

The realisation that the majority of bacteria have never been grown, analysed, or even named, demands new approaches, new techniques and new ways of thinking. Dawn Field and colleagues discuss a new area of science – metagenomics.

# Small world

This is a microbial world; the majority of life on the planet is composed of micro-organisms and they largely run Earth's biogeochemical cycles. These cycles help shape the composition of atmospheric gases and patterns of nutrient availability making them an integral part of Earth's life-support system. Yet our knowledge of this microbial world remains limited.

In recent years, scientists have developed new and extremely powerful ways to detect and characterise this world. It is no exaggeration to say that these techniques are revolutionising the field of microbiology in the same way as Van Leeuwenhoek's sensational discovery of the very existence of microbes using the first simple microscopes in the late 1600s. These new techniques now enable us to look at the complex sets of molecules that make up living cells and to access the information contained within.

## The promise of metagenomics

In the past decade, breakthroughs in our ability to 'read' the content of genome sequences – the heritable information of each individual organism – have led to the exciting field of 'metagenomics', a term first coined by Jo Handelsman in 1998 to study the genomes from all the microbes in a particular environment as opposed to the genome from one organism taken from the environment and grown in a culture in the lab. Metagenomics means we can now get information about communities of microbes taken directly from their natural environments – a litre of seawater, a tablespoon of soil, or a scoop of sludge from a waste-water facility. This also gets over the problem of growing microbes in the lab: many

microbes simply refuse to reproduce in laboratory conditions.

A major difference between this method of studying and more traditional methods is that metagenomic studies do not produce a complete genome sequence of one organism as a single molecule but vast collections of incomplete and anonymous fragments of DNA. The information content (see box) of these fragments has to be reassembled, rather like a jigsaw puzzle, before we see the complete picture of how microbes live and function in their natural environment. Despite the fact that the metagenomic jigsaw has many missing pieces researchers are using this approach to glean a wide range of information from the natural environment. These metagenomes are revealing that microbial communities can be very different beasts, in terms of complexity, than microbiologists have believed from traditional approaches using pure cultures of individual species.

More NERC researchers are adopting metagenomic approaches to environmental science problems. Ian Joint from Plymouth Marine Laboratory (PML) is currently leading a collaboration of nine UK universities, PML and the Centre for Ecology & Hydrology to study marine microbes and their roles

in nature. This project is using metagenomics to study how ocean acidification will affect microbial communities. Rising levels of carbon dioxide in the atmosphere are making the oceans more acidic. Within 100 years the oceans will be more acidic than they have been for 25 million years. Members of the team recently travelled to a special research station in Bergen, Norway, and set about bubbling carbon dioxide through large containers of sea water to change the acid levels to those expected in a hundred years. The team is also testing a number of specific ideas including: do microbes in the

## Genetics – a quick guide

**Genome** – The complete genetic material of an organism containing all the genes.

**Genes** – Genes are segments of DNA that regulate biological activity. They contain the instructions for producing proteins, which make up the structure of cells and direct their activities. Genes determine the inherited characteristics that distinguish one individual from another. Each human has an estimated 30-45,000 genes.

**DNA** – All living cells contain DNA – deoxyribonucleic acid – the organism's blueprint. The DNA molecule carries instructions for making all the structures and materials an organism needs to function.

ocean exist in definable communities, do many chemical movements depend on the microbial community, and is marine microbial activity a major source of the gases in the atmosphere needed for life.

#### A meeting of minds

The explosion of interest in metagenomics has not gone unnoticed by the NERC research community. At a two-day workshop organised by NERC and the Society for General Microbiology more than 200 scientists attended and a real sense of excitement developed among the participants – even those relegated to standing in the lecture theatre doorway due to an unexpectedly large number of attendees. The calibre of talks and the lively discussions demonstrated that a dynamic and interdisciplinary metagenomics community has developed at the international level.


A key theme to emerge from the workshop is that no single technique – not even metagenomics – is going to provide all the answers we want about microbial diversity and function. We are using a combination of approaches in this project including Stable Isotope Probing (SIP) pioneered by Colin Murrell's group at the University of Warwick. In brief, a SIP experiment involves 'feeding' a bacterial community a heavy isotope (often a heavy isotope of carbon). Those metabolically-active bacteria in the environment that can 'eat' this isotope will incorporate the isotope into their DNA as they grow making them easier to identify. It is then possible to separate the 'heavy DNA' from active cells. Using this technique, for example, scientists can isolate the exact type of bacterium responsible for a specific task – such as the degradation of a particular pollutant – from the complex mix of bacteria that form a particular community.

#### Next steps

Metagenomics, combined and integrated with new and traditional experimental approaches and sound ecological knowledge, will pave the way to a new level of understanding of the natural world. We look forward to seeing this young and dynamic community grow and to the discoveries it will make about the 'vast unseen world around us'.

#### The power of metagenomics

DNA is the blueprint of life. In genomes certain pieces of DNA are like 'name tags' and tell scientists where a given sequence falls within the tree of life. By detecting these pieces of DNA, it is possible to build more realistic estimates of the natural abundances of microbes, explore their distributions across the globe, and track changes in these patterns over time, for example, in response to climate change. Other pieces of DNA are responsible for building enzymes, the proverbial power houses of microbial cells. Enzymes are the drivers for the chemical processes within micro-organisms. On a global scale these chemical processes help shape the composition of atmospheric gases and patterns of nutrient availability on Earth. Yet other strips of DNA code for specialist molecules of economic importance, for example, enzymes that are useful in industrial processes because they break down pollutants. By enabling the detection of these types of molecules metagenomics is proving a powerful tool for addressing a wide range of otherwise intractable problems, among them a much improved assessment of biodiversity on Earth, a better understanding of metabolic pathways essential to maintaining life-systems on Earth, and the search for useful molecules, for example, antibiotics.

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