Paper 1

TOWARD A GLOBAL FIELD GUIDE FOR MICROORGANISMS

by

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If one were driving across the desert in Arizona and an elephant walked across the road, one would probably stop and try to understand exactly what was happening. Immediately, one would possibly think, "The elephant must have escaped from somewhere" and, if one were a good citizen, he may try and call the police or animal shelter to inform them. The elephant crossing the road would gain one's attention because, as we all know—elephants are not native to the desert of Arizona.

Although this is an extreme example, this type of scenario happens all the time in the world today. For example, when an American Robin showed up in London, the poor bird's presence was posted on web sites and discussion groups all over the United Kingdom by bird watching groups [1]. They did this because they knew that this bird was out of place because maps are available of where all known species of birds should be. This works because the scientific community and amateur birders have made maps of species over space and time and allows us to know who is out of place.

Unfortunately, knowing what is unusual is much more difficult, if not impossible, for most microorganisms. When the anthrax-letter terrorist attack occurred, there was a mad scramble to gather information about the distribution patterns and diversity of the bacterium that causes anthrax, *Bacillus anthracis,* in order to try and figure out from where the material in the letters may have come. When the bacterium that causes tularemia was detected as part of the Biowatch [2] system, a great debate took place as to whether this was part of the area's background or some escapee from a research lab. To know whether the presence of a microbe is unusual, we need to know what is normal, just as is done in the birding or elephant example given above. Thus we need the same type of maps for microbes that are available in almost any bookstore for birds (relative to space, time, or species).

Although it would be naïve to think we can have something like a bird book for microbes, we must start somewhere. I believe that to begin to tackle this problem we need a global microbial survey. In this paper I discuss the myriad uses for such a survey focusing on those of relevance to national security issues. I also discuss some of the

ongoing efforts to gather this type of information by various groups. Finally, I discuss why these efforts have significant limitations and why I believe a new approach is needed.

I note that, for the purposes of simplicity, I use the general term "microorganism" to refer to both viruses (which are not technically living organisms since they rely on hosts to survive) and true organisms. In addition, within true organisms a diversity of types of microbes exists including ones with which most people are familiar (e.g., bacteria and yeast) as well as some of which most people will not have heard (e.g., archaea). Most of what is discussed here applies to all types of microbes and thus in the interest of keeping things simple I think not too much has been sacrificed.

A. BACKGROUND

1. Current Use Case Studies: Examples of How and Understanding of Microbial Diversity Would Be of Value

a. Use Case I: Passive Forensics

Microorganisms are gaining acceptance as useful tools in forensic studies (characterization of microbes can be used to identify soil origins or to track contacts between people) [3]. The thousands of microbe species present in human skin or in soil, water, or other locations mean that they can potentially be used as forensic tools. Theoretically, one could determine if two people came into close contact by comparing the microbes present in the nasal passages just as comparisons of HIV strains have been used to determine sources of infections [4]. To do this, one needs to have an idea of the patterns of diversity both within and among species of microbes and within and among locations where microbes are found.

b. Use Case II: Active Forensics (Sniffers and Trackers)

Much as one could use analysis of naturally occurring microbes as forensic tools, one could also use microorganisms in an active way. For example, benign microbes could be planted on some material (e.g., a car), and one could determine if someone came in touch with that object and possibly people who contacted those who touched the original object. In the long run, one could even imagine detectors that could register whether someone bearing such microbes passed through a security checkpoint. Using microbes in such an "active" forensics role raises many concerns (e.g., safety,

environmental) but is certainly technically feasible. For this to work, however, one needs to have an idea about the patterns of naturally occurring microbes in order to design an ideal system.

c. Use Case III: Soldier Health

Microbe-caused illnesses have the potential to severely incapacitate individual soldiers and, if communicable, whole units or larger groups. Prior to deployment, we can make predictions about the types of microbes soldiers may encounter in various areas, based on global and other medical work. However, this approach focuses on microbes that we know enough about for diseases caused by them to be reported, recorded, and analyzed. Unquestionably many diseases and ailments are caused by microbes that we have not yet connected to the disease. In addition, some microbes could cause disease in certain circumstances not yet encountered. Therefore, it would be beneficial to have information on the distribution patterns of microbes including those not yet on anyone's watch list.

d. Use Case IV: Natural Versus Unnatural

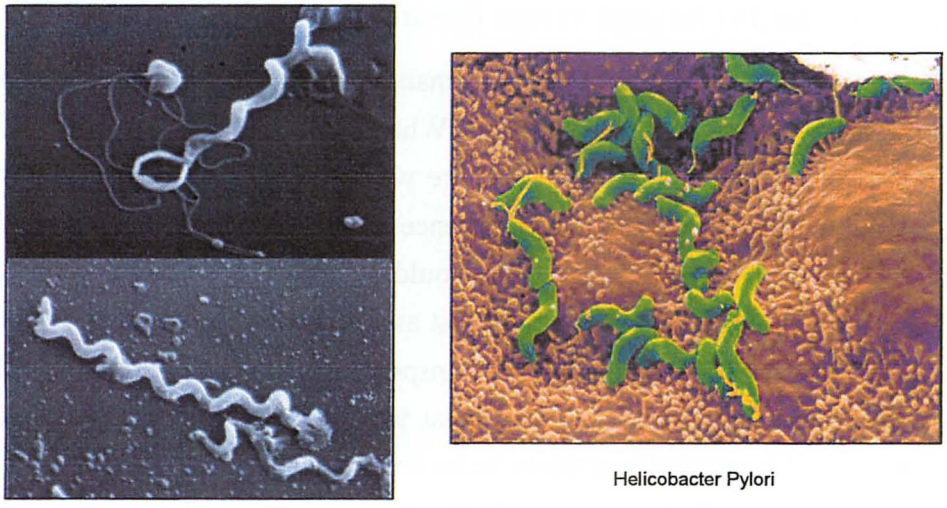
Perhaps the most critical use of information on microbial diversity is that related to the introductory story about the elephant. When a new microbe is identified (e.g., in a disease outbreak, or in biodetectors), how are we to know if its occurrence is unusual. The only way is to ask whether the occurrence could have happened naturally or was likely due to some *unnatural* event. This would have to make use of a combination of spatial, temporal, and genetic information, just as is done by birdwatchers. For example, since flu is able to spread rapidly in public transportation systems like airlines, the sudden occurrence of a strain of flu in New York that was previously only seen in Hong Kong would probably not be considered likely to be unnatural. However, if an outbreak of the strain of flu that caused the 1918 epidemic occurred, one might reasonably suspect something unnatural was occurring. This is because, although flu can move worldwide, there are no known living reservoirs of the 1918 flu. This issue is discussed in much more detail in the DSSG paper by myself and Carla Brodley (see Paper 2). In summary, to identify what is unnatural, we need to know the suite of possible natural things.

2. Difficulty in Surveying Microorganisms as Opposed to Other Types of Species

Imagine one traveled to a never-before-explored island and wanted to make a field guide to the birds there. A key step in this process would be to examine the

appearance of the indigenous birds and an attempt to divide them into different categories. Once this classification was obtained, one could then layer a variety of information onto the classes—vocalizations, behavior, range, etc. When this is done, one frequently finds that the classes based solely on the appearance of birds can be a remarkably good first approximation of the different types. Another way to look at this is that birds that look very similar to each other are usually very closely related and birds that look very different are usually not closely related. This is also true for many types of animals and plants.

Unfortunately, while appearance-based classification can allow for rapid and useful construction of field guides for many organisms, it does not work for most microbes. This is because the physical appearance of particular cells is a very poor guide to what type of microbe at which one is looking. Sometimes very distantly related organisms look virtually identical and very closely related ones look incredibly different. Examples of this abound (see Figure 1-1).



Sources: http://www.ulb.ac.be/sciences/biodic/ImBacterie.html and http://thenightwriterblog.powerblogs.com/files/helicobacter.jpg.

Figure 1-1. Appearances Can Be Deceiving

Left: An image of *Treponema palidum*, the causative agent of syphilis. **Right**: *Helicobacter pylori*, a causative agent of gastric cancers and ulcers. Since spiral shapes are somewhat rare, from microscopic studies these organisms were thought to be related. Pictures are from molecular studies that reveal that these organisms are in fact so distantly related that they are placed in different Phyla (more distant in fact than plants are from animals).

The limited value of the morphology and appearance of microbes makes the task of generating a field guide (and in fact doing any type of field analysis) vastly more

difficult than similar tasks for "macro" organisms. For example, for the bird guide for the hypothetical island, one could send unskilled people into the field to collect birds and record where they were found. These could be sent to a museum and a bird expert could convert the specimens (and their associated location information) into a rough field guide. Another way of thinking about this is to consider birdwatchers who have an appearance-based field guide. For avid birders it is quite easy to assign a bird one sees to a family in a matter of seconds. Generally, sparrows look similar to each other and different from other types of birds. Finches fly in a particular way. Raptors can be readily distinguished from owls [5].

Imagine instead that each bird species simply sampled from all possible morphologies and behaviors randomly—with one species having the head of a warbler, the tail of a pintail duck, the wing angle of a swift, and the flight pattern of a finch. This is basically what happens in many microbes. Thus researchers have needed alternative means to study and understand the distribution of microbes. The alternatives can be divided into two classes—culture-based and culture-independent.

a. Culture-Based Methods

Culture-based methods involve isolating microbes from environmental samples and rearing them in the laboratory. The ideal way is by achieving what is referred to as a "pure culture" in which one is able to grow a single type of some particular microbe in the absence of any other organisms. Usually this involves a combination of physical separation of organisms, dilution of samples, and provision of the right materials and other conditions that the microbe needs to grow (e.g., light, oxygen, carbon dioxide, etc). Once a particular type is grown in pure culture, it can be kept in essence indefinitely in some inactive state (e.g., frozen) and then revived when someone wants to study it.

Thus getting an organism into pure culture is a major achievement as it opens up a large number of avenues for study, allowing one to examine the physiology, pathogenicity, genetics, etc., in controlled conditions. In addition, since cells can be sent around the world, obtaining a pure culture allows researchers in different locations (or at different times) to study in essence the same strain. To aid this sharing, a large number of "culture collections" have been created.[1] To use culture-based methods in surveying microbial diversity, one would take different samples and try to isolate in pure culture

[1] Examples of major culture collections include the American Type Culture Collection (ATCC) in the United States and Deutsch Sammlung von Mikroorganism und Zellculturen (DSMZ) in Germany.

organisms from those samples (hopefully using the same methods for each sample). Then one could characterize the cultures and see how similar/different they are to each other.

Though culturing organisms is critical to experimental studies, it is not of enormous value in microbial surveys for two main reasons. First, it is expensive and time consuming to get organisms into pure culture. With the vast number of microbes and environments one would like to survey, there is simply no way to carry out culturing in large enough numbers to do this. More importantly, many of the types of microbes on the planet cannot currently be cultured in the lab. This means that, if one relied on culturing as the only means of studying organisms, one would only be seeing a small portion of the total system. This is perhaps best understood by a simple experimental test that has become known as the great plate count anomaly (Figure 1-2).

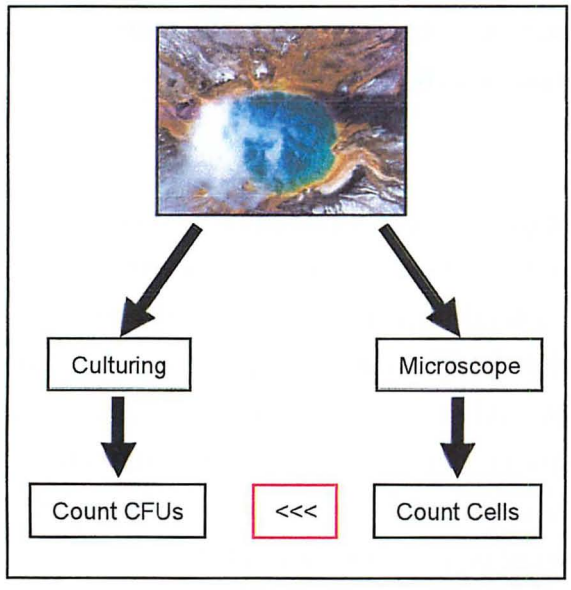


Figure 1-2. The Great Plate Count Anomaly

Suppose one took a sample—let's say 1 gram of soil. Then one took a small subsample of this (say 1 mg) and mixed it with some liquid and then spread out this liquid onto a growth plate (basically, a dish filled with a solid nutrient-rich material much like jello). When one does this, each cell in the subsample that can grow on the plate will grow and divide many times until there is a big pile of cells around the point where the cell landed on the plate. This pile is known as a colony. One can then count the number of colonies that grow. From this, one can estimate the number of colony-forming cells in the whole sample (the subsample was 1:1000 of the whole sample, so one multiplies the number in the subsample by 1,000 to get the whole population). From this type of experiment one can estimate the number of colony-forming units (CFUs) in a sample. Surprisingly, if one takes another subsample from the same original sample and simply looks in the microscope and counts the cells, there are almost always many more cells than there are colony forming units. The difference in cells versus CFUs is astonishing—in some samples (e.g., soil), one can get 100 times as many cells as CFUs. In other words, 99 percent of the cells in the sample do not grow. Thus the difference in cells vs. CFUs has become known as *the great place count anomaly.*

b. Culture-Independent Methods

The great plate count anomaly is just one of many lines of evidence that many microbes on the planet cannot be grown in the lab. In some cases, this is because we have simply not found the right materials to feed the microbes in question. In others, it

may be because the microbes cannot be grown alone but depend on other species to survive (and thus trying to grow them in isolation in the lab will always fail). Whatever the reason, the consequence is simple and devastating—culture based methods only tell us about a tiny fraction of microbes on the planet. This is a great problem because as we said above—appearance is misleading. If we cannot study organisms from their appearance and cannot study them in the lab—what do we do?

A solution to the problems outlined above came in the 1980s—microbes can be studied in the field through analysis of their genetic material [6]. All organisms have some amount of genetic material, either in the form of DNA (what is in most types of organisms) or a related chemical known as RNA (what is in some viruses like HIV and influenza). For any sample that might contain one or many types of microbes, the DNA or RNA can be extracted and characterized. This is analogous to what is done in human forensics with, for example, blood or semen samples. For studies of microbes, the exact type of analysis of the DNA or RNA changes every few years and is not particularly important for purposes of this paper. Currently people are mostly reading molecule sequences. However, in 5 years they may be doing some other type of analysis. What is important is that much can be learned about the microbes present in a sample from analyzing their genetic material including the determination of what type of microbes are present and possibly the prediction of some features of those microbes. For example, one can predict whether a strain is antibiotic resistant or one could detect the presence of one strain of flu but not another, simply by looking at the genetic material. Another important feature is that the genetic material can be stored in *very* small volumes for dozens, if not hundreds, of years for future analysis.

B. THE ULTIMATE GOAL: A GLOBAL FIELD GUIDE TO MICROBES

In an ideal world, what one would need to address the scenarios outlined above and many of the other issues that are or could be of concern relating to microbes is a global field guide. This field guide would include information on the distribution patterns of all types of microbes, including details about genetic variation and changes over time. Just as bird field guides do not say *exactly* where you will find each species, such a field guide would say things like "Microbe X is common in brackish water near sewage outflows" or "Microbe Y's range is expanding westward towards the Rocky Mountains."

Obtaining a global microbial field guide will not be easy to undertake. First, millions, if not hundreds of millions, of species of microbes likely exist. Second, the diversity within individual types of microbes is usually much greater than that for more commonly studied organisms such as plants and animals. Third, the methods needed (e.g., culture-independent molecular studies) are more expensive and complex than standard collection methods. In fact, the obstacles are so great that obtaining a complete global field guide is simply not possible in the immediate future.

Despite these and other obstacles, I believe that a global microbial field guide is a mandatory requirement for national security and public health and for an understanding of the processes on this planet (e.g., weather, carbon cycles). Importantly, starting down the path towards creating a global field guide will produce many tangible benefits along the way. Therefore, in the remainder of this paper, I outline a path towards obtaining a global microbial field guide.

1. What Would a Microbial Field Guide Contain?

Most field guides have two main features: information about distributions of organisms (including time, space, and genetic types) and information on how to find particular types and distinguish them from other similar organisms. For microbes the exact type of information needed would be different than for plants or animals but the principle is the same. For example, one might imagine that some types are found globally but in only certain types of environments, for instance, hot springs. Other types might be limited both by environment and geography. Ideally, what would underlie the field guide would be some type of database containing information about different sampling collections and the organisms found in those samples. In addition, various metadata would be linked to each sample (e.g., temperature, pH, GPS coordinates, time, etc.—see Table 1-1. Organism information would ideally be stored in some type of taxonomic hierarchy [7] and this would be linked to various information about that organism, such as gene and genome sequence data or experimental studies. One could then create maps of organisms (or groups of organisms at different levels in the taxonomic hierarchy) from the database and relate this to the metadata associated with the samples. One could then use this database to search for rules that explain the patterns of different organisms and to see if something found in a new sample was unusual.

Table 1-1. Examples of Metadata That Could Be Collected

Category	Subclasses
Location	Altitude, depth, latitude, longitude
Weather conditions	Temperature, sun levels, pressure, humidity
Time	
Chemical features	pH, salinity, nitrogen
Type of environment	Air, water, land
Biotic associations	Inside animal, outside animals, none
Geological setting	Type of rock

The exact parameters needed for such a database would be best determined by workshops and meetings with people with diverse, related backgrounds including field biologists, epidemiologists, microbiologists, and database specialists.

2. A Global Microbial Field Guide Does Not Require Sampling Every Site on the Planet

One of the comments I have received from many people while discussing this idea of a global field guide is that there are simply too many places on the planet to sample and thus the goal is unattainable. I believe this is based on a misconception about what a field guide is. The task should be envisioned more like a weather map. Weather stations are located in key places, and they gather weather information. Then interpolations are made to build a global weather map based on the weather patterns observed at the stations. In fact, butterfly and bird field guides do not sample every location either and perform the same type of interpolation. Therefore, though the world of microbial diversity is extremely large, to get a useful field guide we do not need to sample everywhere and everything.

3. Current Microbial Surveys and Their Limitations

Using both culture-based and culture-independent methods, a variety of microbial surveys has been made or is underway. It is beyond the scope of this paper to review these. When all the microbial survey projects are tabulated, the overall scope can seem impressive. People are using DNA methods to characterize uncultured microbes from the human internal systems, mouth, and other areas, from soil and water and air, and from a vast diversity of systems and environments. In addition, cultures are being generated from all sorts of new locations. Some surveys look at variation in space and time, and others look at genes and genomes across different types. Some combine culturing and

culture-independent methods. However, despite the seemingly massive scope of all the microbial surveying work being done, because of some major limitations, all of them together will not lead us on a path to have a microbial field guide and/or database. These are discussed in more detail below.

a. Limitation 1: Scale of Projects

Although many large-scale surveys of animal and plant diversity exist, very few are available for microorganisms. Most microbial surveys are investigator-driven projects, funded by one or a few grants, and thus are usually very limited in scope and scale and focus. Only recently (in part related to the threat of bioterrorism) have more top-down or large-scale surveys begun.

b. Limitation 2: Types of Methods Used

Most projects have chosen to either focus on culture-based methods or culture-independent methods. In part this is because the projects are driven by individual investigators, and the people who are trained in culturing diverse organisms are rarely also trained in culture-independent methods (and vice versa). Therefore, some environments have been sampled deeply by one approach but not the other. Ideally it would be better in the long run to have both types of approaches done side by side.

c. Limitation 3: Number of Parameters Being Assayed

In principle, for most of the uses of information on microbial diversity, we need to gather information relating to patterns in space, time and genetics. To return to the bird-watching example, most bird field guides reveal this information—they show maps of spatial distribution, they show information on distribution in different seasons (very important for migratory birds), and they show information on the types of birds one can see. Even better are guides that have historical information overlaid on the seasons since this would show the spread or decrease in particular types over time. The same is needed for microorganisms. This is, in essence, what is done in infectious disease epidemiology (e.g., the recent attempts to survey the populations of influenza virus do this). However, epidemiology (by definition) focuses on microbes known to cause disease. In my opinion, we need to treat microbial surveys more like the bird field guides, where we survey everything, or as much as possible, without any bias towards or against known pathogens.

d. Limitation 4: Lack of Coordination

The number of projects on microbial diversity is very large and is funded by a variety of agencies. For example, projects are funded by a variety of Government agencies, including the National Science Foundation (NSF), National Institutes of Health (NIH), Department of Energy (DOE), Centers for Disease Control (CDC), and many non-Government organizations (NGOs) including, in particular, a few major foundations such as Moore and Sloan. However, most of these projects involve investigator initiated and driven surveys. There is little coordination to these projects to cover every type of environment or organism (with the exception of some recent attempts involving bioweapons).

e. Limitation 5: Preselected Organisms

Most current studies are focused primarily on particular organisms or types of organisms. Since we do not know a priori which microbe we might be interested in, in the future, I believe we need to make such maps for as many types of microbes as possible, and we need to gather the materials such that one could survey for new microbes across the globe very rapidly.

4. Steps to Get to a Global Microbial Field Guide

Due to these and other limitations, it is clear that on the current path of microbial studies, we are not progressing towards anything remotely like a global field guide. This is not to say that all current efforts are useless or in vain. Almost all of them are of some value and some are quite well designed and thought out. However, they are aiming towards much narrower, shorter-term goals. As a country, if we are able to organize the community towards a wider, longer-term approach, we will all benefit. Here I describe six steps that if carried out would lead us towards a global microbial field guide.

a. A Focus on DNA/RNA Analysis

As discussed above, one could go about gathering information on microbial diversity in a number of ways. I believe, however, that the only tenable way to get to a global microbial field guide is to focus almost entirely on analysis of nucleic acids (DNA and RNA). Such a focus would be beneficial for many reasons. First, it is highly amenable to high throughput (and thus low cost) automated processing of samples. This automatism is what allowed the sequence of the human genome (and of many microbial genomes) to be determined for much less money than originally anticipated. Second,

DNA/RNA analysis is highly amenable to archiving since the nucleic acid samples can be stored in small volumes for very long periods of time (discussed more in the next section). Third, because DNA/RNA analysis is being used in some fields, computational and laboratory tools are being developed under other funds. These tools will be of great value in the global microbial field guide work and thus will be essentially a free resource. Fourth, analysis of DNA/RNA has been shown to be highly amenable to comparison across labs and samples because the methods can be standardized.

b. Archiving and Sharing and Databasing of Materials and Results

A key part of the development of all good field guides has been work by many different people in many different locations (and over long periods of time). This is made much easier by the archiving of samples and materials and by making those available to others. This is done routinely for museum collections of birds, mammals, plants, and other "macro" organisms. It is also done in a few locations for pure cultures of particular microbes. However, I have found no that is doing this for DNA/RNA samples isolated from microbial populations in the field. There is one major advantage that a DNA/RNA archive could have over normal museum archives: DNA or RNA samples could be easily sent from the archive to those in the community. This would allow any researcher anywhere to do studies on particular samples at relatively small expense (i.e., they would not have to collect new samples). Making such DNA/RNA samples available would encourage scientists to think globally in terms of types of analyses. For example, today a student interested in bacteria found in hot springs either has to beg for DNA samples from others (who usually do not share) or get permits and collect samples in remote hot springs. In addition, the student may not know exactly how to best collect in hot springs. Imagine instead that for a small fee (to support the archiving and to discourage waste), the student could get 100 DNA samples from hot springs all around the world. This would revolutionize environmental microbial studies.

In addition to sharing samples, it is also important to share information about the samples and results that have come from analyses. Therefore, a key component of this project should be the construction of a database that contains information about all the microbial collections that have been done or are being done. This database should include all the metadata that can be associated with samples and links to other databases such as genome sequence information, satellite imagery, etc.

c. Make Use of Available Archives and Collections

Although no systematic efforts exist to create an archive of DNA/RNA from microbial populations, many collections are available that could be used to rapidly build such an archive. As long as some samples are stored appropriately (e.g., frozen), DNA or DNA can be isolated from them. For example, hundreds of different projects have generated systematic collections of water samples from lakes, oceans, sewers, etc., and have been stored frozen. Others exist for air, soil, animals, plants, and so on. In some cases, these collections are being thrown away. It would not be excessively expensive to take such collections and isolate DNA and/or RNA from each sample and archive it for future use.

d. Encouraging the Participation of Amateurs

Bird and butterfly field guides tend to be much better than field guides for many comparable types of organisms. There are a variety of reasons for this, but one of them is the participation of enormous numbers of amateurs and students in gathering information that is then used for the field guides. This is why, for example, when a rare bird species shows up in London, within days all the birders know about it. Obviously we are not going to be able to have amateur microbe collectors running all around the world helping with collections. However, I do believe there are ways to get amateurs and students to participate in a global microbial surveying effort. One possibility would be to design teaching modules that involve sampling some environment where students send their samples to a center. The center could then do some analysis that would then be returned to the students (hopefully relatively quickly) and also submitted to an archive and database. Even better would be to have kits that could be used in classes (and by amateurs) where they could do some analysis of their own but that would also have them submit samples or results to an archive. This could be analogous to bird and butterfly counts done by amateurs that are very useful in surveying the world.

e. Selection of Model Systems for Initial Studies

The world is a very large place in terms of microbial diversity. Thus I believe it would be important to develop model systems that can show how powerful a global microbial field guide could be. For example, one could select a few types of environments and characterize these in detail (e.g., the human internal systems). Alternatively, one would set target numbers for locations—such as "100 samples per county" that would encourage the participation of local scientists or amateurs in making

sure their communities were covered. It is hard to know exactly what the best model system would be at this point, but I believe a few workshops with a diverse collection of scientists could identify 5-10 model systems or approaches that would be beneficial to use in the first few years.

f. Coordination and Cooperation

For this to really work, it needs to be a global cooperative project. It is for this reason that I believe as much of it as possible should be open. This does not mean that classified or restricted components should not be attached to such a project. But if enough is not in the open, one will not gain the benefits of global participation (and free participation and analysis) that can come from interesting open projects.

Another aspect of coordination and cooperation would be to have Government employees and scientists or other academics collect samples while carrying out other tasks. For example, air samplers could be provided to geologists doing field work so that air samples could be collected from diverse locations that would also have geological information collected. The only negative I can imagine from doing this is that if the project is not viewed positively by the public, seeing Government employees and academics collect samples in diverse locations would probably have a "big brother" feel. There is even occasional discomfort with researchers collecting insects (e.g., farmers sometimes worry about what might be found on their farm; land developers may worry about endangered species being found) and other animals or plants. Thus it would be worth more discussions in this area before having collections made everywhere.

C. NEW DEVELOPMENTS NEEDED AND OTHER ISSUES

There are, of course, many obstacles to the success of making a global microbial field guide. In most cases, the obstacles are simply technologies that need to be developed. I list examples of these in Table 1-2.

Table 1-2. Areas in Need of Development

Area	Detail
Technical needs	Sample processing High throughput DNA/RNA extraction DNA analysis (lab and computational) Archiving
Political needs	Biopiracy conventions
Education and training	Public/amateur participation Design of courses and kits for student participation

D. SUMMARY

What I have tried to do in this essay is outline why a global microbial field guide would be a useful goal. I realize this is may be seen as completely unattainable. But I do not think this is the case. In particular, if we aim for some of the mid-term steps that I outlined above (e.g., DNA collections), we will be able to not only generate a first generation field guide but also we will receive many collateral benefits. Some of these benefits will come directly from the project (e.g., by sharing DNA samples, we will certainly learn a great deal about microbial diversity and help encourage the development of new DNA analysis methods). Other benefits will be indirect. For example, if this becomes an international project it may help keep past bioweapons researchers occupied and employed. I have not proposed an exact plan of action because I think this is something that will need workshops, meetings, conferences, and a series of planning sessions. But the final goal is achievable if we put in the effort. And I do not think the costs would be outrageous. Many museums already have massive collections of insects or other organisms. Here we would need to only collect DNA and then possibly have a distributed team of analyzers who may do the required work at no cost. The only major costs may be in the archiving and in the DNA analysis to be done (e.g., DNA sequencing). Therefore, I believe that this is a project that should be considered for its medical, scientific, and security benefits as well as for the side benefits.

Acknowledgments

Many people advised me regarding this project including multiple DSSG mentors and other DSSG members from my class. In addition, I had some very useful discussions with researchers at Lawrence Livermore National Labs including but not limited to William D. Wilson, Raymond P. Mariella, Jr., and Steve Velsko. Others providing useful input include Claire M. Fraser, Eric Eisenstadt, Randy Murch, Naomi Ward, and Carla Brodley. Any mistakes or omissions, of course, are all the doing of the author and not the advisors. I also would like to thank Phil Gould and Karen Olsen for their work in making the DSSG program a phenomenal experience.

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