Received: 27 September 2017 | Accepted: 6 November 2017
DOI: 10.1111/gcb.14003

RESEARCH REVIEW

WILEY Global Change Biology

Human dissemination of genes and microorganisms in Earth's Critical Zone

Yong-Guan Zhu[1,2] | **Michael Gillings**[3] | **Pascal Simonet**[4] | **Dov Stekel**[5] | **Steven Banwart**[6] | **Josep Penuelas**[7,8]

[1]Key Lab of Urban Environment and Health, Institute of Urban Environment, Chinese Academy of Sciences, Xiamen, China

[2]State Key Lab of Urban and Regional Ecology, Research Center for Eco-environmental Sciences, Chinese Academy of Sciences, Beijing, China

[3]Department of Biological Sciences, Macquarie University, Sydney, NSW, Australia

[4]Environmental Microbial Genomics Group, Université de Lyon, Lyon, France

[5]School of Biosciences, University of Nottingham, Nottingham, UK

[6]Department of Geography, The University of Sheffield, Sheffield, UK

[7]CSIC, Global Ecology Unit, CREAF- CSIC-UAB, Barcelona, Catalonia, Spain

[8]CREAF, Cerdanyola del Vallès, Barcelona, Catalonia, Spain

Correspondence
Yong-Guan Zhu, Key Lab of Urban Environment and Health, Institute of Urban Environment, Chinese Academy of Sciences, Xiamen, China.
Email: ygzhu@iue.ac.cn; ygzhu@rcees.ac.cn
and
Michael Gillings, Department of Biological Sciences, Macquarie University, Sydney, NSW, Australia.
Email: michael.gillings@mq.edu.au

Funding information
National Natural Science Foundation of China, Grant/Award Number: 41571130063; Chinese Academy of Sciences, Grant/Award Number: XDB15020302, XDB15020402; Australian Research Council; European Research Council Synergy, Grant/Award Number: SyG-2013-610028

Abstract

Earth's Critical Zone sustains terrestrial life and consists of the thin planetary surface layer between unaltered rock and the atmospheric boundary. Within this zone, flows of energy and materials are mediated by physical processes and by the actions of diverse organisms. Human activities significantly influence these physical and biological processes, affecting the atmosphere, shallow lithosphere, hydrosphere, and biosphere. The role of organisms includes an additional class of biogeochemical cycling, this being the flow and transformation of genetic information. This is particularly the case for the microorganisms that govern carbon and nitrogen cycling. These biological processes are mediated by the expression of functional genes and their translation into enzymes that catalyze geochemical reactions. Understanding human effects on microbial activity, fitness and distribution is an important component of Critical Zone science, but is highly challenging to investigate across the enormous physical scales of impact ranging from individual organisms to the planet. One arena where this might be tractable is by studying the dynamics and dissemination of genes for antibiotic resistance and the organisms that carry such genes. Here we explore the transport and transformation of microbial genes and cells through Earth's Critical Zone. We do so by examining the origins and rise of antibiotic resistance genes, their subsequent dissemination, and the ongoing colonization of diverse ecosystems by resistant organisms.

KEYWORDS
Anthropocene, human impacts, planetary health, pollution, resistome, urbanization, xenogenetic

1 | INTRODUCTION

Earth's Critical Zone is the thin surface layer of the planet upon which terrestrial life depends. It extends from unaltered bedrock, through the land surface, to the vegetation canopy and atmospheric boundary layer. Critical Zone science is complementary to other integrative system approaches for studying terrestrial, marine, and freshwater environments. Crucially, it includes a mechanistic understanding of shallow lithosphere processes and their interactions with the above-ground ecosystems (Mobley, 2009). It addresses these interactions across wide temporal (subsecond reaction kinetics to geological time spans) and spatial scales (molecular to planetary). The Critical Zone approach recognizes Earth as a physical and geochemical substrate that supports above-ground ecological functions, and extends the lower boundary of ecological function to embrace the lithosphere, and its inputs over geological timescales.

This interdisciplinary research area within geobiology links biological and geochemical processes across temporal and spatial scales. However, the distribution, transport, and recruitment of functional genes have rarely been investigated via the systems perspective framed by Critical Zone science. As investigation of Critical Zone biogeochemical processes extends the analysis of flows and transformations of material and energy to explicitly include biodiversity, a tractable approach may be to describe the geospatial dynamics of the genetic information encoded in functional genes, and the microbes that carry these genes. Above-ground human activities generate impacts that are transmitted through the vertical extent of the Critical Zone, via aquifers, and horizontally within water catchments (Figure 1). Analyzing the vertical and horizontal penetration of genetic material should be part of these investigations (Küsel et al., 2016).

Environmental microbes and genes were traditionally studied in one location, or in one environmental compartment (such as vegetation, the water column, or soil), with little attention paid to the dynamic exchange of microbes and genes across system boundaries and physical scales (Zhu, Gillings, Simonet, Stekel, & Penuelas, 2017). The advent of "omics" tools has facilitated the exploration of Earth's biological "dark matter," but there remains a substantial conceptual gap between the notion of the Earth's biome and its quantitative manifestation in biogeochemical fluxes. Integrating "omics" data into earth system science should generate better models of biogeochemistry and improve understanding of how environmental changes will impact microorganisms and *vice versa*. For instance, incorporating environmental genomics data into biogeochemical models improves predictions about nitrogen cycling (Mock et al., 2016; Reed, Algar, Huber, & Dick, 2014).

Driven by these concepts, there is increasing attention toward system views of the temporal and spatial distribution of microbes and genes in Earth's Critical Zone. Metagenomics has been used to determine the influence of fluvial networks on the co-occurrence of microbes, by examining biofilms in over a hundred streams (Widder et al., 2014). The distribution and origins of fecal bacteria have been determined in large mixed-use watersheds in Michigan, USA, also using omics technologies (Verhougstraete, Martin, Kendall, Hyndman, & Rose, 2015). Similar ecosystem wide approaches have been used to demonstrate how below-ground microbial diversity might be a primary driver of plant diversity and productivity (Bardgett & Van Der Putten, 2014). Questions are also being asked about how surface activities might influence below-ground biota and nutrient cycling, using combinations of omics, biogeochemical, and hydrogeological approaches (Küsel et al., 2016).

These publications are representative of recent efforts to explore the links between microbial biogeography, biogeochemistry, and geological processes. In particular, they reflect a growing interest on the effects that human activities might have on the microbial world (Gillings & Paulsen, 2014). Understanding the role that humans might have in changing the distributions of microorganisms, and in generating selective forces that alter adaptive pressures, is essential if we are to predict how global change will affect microbial activity and function. However, many of the most important processes for Critical Zone function are complex, multigene, and multicell interactions that are difficult to model, due to the complexity and dynamics of

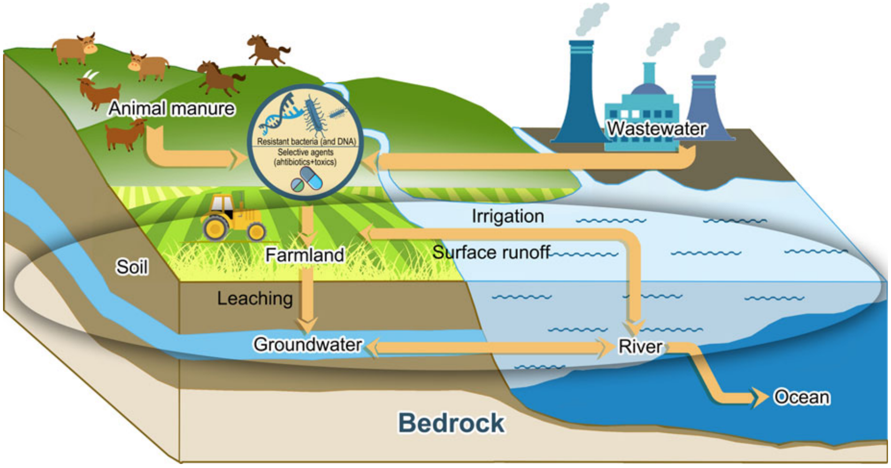

FIGURE 1 Movement of antibiotic resistance genes and bacteria in Earth's Critical Zone. Bacterial cells and their genetic cargoes are released from human dominated ecosystems in wastewater and manure. These same waste streams carry significant quantities of selective agents, promoting recruitment and survival of cells and resistance genes at all destinations. Microbial transport is enhanced by mass movement of soil, produce, and ballast water, and by human tourism. The extent of this movement can be assessed by examining the spread of antibiotic resistance determinants through the Critical Zone. Key hot spots of antibiotic resistance genes are as follows: hospitals, wastewater treatment plants (WWTPs), intensive animal farms, antibiotic manufacturers

genetic and functional diversity within indigenous microbial communities.

There are simpler systems that we can use to understand the influences that humans have on the transport and transformation of genetic information in the Critical Zone. Antibiotic resistance, for instance, is generally a one-gene, one phenotype character and has been the subject of considerable research over the last fifty years. Genes conferring resistance, and the cells that host these genes, could be used as a paradigm for assessing the interactions of gene flow with the diversity of microorganisms in the Critical Zone.

Antibiotic resistance might be a good proxy that can inform more general conclusions about alterations in the distribution and activity of the microorganisms that host specific genes within the Critical Zone. Although antibiotic resistance is ancient (ref), the widespread use of antibiotics in agriculture and medicine has increased the abundance of both resistance genes and the bacteria that host them. These genes and microorganisms are then shed into environmental compartments via human and animal waste streams such as manure, sewage sludge, and wastewater (Figure 1) (Gillings, 2013). As a consequence, antibiotic resistance genes are considered to be emerging environmental contaminants (Pruden et al., 2013). On the one hand, the spread of resistance determinants within the Critical Zone is caused by human activities, and on the other hand, it also threatens human health worldwide. The research history of resistance begins in the 1950s and is thus co-incident with the "Great Acceleration" and the rapidly increasing impact of humans' activity on the planet since this time point (Steffen, Broadgate, Deutsch, Gaffney, & Ludwig, 2015).

2 | NATURAL TRANSPORT AND BIOGEOGRAPHY OF BACTERIA

We live in a world where organismal abundance and gene frequencies have been significantly shaped by human activities. Nevertheless, it is worth reflecting on the historical dynamics of microbial organisms and ecosystems, before the rise of human influence. This allows comparisons with the modern world.

It has been known for some time that microorganisms exhibit the same taxa–area relationships and turnover in species assemblages with distance that are characteristic of larger organisms (Green et al., 2004; Horner-Devine, Lage, Hughes, & Bohannan, 2004). Taxa are distributed nonrandomly in environments such as soil, fresh water, and groundwater, at scales from meters to many thousands of kilometers (Martiny et al., 2006). These patterns are driven by a combination of factors, including the ability to disperse over distance; selection at the destination; and stochastic processes such as drift and mutation (Hanson, Fuhrman, Horner-Devine, & Martiny, 2012). Teasing apart the relative contributions of the processes that generate patterns of microbial biogeography is difficult, and is further complicated by the diversity and complexity of microbial communities themselves (Evans, Martiny, & Allison, 2017; Haggerty & Dinsdale, 2016). The impact of human migration as a transport vector on structuring prokaryotic communities is still poorly understood. Some authors have argued that stochastic events could be more important than deterministic factors such as competition and niche differentiation (Sloan et al., 2006).

At the largest possible temporal and spatial scales, bacteria are the best candidates to survive interplanetary transfer inside rock. Such lithopanspermia is a potential means that life could be transferred between planetary bodies within and outside our solar system (Nicholson, 2009). On Earth, but still across large spatial scales, microorganisms are capable of long-distance dispersal, being ubiquitous and abundant, even in the upper atmosphere (Barberán et al., 2015). Thousands of distinct bacterial taxa, accompanied by other microorganisms, are carried within dust plumes in long-range intercontinental transport events. For instance, Asian aerosols contribute to microbial species richness in North American air (Smith et al., 2013), and dust storms generated in the African Sahara-Sahel transport microorganisms that eventually contribute to bacterial assemblages in European mountain lakes (Perfumo & Marchant, 2010; Peter, Hörtnagl, Reche, & Sommaruga, 2014).

3 | NATURAL RELEASE AND SURVIVAL OF DNA

Microbial biogeography is further complicated by the ability of microorganisms to acquire foreign DNA, and consequently, movement of genes through the Critical Zone can occur independently of organismal movement (Figure 2). DNA released from organisms can transfer to unrelated species either through close contact, or at a distance, when DNA can survive in the environment for extended time periods (Gillings, 2017b).

Extracellular DNA can be readily detected in environmental samples and can originate from dead bacterial, animal, or plant cells. All soils contain significant quantities of extracellular DNA (Frostegård et al., 1999). This DNA can persist in the environment and can be transported away from cell debris. Because DNA can resist physical and biological degradation under some conditions, it has even been proposed as a potential signature of life during interplanetary exploration (Lyon et al., 2010).

Under natural conditions, DNA released via cell lysis is in contact with other cellular components (wall debris, proteins, lipids, RNA, etc.). The presence of both organic compounds and inorganic molecules in soil particles strongly influences the adsorption of DNA (Pietramellara et al., 2009). Consequently, DNA can be protected from enzymatic degradation in soil by adsorption onto soil minerals and humic substances (Levy-Booth et al., 2007). Protection against degradation by DNases of microbial origin is aided by the concomitant adsorption of nucleases (Demanèche, Jocteur-Monrozier, Quiquampoix, & Simonet, 2001). Many studies on survival of DNA in the environment have been conducted using plasmids and antibiotic resistance genes as markers.

The DNA persisting in soil is only a tiny fraction of the total DNA being released at any one time from decaying plants, animals,

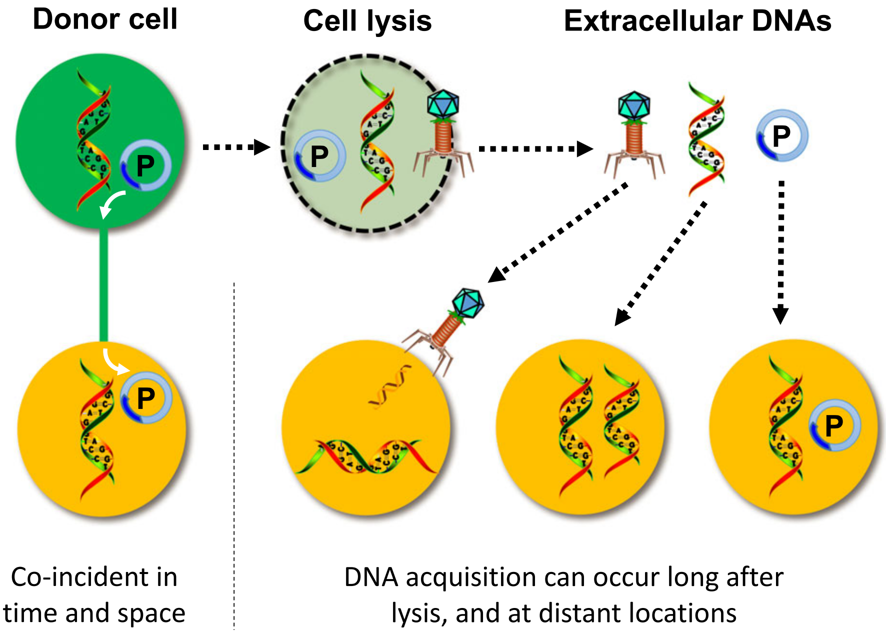

FIGURE 2 Movement of DNA through cells and ecosystems. DNA cargo can move within the cells that originally contained it, or can take advantage of the frequent lateral gene transfer that occurs between bacteria. In the case of transfer by conjugation or nanotube (LHS), DNA is passed directly from one cell to another, often on plasmids (P). When cells lyse through death or bacteriophage attack, they release their DNA content (RHS). This DNA can survive in the environment as naked DNA or encapsulated inside bacteriophage. Such extracellular DNA can be transported by physical processes and be acquired by a new cell at locations distant in both space and time

and microorganisms. This DNA usually undergoes rapid degradation (Ceccherini, Ascher, Pietramellara, Vogel, & Nannipieri, 2007; Pontiroli, Simonet, Frostegard, Vogel, & Monier, 2007; Poté et al., 2010). Degradation is biological and enzymatic, as DNA can survive in autoclaved treatments (Zhu, 2006). Nevertheless, a proportion of extracellular DNA does persist in natural environments, either bound to soil particles, or inside biofilms, where it is an important structural component (Pietramellara et al., 2009; Whitchurch, Tolker-Nielsen, Ragas, & Mattick, 2002). In the long term, persistence eventually requires being taken up by a recipient cell, and incorporated into that cell's genome. The likelihood of this occurring improves with increasing phylogenetic and ecological similarity of donor and recipient (Beiko, Harlow, & Ragan, 2005), and also improves markedly if the donor DNA can confer an adaptive phenotype. This is one reason why genes that confer antibiotic resistance are a good marker for these processes in natural environments.

4 | MOVEMENT AND TRANSPORT OF EXTRACELLULAR DNA

DNA is able to be transported vertically in unsaturated soils, to eventually penetrate groundwater and aquifers, where it can be immobilized through adsorption onto mineral surface or be transported with groundwater flow (Poté et al., 2009). Forced pumping of groundwater for drinking can thus induce rapid flow and associated transport of DNA over considerable distances. DNA can also move upwards in the soil column via capillary action (Ceccherini et al., 2007), potentially allowing subsequent long-distance movement via erosion and runoff.

The presence of extracellular DNA in environmental samples is increasingly being used to perform multitaxa surveys, or to detect rare and elusive species (Zinger et al., 2016). However, the parameters that affect transport and survival of extracellular DNA are not well understood and may compromise some of these experiments (Jerde et al., 2016). Given the problems of differential survival and transport of extracellular DNA, guidelines for the design and interpretation of environmental DNA methods are required (Goldberg et al., 2016).

Experiments to address this problem have used a variety of indicator DNAs. Antibiotic resistance genes known to be associated with humans are a good choice. They have been used to show survival and dissemination of DNA into freshwater sediments in an aquatic environment used for drinking water supply (Thevenon, Adatte, Wildi, & Poté, 2012). Similarly, plasmids (Poté et al., 2003) and bacteriophages (Chetochine, Brusseau, Gerba, & Pepper, 2006) have been used to demonstrate transport over considerable distances in water saturated soil and groundwater. However, the dynamic relationships between DNA transport, immobilization, survival, and the limits of detection are not well established (Hunter et al., 2016).

One way to track and understand dissemination of DNA through the environment and, indeed, throughout Earth's Critical Zone is to use a model system that is tractable and reflects the history of human impacts. Antibiotic resistance genes, their plasmid vectors, and the bacteria that host them are a good candidate for use as a proxy for anthropogenic influences (Gillings et al., 2015). For example, the prevalence of class 1 integron has been verified as a molecular marker for ARGs and used in modeling in a catchment (Amos et al., 2015).

5 | THE EVOLUTIONARY HISTORY OF ANTIBIOTIC RESISTANCE

The genes that we regard as antibiotic resistance genes are, by and large, recently descended from genes whose original functions were *not* to confer resistance to clinical concentrations of antibiotic compounds. Two kinds of event are responsible for the genesis of modern antibiotic resistance genes: mutation of a pre-existing gene within a cell lineage; and co-option of a gene acquired by lateral gene transfer from an unrelated lineage (Gillings, Paulsen, & Tetu, 2017). In the latter case, it has been suggested that many of these laterally transferred genes originally functioned in defensive responses to small signaling molecules arising from antagonistic biota, including those molecules we now use as antimicrobial agents (Davies & Davies, 2010; Davies, Spiegelman, & Yim, 2006; Linares, Gustafsson, Baquero, & Martinez, 2006).

This idea is supported by the observation that natural environments and environmental bacteria contain large numbers of genes that *could* confer resistance to antibiotics whether they were present in clinical contexts. These genes are collectively termed the resistome. The resistome is far larger and far older than the small subset of problematic resistome elements that have recently made their way into human and animal bacteria of clinical importance (Allen et al., 2010). For example, gene families that can confer resistance to particular antibiotic classes are plausibly related to defense mechanisms selected in response to naturally occurring compounds, which induce chemical stress. These gene families date back hundreds of millions of years and can be recovered from ancient environments such as caves and permafrost (Baltz, 2008; Bhullar et al., 2012; D'costa et al., 2011).

The widespread use of antibiotics in healthcare and intensive animal farming since the 1950s has exerted strong selection for rare, individual cells that had recently acquired a mutation or resistome element. As a result of continuing antibiotic use, resistant organisms have rapidly increased in both abundance and distribution (Gillings, 2017b). Under this selection pressure, resistant organisms and their genetic cargo have spread between individuals, species, and continents (Bengtsson-Palme et al., 2015; Hu et al., 2016). These resistance genes are readily identifiable because their recent expansion means they have highly conserved DNA sequences. Carriage of such resistance genes is now a universal feature of gut bacteria in humans and agricultural animals (Pal, Bengtsson-Palme, Kristiansson, & Larsson, 2016).

As a consequence of their universal carriage, resistant bacteria are continually discharged into the environment via wastewater, sewage treatment plants, and animal manure, thus spreading both resistant organisms and resistance genes. These same waste streams also release antibiotics (Grenni, Ancona, & Caracciolo, 2017; Liu, Steele, & Meng, 2017), which have significant effects, and trigger chemical stress responses even at subinhibitory concentrations (Chow, Waldron, & Gillings, 2015). Wastewaters then become giant reactors where complex interactions occur between chemical compounds, molecular responses, cells, resistance genes, and genetic transformation driven by lateral transfer and mutation (Gillings & Stokes, 2012). However, the actual potential of resistance dissemination from wastewater (and WWTPs) to the environment and humans might be less than perceived, but still be a matter for further investigations (Munck et al., 2015).

The broad-scale dissemination of bacterial genes, including resistance genes, is mediated by a number of factors. This transport and transformation is controlled at various nested levels. Firstly, DNA can be released from cells and persist in the environment. From here, it can be taken up and incorporated into bacteria. Secondly, genes can be transported within their host bacteria. Where such bacteria are dispersed by water or wind, their cargo genes are carried with them. Finally, the bacteria themselves can be carried inside animal hosts via mass migration, or in the case of humans, by travel and tourism. For example, Daphnia can act as a refuge for ARGs and thus may contribute to the spread of ARGs in the environment (Eckert, Di Cesare, Stenzel, Fontaneto, & Corno, 2016).

6 | TRACKING THE MOVEMENT OF RESISTANCE GENES IN EARTH'S CRITICAL ZONE

Interest in the dispersal of antibiotic resistance genes and their host bacteria is growing rapidly as the environmental consequences of this dissemination become more apparent. Partly, this is because resistance genes themselves have unique environmental properties and behavior. First, they behave like pollutants, which exhibit environmental exposure routes, and furthermore, they can replicate, making them more akin to an invasive species with multiple cellular hosts (Gillings, 2017a).

Human activities directly promote the invasion and spread of resistance determinants. Wastewater treatment plants occupy a position between human waste streams and the aquatic environment, but do not effectively remove resistance genes, thus distributing them in effluent (Aubertheau et al., 2016; Ben et al., 2017; Karkman et al., 2016). Effluents also contain significant concentrations of selective agents, thus promoting the survival of resistant organisms, potentially at the expense of endemic species (Borruso, Harms, Johnsen, Nielsen, & Brusetti, 2016; Caucci et al., 2016; Koczura, Mokracka, Taraszewska, & Łopacinska, 2016; Lehmann et al., 2016). Application of sewage sludge, or antibiotics alone, increases the abundance of resistance genes and changes the microbial community in soils (Chen et al., 2016; Cleary et al., 2016).

Agricultural activities also strongly promote the environmental spread of resistance through disposal of wastes and application of manure (Heuer, Schmitt, & Smalla, 2011; Sandberg & Lapara, 2016). Similarly, aquaculture is increasingly being recognized as a focal point for enhancing and dispersing resistance in the environment (Muziasari et al., 2016). In both of these cases, the simultaneous release of antibiotics and other selective agents promotes selection of organisms containing resistance genes (He et al., 2016; Liu et al., 2017; Wang, Ben, Yang, Zhang, & Qiang, 2016). This generates opportunities for coselection and fixation of chemical (toxic metals) and resistance determinants in species, and within individual DNA molecules (Johnson et al., 2016; Zhou et al., 2016). An investigation by Di Cesare, Eckert, and Corno (2016), Di Cesare, Eckert, D'Urso et al. (2016) on three WWTPs revealed that heavy metal resistance genes may play a crucial role in the spreading of ARGs via mobile genetic elements.

A combination of phenomena, including the volume of human and agricultural waste streams, and the concomitant release of selective agents, means that resistance genes and resistant organisms can become extraordinarily widespread and abundant over very short time frames. A single multidrug resistant clone of *E. coli* has become globally disseminated since its origin as recently as the year 2000 (Petty et al., 2014).

Antimicrobial resistance in Earth's Critical Zone is thus dependent on human activities, the action of selection in natural environments, and upon natural transport mechanisms, such as rivers, groundwater, and soil movement. At landscape scale, antibiotic resistance genes can move with soil erosion and drainage from top soil to groundwater.

7 | MODELING OF THE DYNAMICS OF RESISTANCE GENES IN THE CRITICAL ZONE

Effective modeling of the spread of antimicrobial resistance is essential for making predictions that can inform policy, practice, and environmental surveillance. Policymakers are interested in models for two reasons. First, they support general policies that can inform handling of antimicrobials in the environment, during production, agricultural use, or wastewater treatment. Second, they inform possible interventions in the face of a specific outbreak of an antibiotic-resistant human or animal pathogen. Models need to be flexible, realistic, and able to be used in different contexts.

However, developing realistic and flexible models that operate on an environmental scale is a significant challenge (Sommer, Munck, Toft-Kehler, & Andersson, 2017). Antimicrobial resistance (AMR) encompasses a broad range of organisms, genes and antimicrobial agents, and mobile genetic elements. Sensitive and resistant organisms live in complex, heterogeneous communities. The processes that drive fixation of resistance occur at microscopic scales. Selection and spread within the Critical Zone can involve slurry tanks (Baker, Hobman, Dodd, Ramsden, & Stekel, 2016), the animal gut (Volkova, Lanzas, Lu, & Gröhn, 2012), wastewater treatment plants (Sharifi, Murthy, Takács, & Massoudieh, 2014), and industrial effluents, while broader dissemination might be driven by soil movement, water percolation, rivers, domestic animals, and wildlife. Some initial linear modeling has been tried to characterize the impact of rainfall on the spread of ARGs in a subalpine river (Di Cesare, Eckert, Rogora, & Corno, 2017).

Mathematical modeling of resistance spread has been applied at a range of scales. Models for laboratory-scale experiments have been valuable for establishing rates of mutation, selection, and the spread of resistance (Bootsma, Van Der Horst, Guryeva, Ter Kuile, & Diekmann, 2012; De Gelder et al., 2004). However, while these models are useful for characterizing key processes, they do not scale up to the required complexity for whole environments. Consideration of the spatial structure of microbial communities, for example, biofilms, gives a more accurate representation of the spread resistance in a community (Lardon et al., 2011). Models of farms or sewage treatment plants have shown that it is possible for resistant organisms or pathogens to persist even in the absence of antibiotic treatment (Sharifi et al., 2014), and can also make predictions about the duration of persistence (Volkova, Lu, Lanzas, Scott, & Gröhn, 2013). However, these models have been limited to considering a single type of bacterium or antimicrobial agent. Therefore, three developments are needed to move forward with environmental scale models that can be effective in understanding and predicting spread or reduction in resistance in the Critical Zone: inclusion of heterogeneity; multiscaling in space and time; and effective global data sharing.

First, models will need to consider a fuller range of organisms, resistance genes, mobile genetic elements, and antimicrobials that reflect the complexity of the observed system (Chen et al., 2016; Perron, Inglis, Pennings, & Cobey, 2015) and the importance of coselection of antibiotic and metal resistance genes (Gullberg, Albrecht, Karlsson, Sandegren, & Andersson, 2014; Pal, Bengtsson-Palme, Kristiansson, & Larsson, 2015). Importantly, different organisms, genes, and mobile genetic elements will behave differently, leading to heterogeneity in growth, transmission, and selection. However, their inclusion will be essential to determine the pace and range of spread or elimination of resistance, and the relative contributions of resistance genes to the emergence of potentially resistant pathogens. This is a considerable modeling challenge, because the number of possible genetic and resistance combinations increases exponentially with the degree of biological complexity to be included. For example, even within a mass action ordinary differential equation framework, to model populations of a single bacterial species in an environment with two different antimicrobials, and two respective resistance genes, that each might be carried on one of two different mobile genetic elements, requires many differential equations, and such models are difficult to parameterize or analyze.

Second, models will need to operate on multiple scales. While the best representation of spread of AMR on a microscopic scale is through individual-based models, such models do not extend to an environmental scale. Therefore, it will be necessary to coarse-grain predictive outcomes of small-scale models into larger scale, multicompartment models that can consider populations of humans, farm animals, and wildlife in their respective geographical compartments. It may also be necessary to use models that combine deterministic with stochastic elements. Deterministic models are capable of simulating large populations of bacteria, while stochastic models can capture rare and random events, for example, the spread of a particular resistance determinant from one species to another. A further feature of such models will be the need to embed geospatial data (Pruden, Arabi, & Storteboom, 2012) and to include factors such as topography, land use, and water flows.

Third, such models will require considerable calibration against real data. Researchers carrying out environmental and field studies will need to share data in a way that is useful for embedding into predictive models. To do this, agreed standards will be required for data capture and sharing, and the development of an international database for resistance in the Critical Zone. Such data could include observations from a wide range of experimental techniques, and data on taxa, species, phenotypes, genomes, resistance genes, mobile genetic elements, antibiotics, heavy metals, and other antimicrobials. Ideally, the data would also include geospatial coordinates so that they can be used in geospatially explicit models. While this challenge alone is considerable, there is considerable precedent for agreed data standards in other areas of high throughput biology, which this development can draw upon.

8 | DISPERSAL OF RESISTANCE GENES IN THE CRITICAL ZONE—A PLANETARY VIEW

Understanding movement of antibiotic resistance through the Critical Zone is complex, and difficult to model. Quantifying the movement of antibiotic resistance genes (ARGs) requires the coupling between the transport of bacterial cells (and resistance genes they carry) and materials (and associated selective agents) and their interactions within the Critical Zone (Figure 2). We can then infer more general principles about the movement and transformation of genes and microorganisms. These principles might then be tested and applied to even more complex, multigene phenotypes of central importance to global biogeochemistry.

Before humans had a major influence on the planet, movement of microorganisms and the genes they carry was mainly driven by natural phenomena, such as air currents and water flow. Without human influence, a relatively small number of microbial cells would be transported to any specific location, therefore chance played a large role in dispersal of bacterial cells/genes. This dispersal did not necessarily result in survival or recruitment, as locally adapted cells were already present, and filled existing niches. With the advent of the Anthropocene, human activities now have large effects on the dispersal of microorganisms and the genes they carry (Table 1). Movement of humans around the globe transports our internal microbiota to new locations at an unprecedented scale. Human migration changes the abundance of resistance genes and successfully transports resistance genes between continents (Bengtsson-Palme et al., 2015; Sun et al., 2016).

The fact that biomass of humans and domestic animals now comprise 35 times that of wild terrestrial mammals (Smil, 2011) may have consequences for the microbial world. Firstly, humans, domestic, and agricultural animals all carry resistance genes in their gut microbiota, thus vastly increasing the abundance and distribution of these genes on the planet. Secondly, on a global scale the fecal microbiota are now mainly represented by the gut microbiota of six species: humans, cattle, sheep, goats, pigs, and chickens. Thus, the overall diversity of bacteria being shed in feces has consequently declined. At the same time, the quantity of fecal microbiota has increased as the biomass of humans and their domesticates approaches five times the global carrying capacity for terrestrial vertebrates (Smil, 2011). Therefore, disposal of both human and animal manures has a significant impact on the dissemination of both microbial organisms and genes (Chen et al., 2016; Jechalke et al., 2013). These cells and genes can contaminate agricultural produce (Bengtsson-Palme, 2017; Jones-Dias et al., 2016), which is then transported between countries.

TABLE 1 Dissemination of genes and microorganisms in Earth's Critical Zone

	Drivers		
	Dispersal	**Stochastics**	**Selection/Recruitment**
Natural forces	Wind transport Ocean currents Freshwater flows	Low cell numbers Population drift	Favors endemic species Local differentiation
Human impacts	Human movement Animal movement Agriculture Ballast water Moving soil/sediment Wastewater flows	High cell numbers Increased evolvability	Codispersal with selective agents Coselection with domesticated hosts

Three phenomena, or drivers, affect microbial/gene spread. These are as follows: opportunity for dispersal; stochastics (the number of foreign cells landing at a particular location, processes that generate local variation such as mutation and drift); and recruitment (the persistence of cells at the new location, often driven by local selection). Historically, these forces generate biogeographic patterns for microorganisms that are similar to those of animals and plants. Human impacts have changed the dynamics of these phenomena and are altering microbial biogeography in the process.

Humans disperse microorganisms by mass movement of materials (Table 1). Transport of ballast water in ships is estimated to move 10^{19} bacteria each day (Endresen, Behrens, Brynestad, Andersen, & Skjong, 2004; Ruiz et al., 2000), spreading diverse microorganisms around the globe and thus reshaping microbial biogeography (Brinkmeyer, 2016; Lohan, Fleischer, Carney, Holzer, & Ruiz, 2016). It has been suggested that anthropogenic movement of soil, sand, and rock now surpasses all natural processes combined (Wilkinson & Mcelroy, 2007), incidentally transporting huge numbers of microbial cells. Wastewater also transports microorganisms and their cargo genes into the environment. With increasing human populations, the volume of wastewater is increasing, but global data on the treatment, reuse, or volumes of wastewater are difficult to assemble (Sato, Qadir, Yamamoto, Endo, & Zahoor, 2013). As an example, antibiotic resistance genes now pollute over 4,000 km of the Chinese coastline at levels up to 100 million genes per gram of sediment (Zhu, Zhao et al., 2017). None of these genes would have been present in this sediment 50 years ago.

Human activities increase the numbers of microorganisms being transported within the Critical Zone and around the Earth ecosystem, thus increasing the chances for successful recruitment (Table 1). Furthermore, during transport, microorganisms are often exposed to pollutants, particularly during discharge of manure and wastewater. Exposure to antibiotics and other coselective agents, even at low doses, can enhance the rate at which bacteria generate diversity via mutation (Kohanski, Depristo, & Collins, 2010), recombination (Guerin et al., 2009), and lateral gene transfer (Prudhomme, Attaiech, Sanchez, Martin, & Claverys, 2006). The simultaneous dispersal of microorganisms and various selective agents increases the genetic variation being generated in those microbial populations, enhancing their potential to evolve (Gillings & Stokes, 2012). Consequently, a subset of the cells dispersed to new locations are adapted to the codispersed pollutants, increasing their probability of recruitment at these new locations. Further, because genes for metal, disinfectant, and antibiotic resistance are often closely linked (Johnson et al., 2016), exposure to any one selective agent drives their coselection and maintains mosaic clusters of resistance determinants (Di Cesare, Eckert, and Corno (2016), Di Cesare, Eckert, D'Urso et al. (2016); Gaze, Abdouslam, Hawkey, & Wellington, 2005; Skurnik et al., 2010). Possession of diverse resistance determinants significantly increases the probability of recruitment at novel destinations by providing a selective advantage over endemic microorganisms (Table 1).

9 | CONCLUDING REMARKS

It is becoming more and more important to understand how human activities cause systematic changes in ecosystems (Alberti, Marzluff, & Hunt, 2017), and especially the effects on the emergence and spread of ARGs in urbanizing Earth's Critical Zone (Zhu, Reid, Meharg, Banwart, & Fu, 2017). To better understand the dynamics of ARGs in the Critical Zone, future studies should emphasize linkages between biogeochemical cycling of nutrients and contaminants with the movement of microorganisms. Under the framework of Critical Zone science, tracking the dynamics of ARGs should give us insights into the interconnections between multiple environmental compartments within the entire Critical Zone. Due to the extreme heterogeneity of the Critical Zone, we should also focus on hot spots for ARG dissemination such as locations receiving high loads of wastewater or manure. Understanding the complex feedbacks between the dynamics of ARGs and interactions with physical, chemical, and biological processes in the Critical Zone is a grand challenge. Progress can only be made by forging interdisciplinary research teams that can manage and interpret the enormous datasets of genomics and biogeochemistry, and by developing predictive models based on these datasets.

ACKNOWLEDGEMENTS

YGZ is supported by Natural Science Foundation of China (41571130063), Chinese Academy of Sciences (XDB15020302 and XDB15020402), MRG is supported by the Australian Research Council, SB is partially supported by NERC grant NE/N007514/1, and JP is supported by the European Research Council Synergy grant SyG-2013-610028 IMBALANCE-P. The authors declare no conflict of interests.

ORCID

Yong-Guan Zhu http://orcid.org/0000-0003-3861-8482
Michael Gillings http://orcid.org/0000-0002-4043-4351
Pascal Simonet https://orcid.org/0000-0002-6329-7361
Dov Stekel https://orcid.org/0000-0002-2492-8079
Steven Banwart https://orcid.org/0000-0001-7223-6678
Josep Penuelas https://orcid.org/0000-0002-7215-0150

REFERENCES

Alberti, M., Marzluff, J., & Hunt, V. M. (2017). Urban driven phenotypic changes: Empirical observations and theoretical implications for eco-evolutionary feedback. *Philosophical Transactions of the Royal Society B*, *372*, 20160029. https://doi.org/10.1098/rstb.2016.0029

Allen, H. K., Donato, J., Wang, H. H., Cloud-Hansen, K. A., Davies, J., & Handelsman, J. (2010). Call of the wild: Antibiotic resistance genes in natural environments. *Nature Reviews Microbiology*, *8*, 251–259. https://doi.org/10.1038/nrmicro2312

Amos, G. C. A., Gozzard, E., Carter, C. E., Mead, A., Bowes, M. J., Hawkey, P. M., ... Wellington, W. M. H. (2015). Validated predictive modelling of the environmental resistome. *The ISME Journal*, *9*, 1467–1476. https://doi.org/10.1038/ismej.2014.237

Aubertheau, E., Stalder, T., Mondamert, L., Ploy, M.-C., Dagot, C., & Labanowski, J. (2016). Impact of wastewater treatment plant discharge on the contamination of river biofilms by pharmaceuticals and antibiotic resistance. *Science of the Total Environment*, *579*, 1387–1398.

Baker, M., Hobman, J.L., Dodd, C.E., Ramsden, S.J., & Stekel, D.J. (2016). Mathematical modelling of antimicrobial resistance in agricultural waste highlights importance of gene transfer rate. *FEMS Microbiology Ecology*, *92*, fiw040. https://doi.org/10.1093/femsec/fiw040

Baltz, R. H. (2008). Renaissance in antibacterial discovery from actinomycetes. *Current Opinion in Pharmacology*, *8*, 557–563. https://doi.org/10.1016/j.coph.2008.04.008

Barberán, A., Ladau, J., Leff, J. W., Pollard, K. S., Menninger, H. L., Dunn, R. R., & Fierer, N. (2015). Continental-scale distributions of dust-associated bacteria and fungi. *Proceedings of the National Academy of Sciences*, *112*, 5756–5761. https://doi.org/10.1073/pnas.1420815112

Bardgett, R. D., & Van Der Putten, W. H. (2014). Belowground biodiversity and ecosystem functioning. *Nature*, *515*, 505–511. https://doi.org/10.1038/nature13855

Beiko, R. G., Harlow, T. J., & Ragan, M. A. (2005). Highways of gene sharing in prokaryotes. *Proceedings of the National Academy of Sciences*, *102*, 14332–14337. https://doi.org/10.1073/pnas.0504068102

Ben, W., Wang, J., Cao, R., Yang, M., Zhang, Y., & Qiang, Z. (2017). Distribution of antibiotic resistance in the effluents of ten municipal wastewater treatment plants in China and the effect of treatment processes. *Chemosphere*, *172*, 392–398. https://doi.org/10.1016/j.chemosphere.2017.01.041

Bengtsson-Palme, J. (2017). Antibiotic resistance in the food supply chain: Where can sequencing and metagenomics aid risk assessment? *Current Opinion in Food Science*, *14*, 66–71. https://doi.org/10.1016/j.cofs.2017.01.010

Bengtsson-Palme, J., Angelin, M., Huss, M., Kjellqvistc, S., Kristianssond, E., Palmgrenb, H., . . . Johanssone, A. (2015). The human gut microbiome as a transporter of antibiotic resistance genes between continents. *Antimicrobial Agents and Chemotherapy*, *59*, 6551–6560. https://doi.org/10.1128/AAC.00933-15

Bhullar, K., Waglechner, N., Pawlowski, A., Koteva, K., Banks, E. D., Johnston, M. D., . . . Wright, G. D. (2012). Antibiotic resistance is prevalent in an isolated cave microbiome. *PLoS ONE*, *7*, e34953. https://doi.org/10.1371/journal.pone.0034953

Bootsma, M., Van Der Horst, M., Guryeva, T., Ter Kuile, B., & Diekmann, O. (2012). Modeling non-inherited antibiotic resistance. *Bulletin of Mathematical Biology*, *74*, 1691–1705. https://doi.org/10.1007/s11538-012-9731-3

Borruso, L., Harms, K., Johnsen, P. J., Nielsen, K. M., & Brusetti, L. (2016). Distribution of class 1 integrons in a highly impacted catchment. *Science of the Total Environment*, *566*, 1588–1594. https://doi.org/10.1016/j.scitotenv.2016.06.054

Brinkmeyer, R. (2016). Diversity of bacteria in ships ballast water as revealed by next generation DNA sequencing. *Marine Pollution Bulletin*, *107*, 277–285. https://doi.org/10.1016/j.marpolbul.2016.03.058

Caucci, S., Karkman, A., Cacace, D., Rybicki, M., Timpel, P., Voolaid, V., . . . Berendonk, T. U. (2016). Seasonality of antibiotic prescriptions for outpatients and resistance genes in sewers and wastewater treatment plant outflow. *FEMS Microbiology Ecology*, *92*, fiw060. https://doi.org/10.1093/femsec/fiw060

Ceccherini, M. T., Ascher, J., Pietramellara, G., Vogel, T. M., & Nannipieri, P. (2007). Vertical advection of extracellular DNA by water capillarity in soil columns. *Soil Biology and Biochemistry*, *39*, 158–163. https://doi.org/10.1016/j.soilbio.2006.07.006

Chen, Q., An, X., Li, H., Su, J., Ma, Y., & Zhu, Y.-G. (2016). Long-term field application of sewage sludge increases the abundance of antibiotic resistance genes in soil. *Environment International*, *92*, 1–10. https://doi.org/10.1016/j.envint.2016.03.026

Chetochine, A. S., Brusseau, M. L., Gerba, C. P., & Pepper, I. L. (2006). Leaching of phage from class B biosolids and potential transport through soil. *Applied and Environmental Microbiology*, *72*, 665–671. https://doi.org/10.1128/AEM.72.1.665-671.2006

Chow, L., Waldron, L., & Gillings, M. (2015). Potential impacts of aquatic pollutants: Sub-clinical antibiotic concentrations induce genome changes and promote antibiotic resistance. *Frontiers in Microbiology*, *6*, 803–817.

Cleary, D. W., Bishop, A. H., Zhang, L., Topp, E., Wellington, E. M., & Gaze, W. H. (2016). Long-term antibiotic exposure in soil is associated with changes in microbial community structure and prevalence of class 1 integrons. *FEMS Microbiology Ecology*, *92*, fiw159. https://doi.org/10.1093/femsec/fiw159

Davies, J., & Davies, D. (2010). Origins and evolution of antibiotic resistance. *Microbiology and Molecular Biology Reviews*, *74*, 417–433. https://doi.org/10.1128/MMBR.00016-10

Davies, J., Spiegelman, G. B., & Yim, G. (2006). The world of subinhibitory antibiotic concentrations. *Current Opinion in Microbiology*, *9*, 445–453. https://doi.org/10.1016/j.mib.2006.08.006

D'costa, V. M., King, C. E., Kalan, L., Morar, M., Sung, W. W. L., Schwarz, C., . . . Wright, G. D. (2011). Antibiotic resistance is ancient. *Nature*, *477*, 457–461. https://doi.org/10.1038/nature10388

De Gelder, L., Ponciano, J. M., Abdo, Z., Joyce, P., Forney, L. J., & Top, E. M. (2004). Combining mathematical models and statistical methods to understand and predict the dynamics of antibiotic-sensitive mutants in a population of resistant bacteria during experimental evolution. *Genetics*, *168*, 1131–1144. https://doi.org/10.1534/genetics.104.033431

Demanèche, S., Jocteur-Monrozier, L., Quiquampoix, H., & Simonet, P. (2001). Evaluation of biological and physical protection against nuclease degradation of clay-bound plasmid DNA. *Applied and Environmental Microbiology*, *67*, 293–299. https://doi.org/10.1128/AEM.67.1.293-299.2001

Di Cesare, A., Eckert, E., & Corno, G. (2016). Co-selection of antibiotic and heavy metal resistance in freshwater bacteria. *Journal of Limnology*, *75*, 59–66.

Di Cesare, A., Eckert, E. M., D'Urso, S., Bertoni, R., Gillan, D., Wattiez, R., & Corno, G. (2016). Co-occurrence of integrase 1, antibiotic and heavy metal resistance genes in municipal wastewater treatment plants. *Water Research*, *94*, 2018–2214.

Di Cesare, A., Eckert, E. M., Rogora, M., & Corno, G. (2017). Rainfall increases the abundance of antibiotic resistance genes within a riverine microbial community. *Environmental Pollution*, *226*, 473–478. https://doi.org/10.1016/j.envpol.2017.04.036

Eckert, E., Di Cesare, A., Stenzel, B., Fontaneto, D., & Corno, G. (2016). Daphnia as a refuge for an antibiotic resistance gene in an experimental freshwater community. *The Science of Total Environment*, *571*, 77–81. https://doi.org/10.1016/j.scitotenv.2016.07.141

Endresen, Ø., Behrens, H. L., Brynestad, S., Andersen, A. B., & Skjong, R. (2004). Challenges in global ballast water management. *Marine Pollution Bulletin*, *48*, 615–623. https://doi.org/10.1016/j.marpolbul.2004.01.016

Evans, S., Martiny, J. B., & Allison, S. D. (2017). Effects of dispersal and selection on stochastic assembly in microbial communities. *The ISME Journal*, *11*, 176–185. https://doi.org/10.1038/ismej.2016.96

Frostegård, A., Courtois, S., Ramisse, V., Clerc, S., Bernillon, D., Gall, F. L., . . . Simonet, P. (1999). Quantification of bias related to the extraction of DNA directly from soils. *Applied and Environmental Microbiology*, *65*, 5409–5420.

Gaze, W. H., Abdouslam, N., Hawkey, P. M., & Wellington, E. M. H. (2005). Incidence of class 1 integrons in a quaternary ammonium compound-polluted environment. *Antimicrobial Agents and Chemotherapy*, *49*, 1802–1807. https://doi.org/10.1128/AAC.49.5.1802-1807.2005

Gillings, M. R. (2013). Evolutionary consequences of antibiotic use for the resistome, mobilome and microbial pangenome. *Frontiers in Microbiology*, *4*, 4–12.

Gillings, M. R. (2017a). Class 1 integrons as invasive species. *Current Opinion in Microbiology*, *38*, 10–16. https://doi.org/10.1016/j.mib.2017.03.002

Gillings, M. R. (2017b). Lateral gene transfer, bacterial genome evolution, and the Anthropocene. *Annals of the New York Academy of Sciences*, *1389*, 20–36. https://doi.org/10.1111/nyas.13213

Gillings, M. R., Gaze, W. H., Pruden, A., Smalla, K., Tiedje, J. M., & Zhu, Y.-G. (2015). Using the class 1 integron-integrase gene as a proxy for anthropogenic pollution. *The ISME Journal*, *9*, 1269–1279. https://doi.org/10.1038/ismej.2014.226

Gillings, M. R., & Paulsen, I. T. (2014). Microbiology of the anthropoceneAnthropocene, *5*, 1–8. https://doi.org/10.1016/j.ancene.2014.06.004

Gillings, M. R., Paulsen, I. T., & Tetu, S. G. (2017). Genomics and the evolution of antibiotic resistance. *Annals of the New York Academy of Sciences*, *1388*, 92–107. https://doi.org/10.1111/nyas.13268

Gillings, M. R., & Stokes, H. W. (2012). Are humans increasing bacterial evolvability? *Trends in Ecology and Evolution*, *27*, 346–352. https://doi.org/10.1016/j.tree.2012.02.006

Goldberg, C. S., Turner, C. R., Deiner, K., Klymus, K. E., Thomsen, P. F., Murphy, M. A., . . . Taberlet, P. (2016). Critical considerations for the application of environmental DNA methods to detect aquatic species. *Methods in Ecology and Evolution*, *7*, 1299–1307. https://doi.org/10.1111/2041-210X.12595

Green, J. L., Holmes, A. J., Westoby, M., Oliver, I., Briscoe, D., Dangerfield, M., . . . Beattie, A. J. (2004). Spatial scaling of microbial eukaryote diversity. *Nature*, *432*, 747–750. https://doi.org/10.1038/nature03034

Grenni, P., Ancona, V., & Caracciolo, A. B. (2017). Ecological effects of antibiotics on natural ecosystems: A review. *Microchemical Journal*, *136*, 25-39 https://doi.org/10.1016/j.microc.2017.02.006

Guerin, E., Cambray, G., Sanchez-Alberola, N., Campoy, S., Erill, I., Da Re, S., … Maze, D. (2009). The SOS response controls integron recombination. *Science*, *324*, 1034. https://doi.org/10.1126/science.1172914

Gullberg, E., Albrecht, L.M., Karlsson, C., Sandegren, L., & Andersson, D.I. (2014). Selection of a multidrug resistance plasmid by sublethal levels of antibiotics and heavy metals. *mBio*, *5*, e01914–01918.

Haggerty, J. M., & Dinsdale, E. A. (2016). Distinct biogeographical patterns of marine bacterial taxonomy and functional genes. *Global Ecology and Biogeography*, *26*, 177–190.

Hanson, C. A., Fuhrman, J. A., Horner-Devine, M. C., & Martiny, J. B. (2012). Beyond biogeographic patterns: Processes shaping the microbial landscape. *Nature Reviews Microbiology*, *10*, 497–506.

He, L.-Y., Ying, G.-G., Liu, Y.-S., Su, H.-C., Chen, J., Liu, S.-S., & Zhao, J.-L. (2016). Discharge of swine wastes risks water quality and food safety: Antibiotics and antibiotic resistance genes from swine sources to the receiving environments. *Environment International*, *92*, 210–219. https://doi.org/10.1016/j.envint.2016.03.023

Heuer, H., Schmitt, H., & Smalla, K. (2011). Antibiotic resistance gene spread due to manure application on agricultural fields. *Current Opinion in Microbiology*, *14*, 236–243. https://doi.org/10.1016/j.mib.2011.04.009

Horner-Devine, M. C., Lage, M., Hughes, J. B., & Bohannan, B. J. (2004). A taxa–area relationship for bacteria. *Nature*, *432*, 750–753. https://doi.org/10.1038/nature03073

Hu, Y., Yang, X., Li, J., Lv, N., Liu, F., Wu, J., … Zhu, B. L. (2016). The Bacterial Mobile Resistome Transfer Network Connecting the Animal and Human Microbiomes. *Applied and Environmental Microbiology*, *82*, 6672–6681.

Hunter, M. E., Dorazio, R. M., Butterfield, J. S., Meigs-Friend, G., Nico, L. G., & Ferrante, J. A. (2016). Detection limits of quantitative and digital PCR assays and their influence in presence–absence surveys of environmental DNA. *Molecular Ecology Resources*, *17*, 221–229.

Jechalke, S., Schreiter, S., Wolters, B., Dealtry, S., Heuer, H., & Smalla, K. (2013). Widespread dissemination of class 1 integron components in soils and related ecosystems as revealed by cultivation-independent analysis. *Frontiers in Microbiology*, *4*, 420–427.

Jerde, C. L., Olds, B. P., Shogren, A. J., Andruszkiewicz, E. A., Mahon, A. R., Bolster, D., & Tank, J. L. (2016). Influence of stream bottom substrate on retention and transport of vertebrate environmental DNA. *Environmental Science & Technology*, *50*, 8770–8779. https://doi.org/10.1021/acs.est.6b01761

Johnson, T.A., Stedtfeld, R.D., Wang, Q., Cole, J.R., Hashsham, S.A., Looft, T., … Tiedje, J.M. (2016). Clusters of antibiotic resistance genes enriched together stay together in swine agriculture. *mBio*, *7*, e02214–e02215.

Jones-Dias, D., Manageiro, V., Ferreira, E., Barreiro, P., Vieira, L., Moura, I. B., & Caniça, M. (2016). Architecture of class 1, 2, and 3 integrons from gram negative bacteria recovered among fruits and vegetables. *Frontiers in Microbiology*, *7*, 1400–1411.

Karkman, A., Johnson, T. A., Lyra, C., Stedtfeld, R. D., Tamminen, M., Tiedje, J. M., & Virta, M. (2016). High-throughput quantification of antibiotic resistance genes from an urban wastewater treatment plant. *FEMS Microbiology Ecology*, *92*, fiw014. https://doi.org/10.1093/femsec/fiw014

Koczura, R., Mokracka, J., Taraszewska, A., & Łopacinska, N. (2016). Abundance of class 1 integron-integrase and sulfonamide resistance genes in river water and sediment is affected by anthropogenic pressure and environmental factors. *Microbial Ecology*, *72*, 909–916. https://doi.org/10.1007/s00248-016-0843-4

Kohanski, M. A., Depristo, M. A., & Collins, J. J. (2010). Sublethal antibiotic treatment leads to multidrug resistance via radical-induced mutagenesis. *Molecular & Cellular Biochemistry*, *37*, 311–320. https://doi.org/10.1016/j.molcel.2010.01.003

Küsel, K., Totsche, K. U., Trumbore, S. E., Lehmann, R., Steinhäuser, C., & Herrmann, M. (2016). How deep can surface signals be traced in the critical zone? Merging biodiversity with biogeochemistry research in a central German Muschelkalk landscape. *Frontiers in Earth Science*, *4*, 32–46.

Lardon, L. A., Merkey, B. V., Martins, S., Dötsch, A., Picioreanu, C., Kreft, J. U., & Smets, B. F. (2011). iDynoMiCS: Next-generation individual-based modelling of biofilms. *Environmental Microbiology*, *13*, 2416–2434. https://doi.org/10.1111/j.1462-2920.2011.02414.x

Lehmann, K., Bell, T., Bowes, M. J., Amos, G. C., Gaze, W. H., Wellington, E. M., & Singer, A. C. (2016). Trace levels of sewage effluent are sufficient to increase class 1 integron prevalence in freshwater biofilms without changing the core community. *Water Research*, *106*, 163–170. https://doi.org/10.1016/j.watres.2016.09.035

Levy-Booth, D. J., Campbell, R. G., Gulden, R. H., Hart, M. M., Powell, J. R., Klironomos, J. N., … Dunfield, K. E. (2007). Cycling of extracellular DNA in the soil environment. *Soil Biology and Biochemistry*, *39*, 2977–2991. https://doi.org/10.1016/j.soilbio.2007.06.020

Linares, J. F., Gustafsson, I., Baquero, F., & Martinez, J. L. (2006). Antibiotics as intermicrobial signaling agents instead of weapons. *Proceedings of the National Academy of Sciences*, *103*, 19484–19489. https://doi.org/10.1073/pnas.0608949103

Liu, X., Steele, J. C., & Meng, X.-Z. (2017). Usage, residue, and human health risk of antibiotics in Chinese aquaculture: A review. *Environmental Pollution*, *223*, 161–169. https://doi.org/10.1016/j.envpol.2017.01.003

Lohan, K. P., Fleischer, R., Carney, K., Holzer, K., & Ruiz, G. (2016). Amplicon-Based pyrosequencing reveals high diversity of protistan parasites in ships' ballast water: Implications for biogeography and infectious diseases. *Microbial Ecology*, *71*, 530–542. https://doi.org/10.1007/s00248-015-0684-6

Lyon, D. Y., Monier, J.-M., Dupraz, S., Freissinet, C., Simonet, P., & Vogel, T. M. (2010). Integrity and biological activity of DNA after UV exposure. *Astrobiology*, *10*, 285–292. https://doi.org/10.1089/ast.2009.0359

Martiny, J. B. H., Bohannan, B. J., Brown, J. H., Colwell, R. K., Fuhrman, J. A., Green, J. L., … Staley, J. T. (2006). Microbial biogeography: Putting microorganisms on the map. *Nature Reviews Microbiology*, *4*, 102–112. https://doi.org/10.1038/nrmicro1341

Mobley, M. L. (2009). Monitoring Earth's critical zone. *Science*, *326*, 1067–1068.

Mock, T., Daines, S. J., Geider, R., Collins, S., Metodiev, M., Millar, A. J., … Lenton, T. M. (2016). Bridging the gap between omics and earth system science to better understand how environmental change impacts marine microbes. *Global Change Biology*, *22*, 61–75. https://doi.org/10.1111/gcb.12983

Munck, C., Albertsen, M., Telke, A., Ellabaan, M., Nielsen, P. H., & Sommer, M. O. A. (2015). Limited dissemination of the wastewater treatment plant core resistome. *Nature Communications*, *6*, 8452. https://doi.org/10.1038/ncomms9452

Muziasari, W. I., Pärnänen, K., Johnson, T. A., Lyra, C., Karkman, A., Stedtfeld, R. D., … Virta, M. (2016). Aquaculture changes the profile of antibiotic resistance and mobile genetic element associated genes in Baltic Sea sediments. *FEMS Microbiology Ecology*, *92*, fiw052. https://doi.org/10.1093/femsec/fiw052

Nicholson, W. L. (2009). Ancient micronauts: Interplanetary transport of microbes by cosmic impacts. *Trends in Microbiology*, *17*, 243–250. https://doi.org/10.1016/j.tim.2009.03.004

Pal, C., Bengtsson-Palme, J., Kristiansson, E., & Larsson, D. J. (2015). Co-occurrence of resistance genes to antibiotics, biocides and metals reveals novel insights into their co-selection potential. *BMC Genomics*, *16*, 964. https://doi.org/10.1186/s12864-015-2153-5

Pal, C., Bengtsson-Palme, J., Kristiansson, E., & Larsson, D. J. (2016). The structure and diversity of human, animal and environmental resistomes. *Microbiome*, *4*, 54. https://doi.org/10.1186/s40168-016-0199-5

Perfumo, A., & Marchant, R. (2010). Global transport of thermophilic bacteria in atmospheric dust. *Environmental Microbiology Reports*, *2*, 333–339. https://doi.org/10.1111/j.1758-2229.2010.00143.x

Perron, G. G., Inglis, R. F., Pennings, P. S., & Cobey, S. (2015). Fighting microbial drug resistance: A primer on the role of evolutionary biology in public health. *Evolutionary Applications*, *8*, 211–222. https://doi.org/10.1111/eva.12254

Peter, H., Hörtnagl, P., Reche, I., & Sommaruga, R. (2014). Bacterial diversity and composition during rain events with and without Saharan dust influence reaching a high mountain lake in the Alps. *Environmental Microbiology Reports*, *6*, 618–624. https://doi.org/10.1111/1758-2229.12175

Petty, N. K., Zakour, N. L. B., Stanton-Cook, M., Skippington, E., Totsikaa, M., Fordea, B. M., … Beatson, S. A. (2014). Global dissemination of a multidrug resistant Escherichia coli clone. *Proceedings of the National Academy of Sciences*, *111*, 5694–5699. https://doi.org/10.1073/pnas.1322678111

Pietramellara, G., Ascher, J., Borgogni, F., Ceccherini, M., Guerri, G., & Nannipieri, P. (2009). Extracellular DNA in soil and sediment: Fate and ecological relevance. *Biology and Fertility of Soils*, *45*, 219–235. https://doi.org/10.1007/s00374-008-0345-8

Pontiroli, A., Simonet, P., Frostegard, A., Vogel, T. M., & Monier, J.-M. (2007). Fate of transgenic plant DNA in the environment. *Environmental Biosafety Research*, *6*, 15–35. https://doi.org/10.1051/ebr:2007037

Poté, J., Ceccherini, M. T., Rosselli, W., Wildi, W., Simonet, P., & Vogel, T. M. (2003). Fate and transport of antibiotic resistance genes in saturated soil columns. *European Journal of Soil Biology*, *39*, 65–71. https://doi.org/10.1016/S1164-5563(03)00003-7

Poté, J., Ceccherini, M. T., Rosselli, W., Wildi, W., Simonet, P., & Vogel, T. M. (2010). Leaching and transformability of transgenic DNA in unsaturated soil columns. *Ecotoxicology and Environmental Safety*, *73*, 67–72. https://doi.org/10.1016/j.ecoenv.2009.09.009

Poté, J., Mavingui, P., Navarro, E., Rosselli, W., Wildi, W., Simonet, P., & Vogel, T. M. (2009). Extracellular plant DNA in Geneva groundwater and traditional artesian drinking water fountains. *Chemosphere*, *75*, 498–504. https://doi.org/10.1016/j.chemosphere.2008.12.048

Pruden, A., Arabi, M., & Storteboom, H. N. (2012). Correlation between upstream human activities and riverine antibiotic resistance genes. *Environmental Science & Technology*, *46*, 11541–11549. https://doi.org/10.1021/es302657r

Pruden, A., Larsson, D. J., Amézquita, A., Collignon, P., Brandt, K. K., Graham, D. W., … Zhu, Y.-G. (2013). Management options for reducing the release of antibiotics and antibiotic resistance genes to the environment. *Environmental Health Perspectives*, *121*, 878–885. https://doi.org/10.1289/ehp.1206446

Prudhomme, M., Attaiech, L., Sanchez, G., Martin, B., & Claverys, J.-P. (2006). Antibiotic stress induces genetic transformability in the human pathogen *Streptococcus pneumoniae*. *Science*, *313*, 89–92. https://doi.org/10.1126/science.1127912

Reed, D. C., Algar, C. K., Huber, J. A., & Dick, G. J. (2014). Gene-centric approach to integrating environmental genomics and biogeochemical models. *Proceedings of the National Academy of Sciences*, *111*, 1879–1884. https://doi.org/10.1073/pnas.1313713111

Ruiz, G. M., Rawlings, T. K., Dobbs, F. C., Drake, L. A., Mullady, T., Huq, A., & Colwell, R. R. (2000). Global spread of microorganisms by ships. *Nature*, *408*, 49–50. https://doi.org/10.1038/35040695

Sandberg, K. D., & Lapara, T. M. (2016). The fate of antibiotic resistance genes and class 1 integrons following the application of swine and dairy manure to soils. *FEMS Microbiology Ecology*, *92*, fiw001. https://doi.org/10.1093/femsec/fiw001

Sato, T., Qadir, M., Yamamoto, S., Endo, T., & Zahoor, A. (2013). Global, regional, and country level need for data on wastewater generation, treatment, and use. *Agricultural Water Management*, *130*, 1–13. https://doi.org/10.1016/j.agwat.2013.08.007

Sharifi, S., Murthy, S., Takács, I., & Massoudieh, A. (2014). Probabilistic parameter estimation of activated sludge processes using Markov Chain Monte Carlo. *Water Research*, *50*, 254–266. https://doi.org/10.1016/j.watres.2013.12.010

Skurnik, D., Ruimy, R., Ready, D., Ruppe, E., de-Bauduin, C. B., Djossou, F., … Andremont, A. (2010). Is exposure to mercury a driving force for the carriage of antibiotic resistance genes? *Journal of Medical Microbiology*, *59*, 804–807. https://doi.org/10.1099/jmm.0.017665-0

Sloan, W. T., Lunn, M., Woodcock, S., Head, I. M., Nee, S., & Curtis, T. P. (2006). Quantifying the roles of immigration and chance in shaping prokaryote community structure. *Environmental Microbiology*, *8*, 732–740. https://doi.org/10.1111/j.1462-2920.2005.00956.x

Smil, V. (2011). Harvesting the biosphere: The human impact. *Population and Development Review*, *37*, 613–636. https://doi.org/10.1111/j.1728-4457.2011.00450.x

Smith, D. J., Timonen, H. J., Jaffe, D. A., Griffin, D. W., Birmele, M. N., Perry, K. D., … Roberts, M. S. (2013). Intercontinental dispersal of bacteria and archaea by transpacific winds. *Applied and Environmental Microbiology*, *79*, 1134–1139. https://doi.org/10.1128/AEM.03029-12

Sommer, M. O. A., Munck, C., Toft-Kehler, R. V., & Andersson, D. I. (2017). Prediction of antibiotic resistance: Time for a new preclinical paradigm? *Nature Reviews Microbiology*, *15*, 689–696. https://doi.org/10.1038/nrmicro.2017.75

Steffen, W., Broadgate, W., Deutsch, L., Gaffney, O., & Ludwig, C. (2015). The trajectory of the Anthropocene: The great acceleration. *The Anthropocene Review*, *2*, 81–98. https://doi.org/10.1177/2053019614564785

Sun, M., Ye, M., Schwab, A. P., Li, X., Wan, J. Z., Wei, Z., … Jiang, X. (2016). Human migration activities drive the fluctuation of ARGs: Case study of landfills in Nanjing, eastern China. *Journal of Hazardous Materials*, *315*, 93–101. https://doi.org/10.1016/j.jhazmat.2016.04.077

Thevenon, F., Adatte, T., Wildi, W., & Poté, J. (2012). Antibiotic resistant bacteria/genes dissemination in lacustrine sediments highly increased following cultural eutrophication of Lake Geneva (Switzerland). *Chemosphere*, *86*, 468–476. https://doi.org/10.1016/j.chemosphere.2011.09.048

Verhougstraete, M. P., Martin, S. L., Kendall, A. D., Hyndman, D. W., & Rose, J. B. (2015). Linking fecal bacteria in rivers to landscape, geochemical, and hydrologic factors and sources at the basin scale. *Proceedings of the National Academy of Sciences*, *112*, 10419–10424. https://doi.org/10.1073/pnas.1415836112

Volkova, V. V., Lanzas, C., Lu, Z., & Gröhn, Y. T. (2012). Mathematical model of plasmid-mediated resistance to ceftiofur in commensal enteric *Escherichia coli* of cattle. *PLoS ONE*, *7*, e36738. https://doi.org/10.1371/journal.pone.0036738

Volkova, V. V., Lu, Z., Lanzas, C., Scott, H. M., & Gröhn, Y. T. (2013). Modelling dynamics of plasmid-gene mediated antimicrobial resistance in enteric bacteria using stochastic differential equations. *Scientific Reports*, *3*, 2463. https://doi.org/10.1038/srep02463

Wang, J., Ben, W., Yang, M., Zhang, Y., & Qiang, Z. (2016). Dissemination of veterinary antibiotics and corresponding resistance genes from a concentrated swine feedlot along the waste treatment paths. *Environment International*, *92*, 317–323. https://doi.org/10.1016/j.envint.2016.04.020

Whitchurch, C. B., Tolker-Nielsen, T., Ragas, P. C., & Mattick, J. S. (2002). Extracellular DNA required for bacterial biofilm formation. *Science*, *295*, 1487. https://doi.org/10.1126/science.295.5559.1487

Widder, S., Besemer, K., Singer, G. A., Ceolae, S., Bertuzzof, E., Quinceg, C., … Battin, T. J. (2014). Fluvial network organization imprints on microbial co-occurrence networks. *Proceedings of the National Academy of Sciences*, *111*, 12799–12804. https://doi.org/10.1073/pnas.1411723111

Wilkinson, B. H., & Mcelroy, B. J. (2007). The impact of humans on continental erosion and sedimentation. *Geological Society of America Bulletin*, *119*, 140–156. https://doi.org/10.1130/B25899.1

Zhou, B., Wang, C., Zhao, Q., Wang, Y., Huo, M., Wang, J., & Wang, S. (2016). Prevalence and dissemination of antibiotic resistance genes and coselection of heavy metals in Chinese dairy farms. *Journal of Hazardous Materials*, *320*, 10–17. https://doi.org/10.1016/j.jhazmat.2016.08.007

Zhu, B. (2006). Degradation of plasmid and plant DNA in water microcosms monitored by natural transformation and real-time polymerase chain reaction (PCR). *Water Research*, *40*, 3231–3238. https://doi.org/10.1016/j.watres.2006.06.040

Zhu, Y.-G., Gillings, M. R., Simonet, P., Stekel, D., & Penuelas, J. (2017). Microbial mass movements. *Science*, *357*, 1099–1100. https://doi.org/10.1126/science.aao3007

Zhu, Y.-G., Reid, B. J., Meharg, A. A., Banwart, S. A., & Fu, B.-J. (2017). Optimizing Peri-URban Ecosystems (PURE) to re-couple urban-rural symbiosis. *Science of the Total Environment*, *586*, 1085–1090. https://doi.org/10.1016/j.scitotenv.2017.02.094

Zhu, Y.-G., Zhao, Y., Li, B., Huang, C.-L., Zhang, S.-Y., Yu, S., . . . Su, J.-Q. (2017). Continental-scale pollution of estuaries with antibiotic resistance genes. *Nature Microbiology*, *2*, 16270. https://doi.org/10.1038/nmicrobiol.2016.270

Zinger, L., Chave, J., Coissac, E., Iribar, A., Louisanna, E., Manzi, S., . . . Taberlet, P. (2016). Extracellular DNA extraction is a fast, cheap and reliable alternative for multi-taxa surveys based on soil DNA. *Soil Biology and Biochemistry*, *96*, 16–19. https://doi.org/10.1016/j.soilbio.2016.01.008

How to cite this article: Zhu Y-G, Gillings M, Simonet P, Stekel D, Banwart S, Penuelas J. Human dissemination of genes and microorganisms in Earth's Critical Zone. *Glob Change Biol*. 2017;00:1–12. https://doi.org/10.1111/gcb.14003