing elements of scientific expertise. In short, prediction and discovery around releasing the full value is currently very limited and inefficient. To improve this situation key obstacle to research need to be tackled in a co-ordinated way, which in turn will improve the provision of microbial resources beyond what is currently supplied by individual microbial resource collections.

Broadening the range of microorganisms available needs to be accompanied by addressing gaps in data about such resources. Currently there is a lack of both primary data and meta-data describing organisms as well as second-order knowledge on their full value (i.e. the potential functions and uses of microbial resources and associated biological systems). Critical in this is ensuring correct and valid taxonomy.

KEEPING PACE WITH CHANGING TAXONOMY

mBRCs must ensure the correct naming of organisms as most data is currently linked through the name and import decisions on quarantine, health and safety and biosecurity are taken as a result of knowing the name of a strain. One of the most fundamental problems of managing a collection of microorganisms is keeping pace with the taxonomy and resultant name changes being introduced for species. Although this is addressed by many mBRCs who have the relevant expertise, many collections require support. This is highlighted when databases are brought together; a specific case in point being the tremendous amount of time taken up during the integration of MINE – Microbial Information Network Europe data [4,5].

This was again highlighted during the CABRI – Common Access to Biological Resources and Information project (http://www.cabri.org/) [6], where a special "search by synonyms" feature was included. In producing a MIRRI information system this issue raised its head once again. Some attempts have been made but the problem is still encountered by databases such as the World Data Centre for Microorganisms (WDCM) when it lists the numbers of species (names) held by its registered collections (http://www.wdcm.org/) and demonstrated by species lists and strain number linkages shown when Straininfo.net (http://www.straininfo.net/) is searched. There are very few tools that can cope with this centrally and to get every name right for the 2 million plus strains in the WDCM database would be a tremendous task; several attempts have been made to do this over the years. It is not a simple process that can be achieved by electronic means. The publications where the name changes were made or where valid names were published need to be referred to in order to ensure the name change was appropriate in each case. In several cases changes are the result of splitting the species into two or more species; name changes cannot be made until relevant properties that are the basis for the name change are checked. What MIRRI can achieve centrally is to indicate where possible problems are present in its database content and offer tools to enable all possible strains linked to the name that is searched for to be found. This requires coordinated action which MIRRI can help achieve through its expert platforms and linkages to global networks.

A number of taxonomic or nomenclatural databases are available to link mBRC strain data to currently recognized scientific names. For fungi, MycoBank (http://www.mycobank.org) provides information on nomenclature and taxonomy and Index Fungorum (http://www.indexfungorum.org) which addresses fungal nomenclature are the key examples. For bacteria, Leibniz Institute DSMZ-German Collection of Microorganisms and Cell Cultures (http://www.dsmz.de/) publishes monthly updates of bacterial nomenclature and taxonomy (http://bacdive.dsmz.de/api/pnu/). Another highly visited website is the *List of prokaryotic names with standing in nomenclature* available at http://www.bacterio.net/; it is rich in terms of data but has limitations in terms of interoperability since data are not stored in a database but in html pages and there are no real web services allowing to easily link and retrieve data. Therefore, MIRRI created a bacterial names search engine with associated web services, working exactly like MycoBank (http://www.mycobank.org/bacteria). The Catalogue of Life (CoL; http://www.catalogueoflife.org) initiative is another solution to access taxonomic information that is not just specialized for Fungi or Bacteria but integrates higher organisms as well. The Encyclopedia of Life project (EOL; http://eol.org)offers species descriptions and associated metadata on the many life-forms on Earth - of animals, plants, fungi, protists and bacteria. Like CoL, EOL is an aggregator of data obtained from other databases such as MycoBank or Index Fungorum, for example. For the management of names, mBRCs should avoid the duplication of effort in maintaining their own nomenclature and taxonomic databases since this task is far too complex and would require important dedicated resources that are, most of the time, not available. MycoBank is an example that is delivering a number of web services that can be used to link mBRC's strains to a central and curated system that could be utilised.

A CALL FOR A COORDINATED ACTION ON DATA

As new data is accumulated on a massive and accelerating scale, the huge quantity of existing data needs to be used in a more focussed and intelligent way. Ensuring data on microbial strains is interoperable with other data sets allows meta-data analysis and new knowledge generation. Integration of habitat, taxonomic, genomic and phenotypic data can be interrogated smartly to reveal interesting chemistry and utilisable metabolic information in the search for chemical leads. Data accumulation aligned to the needs of potential users will ensure relevance of the microbial resources and facilitate their uptake and use to provide innovative solutions and discover active compounds. A coordinated approach across the mBRCs will enable the prioritisation of data interoperability, linkage of relevant isolated data sets and an obligation of member collections to ensure quality of data. To seek mechanisms to add value will increase the data offer and provide transparency to reveal new uses. The way forward to develop an Information System for European culture collections (mBRCs) has been described by MIRRI partners [7]. The authors describe the indispensable information about the microorganisms preserved in mBRC repositories, such as taxonomical descriptions, origins, physiological and biochemical characteristics, bibliographic references, etc. They summarise that information currently accessible in databases rarely adheres to common standard protocols. They are concerned that the resultant heterogeneity between culture collections, in terms of both content and format, notably hampers microorganism-based research and development. The optimized exploitation of these resources thus requires standardized, and simplified access to the associated information [7].

MIRRI'S DATA OFFER (INTEROPERABILITY TO FACILITATE DATA MINING)

MIRRI will connect its data to other relevant data sets to facilitate the generation of knowledge, following the principles laid down in the report "*Riding the wave. How Europe can gain from the rising tide of scientific data*" [8], where the benefits of accelerating the development of a fully functional e-infrastructure for scientific data is described. Interrogating member collections strain data at several levels will enable the identification of potential chemical entities and properties to deliver solutions and indicate where to find them. Utilising phylogenetic hierarchy to extend individual strain data to relatives, or chemistry through host and substrates can lead to a broader range of organisms that have the potential property sought. Additionally, when discoveries are made environments can be identified where more microbial diversity with the property can be found. MIRRI will seek data holding partners and through initiatives of ELIXIR and BioMed Bridges will ensure interoperability of its community data to facilitate accelerated discovery and innovation.

There needs to be better interrogation of the hidden value of organisms in the field. Such interrogation should enable exploration, discovery, description and generation of knowledge, not just present the data available. It needs to be:

- specialised – specific collections in a MIRRI matrix have complementary expertise
- targeted - collections become economically and

scientifically relevant

- focussed in line with demand and address current and near future needs
- vision-driven - appropriately forward looking and exploratory

The data offering needs to be clearer. Specifically:

- databases need to be coordinated across collections
- integration of data across and between collections
- implementation of shared minimum data sets
- implementation of quality standards

Datasets across and beyond collections need to exist at different levels. These need to be integrated and then data-mined. These cover:

- ecosystem and habitat
- strain properties to the extent available
- geographical locations
- International Nucleotide Sequence Database Collaboration (INSDC) – strain number – phenotype – downstream properties linkages
- unambiguous databases of phenotypic properties – e.g. enzymes, metabolites and including chemotaxonomic information
- phylogenetic information

A short term target for MIRRI is to identify the databases that it needs to link to, or even develop, and ways to integrate them. By applying data standards and ensuring interoperability in the medium term, MIRRI users will have access to a data landscape that can be mined for useful properties. MIRRI's data offering will change the game on discovery and exploitation by facilitating the identification of the yet to be discovered value of microbial resources.

The data integration and thus value-added needs to be delivered in three steps:

- Utilise standards for the integration of data within mBRCs according to defined and controlled data models and ontologies; providing a trusted, good and accurate interface. Increase the level of data on the mBRC's own strains from paper information into an electronic format.
- Collaborate with ELIXIR and other ESFRI Research Infrastructures to facilitate data mining across databases and begin to deliver comprehensive and innovative data. This envisages plugging into investment in Big Data and HPC to add information, thus value into the existing large volumes of data in mBRCs. This is a scientific enterprise – with data mining and integration at its heart. The goal is to offer novel data sets and data combinations to very well informed customers who are then able to use such data sets in creating new knowledge and opportunities.
- Turning new data into new knowledge and making that knowledge available through integrated and open knowledge networks. Knowledge presents the hidden value in recognisable terms for investment. It envisages the creation of a knowledge collaboration based on data networking.

It is the gold standard of a publicly-funded shared knowledge that integrates MIRRI met a data with, for example, EU-OPENSCREEN in a way that casts light on G8 aspirations for new antimicrobials. The G8 ministers released a joint statement on 14 June 2013, identifying antimicrobial drug resistance as a "major health security challenge of the 21st century." According to the statement, concrete actions will include coordinated efforts to rein in the use of existing antimicrobials, the development of rapid diagnostics to inform antimicrobial use, incentives for the development of new antimicrobials, international cooperation and surveillance data on drug resistance and theoretical and applied research to better understand the origin, spread, evolution, and development of resistance and the role of the innate immune system [9]. Such activities require microbial data access and integration, thus, data path-finding will drive the engine of MIRRI.

TOWARDS AN INTEGRATED PORTAL OF MBRCS

MIRRI produced a data policy and strategy during its preparatory phase laying down some key design principles in order to establish an integrated portal for mBRCs. These design principles presented some initial ideas and laid them open for discussion and implementation in the MIRRI construction phase.

1. A common standard should be used for exchanging information about microorganisms kept in mBRCs or that may finally be deposited in mBRCs
2. Proper training is needed to involve all mBRCs in the process of establishing a common portal
3. Suppliers of software that is used to manage data about individual mBRCs should be encouraged to provide support for the common exchange format
4. A common portal should contain information of all mBRCs worldwide (currently the WDCM holds data on over 700 mBRCs but this is only a small fraction of the research collections that exist globally)
5. A common portal must supply high-quality information to its endusers; quality control and quality assurance measures must be taken in all intermediate layers on which a common portal is built
6. A common portal of mBRCs should be integrated with as many external international data and resource providers as possible (sequence databases, compound databases, molecular pathway and interaction databases, publication databases, taxonomic databases, patent repositories, standards organisations, …)
7. The information content of a common portal should be as rich as possible
8. A central index must be maintained with recent administrative information about all mBRCs

9. The common exchange format and quality standards will facilitate the connection of data across the many holders and also facilitate the collection of recent dumps of the catalogs of all mBRCs when integrated access is required

10. There should be only one central index of mBRCs and one integrated common portal of the organisms kept in these mBRCs

Many of the design decisions listed above have already have been taken up and are being considered for the establishment of MIRRI. The flowchart (Figure 1) produced by a small working group within the MIRRI partnership demonstrates how some existing initiatives can be drawn together for the basis of this. For example, between Strain Info and BacDive at DSMZ, but possibly also with SILVA [10], and the WDCM global catalogue, and other data providers. The StrainInfo team, in collaboration with the Genomic Standards Consortium, has proposed the Microbiological Common Language (MCL) [11]. This standard would need further development as more use cases are set up that makeuse of MCL. In collaboration with Strain Info, some 20 collections already export their mBRC catalogues in MCL format and the BioLomics software package developed by Vincent Robert (CBS, the Netherlands) as well as BRC-Lims developed by the French network mBRC network (http://www.fbrcmi.fr/) provide native support for this export language. The WDCM are already providing data services [11], and help collections establish their online catalogues using common data sets. UGD, the USMI Galaxy Demonstrator (http://bioinformatics.hsanmartino.it:8080/), was developed in the MIRRI preparatory phase in order to support data curation and integration of catalogs with external resources. It makes it possible to integrate collections' data with other bioinformatics databases with little development requirements by leveraging on Galaxy, a well known and adopted tool.

It is important that such established systems are made interoperable and work together to provide the user with a clear and common access to the resources and associated data available. The EMBRIC project (http://www.embric.eu/) is providing some means to interconnect such data banks and services and particularly is looking to ensure that dynamic links between mBRC data and sequence data bases are made. EMBRIC work package 4 on data services and reporting standards have presented relevant reports, practices, standards and tools as deliverables of the project (http://www.embric.eu/deliverables).

BUILDING MIRRI

The heart of the MIRRI will be built around an open access infrastructure for handling of and access to expertise, resources and associated data. MIRRI will adhere to the European Charter for Access to Research Infrastructures; this charter sets out non-regulatory principles and guidelines as a reference when defining access policies for RIs and promotes interaction with business, industry and public services (https://ec.europa.eu/research/infrastructures/index_en.cfm?pg=access). MIRRI will provide open access for data and materials generated with public funding establishing clear rights on access and use but where it adds value it may develop tools for which it charges. mBRCs will continue to charge for supply of strains to cover a fraction

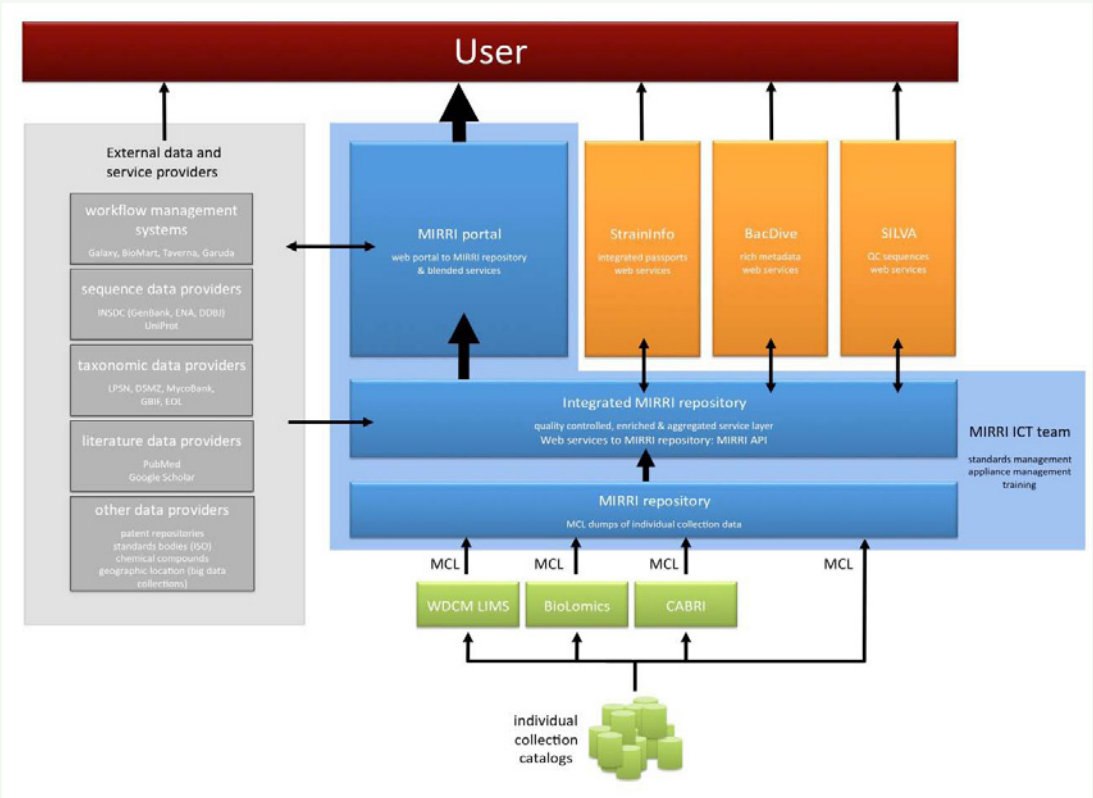

Figure 1 The MIRRI information schematic extracted from the MIRRI data strategy.

of their maintenance costs. Some services will be market driven and where commercial approaches will be in line with the legal mechanisms establishing MIRRI.

MIRRI partner mBRCs make a number of commitments when they join the MIRRI infrastructure which are laid out in the MIRRI partner Charter [12].The Partner Charter defines criteria that are to be met by the partners and criteria for resource and service providers (mBRCs) that include commitments to high quality data provision, participation in a coordinated approach to accession of new strains, quality management, best practices on Access and Benefit Sharing and biosecurity and participation in applicable cluster activities and the implemention of resulting harmonised practices, strategies and policies. Regarding data management and dissemination, the MIRRI partners guarantee FAIR (Findable, Accessible, Interoperable and Reusable) access to microbial resources they bring to MIRRI by complying with the general requirements of MIRRI. They commit themselves to provision of data and information to meet MIRRI's data management and delivery need.

CONCLUSION

Delivery of high quality microbial resources with facilities to data mine associated data sets is needed to facilitate research and accelerate the discovery of new products and stimulate innovative microbial solutions to the worlds greatest challenges, described in the sustainable development goals [13]. MIRRI will facilitate this by ensuring dynamic links between microbial strain data and other relevant data sets such as DNA and protein sequences, ecological data, metabolites, geographical data and phylogenetic relationships [14]. MIRRI will deliver a coordinated accession policy to broaden coverage of resources, increase capacity to store and deliver more characterised microorganisms to researchers. Underpinning these laudible goals is facilitating interoperability between the data held in a multitude of places to enable dynamic linkage and adoption of common standards to ensure quality and accessibility of data. MIRRI cannot achieve this alone and works through clusters of European Research Infrastructures, specialist communities and global partnerships to achieve it.

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