EXPLORING THE MICROBIOLOGICAL COMMONS.

CONTRIBUTIONS OF BIOINFORMATICS AND INTELLECTUAL PROPERTY RIGHTS
IN SHARING BIOLOGICAL INFORMATION

Tom Dedeurwaerdere (FRS-FNRS/UCL)

Bibliographical reference

Self-archived author copy
This copy is for your personal, non-commercial use only.
For all other uses permission shall be obtained from the copyright owner.

Copyright © 1999-2014 John Wiley & Sons, Inc. All Rights Reserved
EXPLORING THE MICROBIOLOGICAL COMMONS

Contributions of bioinformatics and intellectual property rights in sharing biological information

Peter Dawyndt, Tom Dedeurwaerdere, and Jean Swings

Objectives

As scientists and user groups become better connected with each other, particularly through the Internet, and as research focuses on issues of global importance such as climate change, human health, and biodiversity, there is a growing need to systematically address data access and sharing issues beyond national jurisdictions, and thereby create greater value from international cooperation. The goal should be to ensure that both researchers and the broader public receive the optimum return on public investments, and to build on the value chain of investments in research and research data (Stiglitz et al. 2000). Data sharing of microbiological information is essential for the rapid translation of research results into knowledge, products, and procedures to improve matters of general interest such as the exploration, conservation, and exploitation of biodiversity. At present, widespread national, international, and cross-disciplinary sharing of themselves. The research data is no longer merely a technological matter, but also a complex social process in which researchers have to balance different pressures and interests. Purely regulatory approaches to data sharing are not likely to be successful without considering these factors, as technology on its own will not fulfill the promise of e-science. Information and communication technologies (ICT) merely provide the physical infrastructure. It is up to national governments, international agencies, research institutions, and scientists themselves to ensure that the institutional, financial, and economic, legal and cultural and behavioral aspects of data sharing are taken into account (Arzberger et al. 2004).

In an attempt to point out the different technological shortcomings and conflicts of interest – and find ways to overcome the opposing forces that prevent the sharing of biodiversity data – it is timely to bring together information shareholders workshop addressed the

Peter Dawyndt works as a research professor at Ghent University, Department of Applied Mathematics and Computer Science, where he is teaching courses in Computer Science. His main research interest is the design of a self-learning reasoning system for landscaping bacterial diversity, used as a figure of speech for taxonomic modeling. He is regarded as the founding father of the StrainInfo.net bioportal (www.StrainInfo.net).

Tom Dedeurwaerdere is director of research at the Centre for Philosophy of Law and professor at the Faculty of Philosophy, both at the Catholic University of Louvain. Bibliographical information on his publications can be found on the website: www.cpdr.ucl.ac.be/perso/dedeurwaerdere

Jean Swings has been research manager for microbiology at Plant Genetic Systems, director of the laboratory of microbiology as full professor and director of the BCCM™/LMG bacteria collection in Belgium from 1992 to 2005. He is author of more than 280 publications in international peer reviewed journals. During 2002-2004 he was the elected president of the World Federation of Culture Collections.

Email: Peter.Dawyndt@ugent.be

Email: Dedeurwaerdere@cpdr.ucl.ac.be

Email: Jean.Swings@ugent.be
problematic nature of data sharing in the particular case of microbes. Microbes are the smallest life forms, but together they represent the single largest mass of life on earth. As a result they are often given scant attention or avoided in general biodiversity projects, but analogous to the role of dark matter that is invisibly hidden across the universe, microbes cannot be neglected, being responsible for the creation, maintenance, and restoration of balance in virtually all ecosystems. All life on earth is inextricably intertwined with micro-organisms that are critical to maintaining the health of organisms that depend on them for nutrients, minerals, and energy recycling, as well as, conversely, causing infectious disease when they overlap with susceptible hosts. Microbes show the greatest diversity of all living creatures, using biological and chemical processes that exist nowhere else in nature. Consequently, we can look to the bacterial world as a vast, mostly untapped resource of biotechnological potential, and we can study microbes to understand the majority of life processes so as to further unravel the basic mechanisms of life on earth.

Because of this interplay of the micro-organisms with their surroundings – from individual cells to entire ecosystems – the idea of transferring our studies of micro-organisms to a technological platform that seamlessly integrates all available knowledge is very attractive. This would enable the construction of dynamic self-learning systems for automated information acquisition and knowledge creation. As such, the workshop on exploring and exploiting the microbiological commons is part of a pilot project aiming at gathering expertise and new ideas in the process of building up a European biological resources platform. In particular, its goal was to constitute a reference group for a strategic research programme on a cross-cutting theme of interest to the platform as a whole.

For several reasons the bacterial world seemed an ideal prototype as a starting point for a biodiversity data exchange platform. Notwithstanding their broad metabolic diversity, there are at present no more than 6,000 validly described species, which result in a fairly limited number of anchor points for an information system. Moreover, the polyphasic approach underlying most microbial screening studies has made available large data sets on standardised observational features that reflect the phenotypic and genotypic diversity encountered among bacteria. In addition, the limited genome size that is the groundwork of bacterial life has been a strong factor leading to sequencing the complete genome of some 200 bacterial organisms, with a least another 650 complete genome sequencing projects that will reach their final stage in the near future (Genomes online database n.d.).

An integrated and combined access to this multifaceted information realm opens perspectives for the implementation of new applications. Moreover, this new set of tools for studying biological building blocks and pathways will lay the foundation for even more complex future projects. These may include the complete mapping of an organism’s protein and metabolism networks, as well as the creation of biological models that can pave the way for theoretical models on bacterial speciation and their complex ecological dynamics (Gevers et al. 2005). The development of tools for automated species identification undoubtedly requires access to sets of skills that are not typically encountered among systematists or within the departments and institutions in which the bulk of formal taxonomic identifications are conducted. Developing solid approaches requires novel collaborations between microbiologists, engineers, mathematicians, computer scientists, and personnel who have significant knowledge of both applied biology and computing science, not to forget the legal aspects of sharing biological resources and software tools in the public domain. By engaging seemingly unrelated disciplines, traditional gaps in terminology, approach, and methodology might be gradually eliminated. With roadblocks to potential collaboration removed, a true meeting of minds can take place: one that broadens the scope of investigation into biodiversity problems, yields fresh and possibly unexpected insights, and may even give birth to new hybrid, analytically sophisticated disciplines.

**State of the art**

The implementation of such a cross-cutting research programme makes sense only on the
basis of a common diagnosis of the problems that have to be faced and the elaboration of a fundamental hypothesis that guides the research.

Relying on recent Colloquia Reports of the American Society of Microbiology (n.d.), one can already point to some key elements that are part of such a diagnosis. The enhanced recourse to genetic screening and bioinformatics within microbiology is causing a profound change in the organisation of research and development in biotechnology. In particular, biological resources are being increasingly explored through computational means and information is extracted by combining a wealth of data from different sources and scales of interaction. Also, contemporary research shows the necessity of moving towards a systems biological perspective: the way that genes are expressed in an organism depends on the ecosystemic properties of its environment. In analysing the properties of micro-organisms, genetic information has to be combined with behavioural and environmental data. Moreover, in such diverse fields as antibiotics, food research, or bio-security, important new insights are to be expected from the possibility of enhancing our knowledge on the principles underlying the generation of microbiological diversity through new computational and experimental techniques.

As a consequence of this reorganisation of research and development in biotechnology, users and scientists have become more interconnected in the innovation chain. Three factors play a key role in the necessity of this dynamic user–scientist interaction.

First, the adoption of a systems biological perspective requires combining information from a broad range of actors. In particular, knowledge of the behavioural properties of organisms in the real world requires gathering data from a diverse set of “information shareholders”, ranging from traditional communities for data on slow ecosystem variables to industries for data on fermentation processes. For instance, a study of the genetic diversity of Vibrio cholerae strains isolated in different geographical regions of Brazil has revealed the close evolutionary lineage between different cholera-causing strains in completely different geographical regions (Thompson et al. 2003). This study relied on a combination of the clinical data on cholera, the environmental data on Vibrio cholerae and the genomic fingerprinting data of the collected strains. As this example shows, organising and combining information from different information shareholders has become a key issue.

Second, the multi-actor nature of the information-gathering process has raised new social issues. Indeed, public concerns have been raised about the appropriate protection of the rights of the information shareholders, for example in the use of clinical data or in bioprospecting. In this context, opting for a certain mode of organising the information-gathering process is not only a technical choice, but a choice of a certain set of social values, such as obtaining prior informed consent, protecting privacy, or sharing the benefits of the process.

Therefore, the path of technical innovation in biotechnology has become more reflexive (Beck 1997, pp. 11–19), in a similar manner to what has happened in other fields such as the Internet (Dedeurwaerdere 2002). Moreover, in this multi-actor process, protecting the rights of the shareholders cannot be the sole responsibility of the scientist: it also depends on the distribution of the bundle of rights granted to both the intermediaries in the process of data sharing and the end users of the data.

Finally, the recourse to bioinformatics and database management has introduced a new type of technical actor to the process: the information and communication technologies themselves. Indeed, the role of information and communication technology goes far beyond its use as a passive tool for data gathering and exchange. Instead, it makes an active contribution to the process of knowledge generation itself. For instance, in the case of integrated strain databases, self-learning systems organise data across different scales and show new types of linkages in an unanticipated manner (Dawyndt et al. 2005). Also, computer simulations based on self-organising networks produce new patterns of biodiversity out of existing data sets, allowing the extension of our knowledge beyond the existing culturable micro-organisms (Abe et al. 2003; Kohonen 1990). The self-organising character of these computational processes also requires a closer interaction between the provider and the user of the information. Indeed, these processes produce a
plurality of possible paths of development and the user plays a key role in producing the appropriate feedback information for selecting between these paths.

The fundamental hypothesis of the research, drawing on these insights, is that this reorganisation of the innovation chain implies a reversible interaction between scientists and innovators on the one hand and the end users of the new products (such as for food, drugs, or environmental technologies) on the other:

- On the one hand, a combination of information from genetic screening, bioinformatics, know-how and traditional knowledge, and so on, generates new knowledge and different possible paths of innovation, often in an unpredictable manner.
- On the other hand, end users should (1) provide the criteria for selecting between the different paths of development, (2) provide input to the innovation process by bringing in information from the behavioural environment of the products and (3) provide appropriate guarantees for the protection of the rights of the information shareholders.

Some projects that rely on such a reversible interaction between users and scientists have already been developed, such as the Iceland Health Sector database, which combines health sector databases with genealogical and human genomics data in order to generate knowledge about the interplay between genes, environment, disease, treatment, and outcomes in an innovative way. No study has been undertaken in a more systematic way on the generic concept of a global microbial information system for knowledge generation as such. That is why in this pilot project we want to focus on one particular case study where a sufficiently comprehensive dataset already exists, permitting dealing with these issues in a more systematic way.

The pilot project for exploring the microbiological commons focuses on one main component of this ongoing transformation of the innovation chain. This is the role of bioinformatics and intellectual property rights for knowledge generation, data access, and data sharing. As has been mentioned above, one of the advantages of focusing on this case is the existence of available large data sets on standardised and reproducible observational features, of both a genetic and phenotypic nature. Moreover, from the point of view of intellectual property rights, it is also a key area where the most advanced experiments with institutions for exchanging and sharing data and biological material have been developed (such as public sequence databases and the Mosaics project at the Belgium Coordinated Collections of Micro-organisms (n.d.)). These new institutions emerged as collaborative efforts creating appropriate data sharing for the exploration of the microbiological commons.

**Bioinformatics for knowledge generation**

The use of bioinformatics in the building of global databases in microbiology aims at pinpointing the key technologies and necessary building blocks that should make it possible to (1) build an accumulative knowledge repository that captures the reams of experimental data and meta-data about micro-organisms and to (2) develop general data mining tools for knowledge discovery in this data-rich environment, in order to (3) establish dynamically updated and flexible portals upon the observed bacterial diversity and related biotechnological innovations, with the ultimate goal of (4) valorising newly discovered insights as new applications or end-products (Dawyndt et al. 2001). This leitmotiv is schematically represented in Fig. 1. The reality is that all those involved in the initial stages of the design of automatic and dynamic models upon the raw material that is at the heart of bio-discovery research are in a period of intense experimentation, the outcome of which is difficult to predict. However, it is strongly believed that – although some of the visions may change in their details – prototyping and lack of dogmatism are undoubtedly the way forward. One of the primary goals of the bio-informatics sessions is to streamline some of these pioneering initiatives and mould the different insights they have produced into a more integrative approach.

With the rapid emergence of data formats and applications in bioinformatics supporting a veritable cottage industry of databases and web-services, the design of commonly accepted and
implemented data formats and interrogation languages has become of paramount importance if they are to support holistic scenarios. The issue of querying databases in environments where the distributed data sources have different schemas, known as the schema integration problem, has been addressed extensively in literature. Multiple common schema design initiatives for the standardisation of data exchange between distributed microbial data providers have arisen over the past two decades. Microbial Information Network Europe (MINE) and Common Access to Biotechnological Resources and Information (CABRI) are standard schemas designed specifically to disseminate information on micro-organisms, while the Global Biodiversity Information Facility (GBIF) supports both Access to Biological Collection Data (ABCD) and Darwin Core as standard schemas to cover all information about the complete biodiversity on earth. Standards for managing biodiversity content have hardly been a riveting topic for researchers. But they are a key to a host of issues that affect scientists and user groups, such as searching, data mining, and functionality, and the creation of stable, long-term archives of research results.

Successful database integration, however, requires not only the development of common schemas which allow searching the different information sources from a logical single point of access, but also needs the collected information to be normalised and corrected wherever necessary. Database annotations lack the prestige of published articles, as their value is largely ignored by citation metrics, and their upkeep is often regarded as a thankless task. The curation of databases has consequently lacked the quality control typical of good journals. These data integration issues are complementary to their schema integration counterparts, but do not seem to have been fully addressed within the problem domain of microbiology or that of the life sciences in general. Instead of striving for one single physical knowledge base containing a large amount of the accumulated information gathered on bacterial diversity, it should be anticipated that the future microbial information landscape might see a large number of high added-value information providers evolving as overlays to vast but largely automated knowledge archives and databases. This observation urges the need to establish a solid divide and conquer strategy for the management of distributed microbial information providers. Such a holistic data integration strategy is sensible as it acknowledges the fact that the value and nature of scientific information are heterogeneous.

The most prominent user-added value resulting from the integration process of microbiological commons is the establishment of information gateways that seamlessly glue together related pieces of the puzzle of common knowledge. As such, they are capable of enhancing manual navigation between distributed and heterogeneous microbial information sources, cross-checking and fusing the information disseminated by different data providers, providing the automated execution of dynamic distributed queries and exploiting large scale data mining activities for the discovery of new patterns and principles behind bacterial diversification processes. This quest requires the design of objective exploratory data analysis strategies with clear applications to biotechnological innovation. As such, mathematics and computer science might increasingly benefit from their involvement with biology, just as mathematics and computer science have already benefited and will continue to benefit from their historical involvement with physical problems (Cohen 2004). Breaking down terminological
barriers between disciplines should also enhance interdisciplinary understanding and serendipity.

Despite the slew of unresolved issues, it is anticipated that the people and the ideas brought together during the workshop might give further impetus to global action in the integration of microbial data sources, instead of just wishful thinking. Getting there will require novel forms of collaboration between microbiologists, mathematicians, computer scientists, and other stakeholders. After all, it is unwise to put all your eggs in the basket of any one solution. Diversity is the best bet.

**Intellectual property rights for data access and sharing**

Our hypothesis of a reversible interaction between user groups and scientists, in the exploration and exploitation of the microbiological commons, calls for innovative answers in the field of intellectual property rights and institutions for data access and sharing.

As a depletable good, microbial biodiversity in nature shares some of the properties of private goods, and it is de facto public in consumption or often kept in public access in order to ensure its sustainable use, it shares some properties of public goods. As such, it can be appropriately described as a “common pool resource” (Polski 2005). However, the growing importance of the digital infrastructure in the exploration and exploitation of the microbiological commons and the related possibility of making access to data more exclusive call for the creation of a second type of “commons”, a microbiological information commons.

In the field of microbiology there are already initiatives for sharing knowledge through databases and gathering knowledge from different fields, such as within the CABRI network (Common Access to Biological Resources and Information, n.d) or the ongoing GBIF project...
From a governance perspective, these networks face the increasing pressure from the development of global markets. In particular, the development of global intellectual property rights has led to a competition for the ownership of previously shared resources. At the same time, the role of the state in the provision of services of general interest, such as public collections and databases, is gradually shifting from direct intervention to the regulation of markets or quasi-markets. In the context of this new role of the state, cost-effective access can, for example, be guaranteed through introducing a general research exemption for database access for non-commercial research. In a similar manner, the exchange of biological material can be regulated through compulsory clauses in contractual arrangements for the exchange of biological material, specifying the origin of the resource and/or prior informed consent.

In this special issue we analyse the institutional conditions for the development of database-sharing in this context of global intellectual property rights. In particular, we rely on contemporary insights in theories of governance which show the necessity of developing new forms of collective action in order to deal both with the insufficiencies of market solutions and the limits of the new forms of regulation in the context of the construction of a research commons for scientific data (Hess and Ostrom 2003; Reichman and Ulhir 2003). For instance, in the field of digital communication the development of e-print repositories such as that at Cornell University Library (n.d.) and BioMedCentral (n.d.) or the development of trusted digital repositories for knowledge of general interest, such as public collections and/or prior informed consent.

arrangements in knowledge networks seem necessary to go beyond market insufficiencies created by the unpredictable character of an automated knowledge creation process and to create new partnerships between the diverse set of both public and private actors that are involved in the entire innovation chain.

These insights in contemporary governance theory allow us also to cast the stake of intellectual property rights in an entirely different perspective. Indeed, if we look at the innovation process as it is represented in the pyramid in Fig. 1, we see that the value of a biological resource is created progressively through the various steps of the process of value creation – from the extraction and accumulation of the information on the resource, through the laboratory screening and modelling process, to the development and new applications of the product. However, the current intellectual property right system creates an incentive only at the top end of the pyramid – the application – and does not address stakeholders in the entire innovation chain. Under such conditions, it seems more appropriate to adopt a dynamic framework to economic valuation (Driesden 2003). Such a dynamic approach incorporates the conditions of bounded rationality and also takes into account the dynamics of economic change outside the view of a static equilibrium situation. Accordingly, in this framework, the focus shifts from a concern about the optimal allocation of existing resources to a concern about issues of adaptive efficiency, such as knowledge acquisition throughout the entire process of value creation and incentives for the preservation of future option value under conditions of uncertainty (Dedeurwaerdere 2004).

The diagnosis of the necessity of taking into account a dynamic conception of economic efficiency in the definition of intellectual property rights joins the analyses of authors such as Jerome Reichman or Timothy Swanson, who see that new tools of regulation are needed to adapt the existing regime of intellectual property rights to a new situation, but also reveal a change in the underlying beliefs of the classical paradigm of intellectual property rights (Reichman 1994; Swanson 1997). These authors distance themselves from those who see the difficulties posed by intellectual property rights on genetic resources as only a simple technical legal issue. In order to capture the originality of the new legal tools that
are required, another reading of current changes is necessary – a reading which does not reduce them to a simple technical adjustment by sector of activity. For this, new legal tools that incorporate a more dynamic approach to efficiency need to be developed and worked out in detail in the biodiversity regime. For example, Reichman proposes evolving from a paradigm that functions by the hybridisation of existing tools based essentially on patent and copyright, to a new paradigm in terms of a liability regime, allowing the *ex post* compensation of the prior link in the innovation chain (Reichman 2000, pp. 1776–1796). Others have proposed the creation of societies of traditional knowledge and/or know-how, to foster both the wide diffusion of knowledge and appropriate protection (Drahos 2000). These alternative proposals still have a long way to go in order to become fully operational for data sharing in the microbiological commons, but they are certainly the way forward in creating incentives for innovation throughout the entire process of value creation.

This special issue gathers a set of original papers that were discussed at the first workshop that was organised on microbiological commons. As a new field of research, it has since been further developed at meetings of the International Association of Common Property and in European and Belgian inter-university research networks. In a series of two parallel sessions the workshop aimed to gather the relevant expertise for furthering the development of a prototype for information fusion (the bioinformatics sessions) and designing the appropriate intellectual property rights and institutions for database sharing (the governance sessions).

Fashioning complex computational concepts is one thing, but bringing them into practice is yet another issue. Therefore, the technical sessions of the workshop discussed prototypes for landscaping the microbial world, that is, the development of automated, dynamic, and interactive information systems for knowledge accumulation, exploration, and exploitation. Many practical questions remain open and were discussed in the major topics at the first series of sessions of the workshop (the bioinformatics sessions): (1) what are the key ICT technologies that power the construction of distributed information networks, (2) what are the necessary services for implementing an integrated biological information framework established as a community-wide effort and (3) how can state-of-the-art data mining methods lead to knowledge discovery in databases and what are the precursors for their application in the biotechnological innovation chain.

The analysis of the role of intellectual property rights and collaborative knowledge networks for the development of appropriate data access and sharing in microbiology was the subject of the second series of sessions of the workshop (the governance sessions). The session was organised in three sub-sessions, dealing respectively with (1) case studies of existing institutions for collaborative database management (public sequence databases, GBIF, and CABRI); (2) new approaches for developing appropriate bundle of rights for database fusion and information sharing (such as cooperative licence agreements and *sui generis* database protection) and (3) institutional design of the microbiological information commons, drawing on a list of necessary databases that should be combined in the realisation of the pilot project (taxonomic data, biological resource data, scientific literature, and observational data (such as 16S rRNA, FAME, MLSA, and DNA stocks)). This special issue is based on a substantial reworking of the original papers presented in this second session on the social science and institutional challenges of the microbiological commons.

Notes

1. The initiative for this platform results from consultations between participants of several European research projects (EBRCN, EUROGENTEST, MOSAICC, TEDDY). A proposal was submitted to the EU in December 2004, in the context of a consultation on future technology
 platforms. Several meetings were planned in 2005 in order to gradually enlarge and compose the core group of the platform.

2. The Iceland Health Sector (IHS) database will collect information from anonymous patient records from Iceland’s National Health Service and store the data in a computer system for clinical and statistical analysis, with legal protection against infringement or abuse. The database can be linked to an existing genealogical database. The initiative also allows the cross-referencing of IHS data with genomics data which was obtained and analysed with the informed consent of Icelandic donors (OECD 2001, p. 37).

3. The International Nucleotide Sequence database, publicly accessible through the DNA Databank of Japan (n.d.), EMBL Nucleotide Sequence Database (n.d.) and GenBank portals (n.d.).

References


Genomes Online Database n.d. Available from: http://


