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1 Human dissemination of genes and microorganisms

2

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29

30 **Abstract**

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

50

51

52 **Introduction**

53 Earth's Critical Zone is the thin surface layer of the planet upon which terrestrial life
54 depends. It extends from unaltered bedrock, through the land surface, to the
55 vegetation canopy and atmospheric boundary layer. Critical Zone science is
56 complementary to other integrative systems approaches for studying terrestrial,
57 marine and freshwater environments. Crucially, it includes a mechanistic
58 understanding of shallow lithosphere processes and their interactions with the above-
59 ground ecosystems (Mobley 2009)

60 . It addresses these interactions across wide temporal (sub-second reaction kinetics to
61 geological time spans) and spatial scales (molecular to planetary). The Critical Zone
62 approach recognizes Earth as a physical and geochemical substrate that supports
63 above ground ecological functions, and extends the lower boundary of ecological
64 function to embrace the lithosphere, and its inputs over geological time scales.

65

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

78

79 Environmental microbes and genes are traditionally studied in one location, or in one
80 environmental compartment (such as vegetation, the water column, or soil), with little
81 attention paid to the dynamic exchange of microbes and genes across system

82 boundaries and physical scales. The advent of "omics" tools has facilitated the
83 exploration of Earth's biological 'dark matter', but there remains a substantial
84 conceptual gap between the notion of the Earth's biome and its quantitative
85 manifestation in biogeochemical fluxes. Integrating "omics" data into earth system
86 science should generate better models of biogeochemistry and improve understanding
87 of how environmental changes will impact microorganisms. For instance,
88 incorporating environmental genomics data into biogeochemical models improves
89 predictions about nitrogen cycling (Mock, et al. 2016; Reed, et al. 2014).

90

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

103

104 These publications are representative of recent efforts to explore the links between
105 microbial biogeography, biogeochemistry and geological processes. In particular, they
106 reflect a growing interest on the effects that human activities might have on the
107 microbial world (Gillings and Paulsen 2014). Understanding the role that humans
108 might have in changing the distributions of microorganisms, and in generating
109 selective forces that alter adaptive pressures, are essential if we are to predict how
110 global change will affect microbial activity and function. However, many of the most
111 important processes for Critical Zone function are complex, multi-gene and multi-cell

112 interactions that are difficult to model, due to the complexity and dynamics of genetic
113 and functional diversity within indigenous microbial communities.

114

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

122

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

136

137 **Natural transport and biogeography of bacteria**

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

142

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

157

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

170

171 **Natural release and survival of DNA**

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

177

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

184

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

194

195 The DNA persisting in soil is only a tiny fraction of the total DNA being released at
196 any one time from decaying plants, animals and microorganisms. This DNA usually
197 undergoes rapid degradation (Ceccherini, et al. 2007; Pontiroli, et al. 2007; Poté, et al.
198 2010). Degradation is biological and enzymatic, since DNA can survive in autoclaved
199 treatments (Zhu 2006). Nevertheless, a proportion of extracellular DNA does persist
200 in natural environments, either bound to soil particles, or inside biofilms, where it is
201 an important structural component (Pietramellara, et al. 2009; Whitchurch, et al.

202 2002). In the long term, persistence eventually requires being taken up by a recipient
203 cell, and incorporated into that cell's genome. The likelihood of this occurring
204 improves with increasing phylogenetic and ecological similarity of donor and
205 recipient (Beiko, et al. 2005), and also improves markedly if the donor DNA can
206 confer an adaptive phenotype. This is one reason why genes that confer antibiotic
207 resistance are a good marker for these processes in natural environments.

208

209 **Movement and transport of extracellular DNA.**

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

217

218 The presence of extracellular DNA in environmental samples is increasingly being
219 used to perform multi-taxa surveys, or to detect rare and elusive species (Zinger, et al.
220 2016). However, the parameters that affect transport and survival of extracellular
221 DNA are not well understood, and may compromise some of these experiments
222 (Jerde, et al. 2016). Given the problems of differential survival and transport of
223 extracellular DNA, guidelines for the design and interpretation of environmental
224 DNA methods are required (Goldberg, et al. 2016).

225

226 Experiments to address this problem have used a variety of indicator DNAs.
227 Antibiotic resistance genes known to be associated with humans are a good choice.
228 They have been used to show survival and dissemination of DNA into freshwater
229 sediments in an aquatic environment used for drinking water supply (Thevenon, et al.
230 2012). Similarly, plasmids (Poté, et al. 2003) and bacteriophages (Chetochine, et al.
231 2006) have been used to demonstrate transport over considerable distances in water

232 saturated soil and groundwater. However, the dynamic relationships between DNA
233 transport, immobilization, survival, and the limits of detection are not well established
234 (Hunter, et al. 2016).

235

236 One way to track and understand dissemination of DNA through the environment, and
237 indeed, throughout Earth's Critical Zone is to use a model system that is tractable and
238 reflects the history of human impacts. Antibiotic resistance genes, their plasmid
239 vectors, and the bacteria that host them are a good candidate for use as a proxy for
240 anthropogenic influences (Gillings, et al. 2015).

241

242 **The evolutionary history of antibiotic resistance**

243 The genes that we regard as antibiotic resistance genes are, by and large, recently
244 descended from genes whose original functions were *not* to confer resistance to
245 clinical concentrations of antibiotic compounds. Two kinds of event are responsible
246 for the genesis of modern antibiotic resistance genes: mutation of a pre-existing gene
247 within a cell lineage; and co-option of a gene acquired by lateral gene transfer from an
248 unrelated lineage (Gillings, et al. 2017). In the latter case, it has been suggested that
249 many of these laterally transferred genes originally functioned in defensive responses
250 to small signaling molecules arising from antagonistic biota, including those
251 molecules we now use as antimicrobial agents (Davies and Davies 2010; Davies, et al.
252 2006; Linares, et al. 2006).

253

254 This idea is supported by the observation that natural environments and
255 environmental bacteria contain large numbers of genes that *could* confer resistance to
256 antibiotics if they were present in clinical contexts. These genes are collectively
257 termed the resistome. The resistome is far larger and far older than the small subset of
258 problematic resistome elements that have recently made their way into human and
259 animal bacteria of clinical importance (Allen, et al. 2010). For example, gene families
260 that can confer resistance to particular antibiotic classes are plausibly related to
261 defense mechanisms selected in response to naturally-occurring compounds which

262 induce chemical stress. These gene families date back hundreds of millions of years,
263 and can be recovered from ancient environments such as caves and permafrost (Baltz
264 2008; Bhullar, et al. 2012; D'Costa, et al. 2011).

265

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

276

277 As a consequence of their universal carriage, resistant bacteria are continually
278 discharged into the environment via waste water, sewage treatment plants and animal
279 manure, thus spreading both resistant organisms and resistance genes. These same
280 waste streams also release antibiotics (Grenni, et al. 2017; Liu, et al. 2017), which
281 have significant effects, and trigger chemical stress responses even at sub-inhibitory
282 concentrations (Chow, et al. 2015). Waste waters then become giant reactors where
283 complex interactions occur between chemical compounds, molecular responses, cells,
284 resistance genes, and genetic transformation driven by lateral transfer and mutation
285 (Gillings and Stokes 2012).

286

287 The broad-scale dissemination of bacterial genes, including resistance genes, is
288 mediated by a number of factors. This transport and transformation is controlled at
289 various nested levels. Firstly, DNA can be released from cells and persist in the
290 environment. From here it can be taken up and incorporated into environmental
291 bacteria. Secondly, genes can be transported within their host bacteria. Where such

292 bacteria are dispersed by water or wind, their cargo genes are carried with them.
293 Finally, the bacteria themselves can be carried inside animal hosts via mass migration,
294 or in the case of humans, by travel and tourism.

295

296 **Tracking the movement of resistance genes in Earth's Critical Zone**

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

303

304 Human activities directly promote the invasion and spread of resistance determinants.
305 Waste water treatment plants occupy a position between human waste streams and the
306 aquatic environment, but do not effectively remove resistance genes, thus distributing
307 them in effluent (Aubertheau, et al. 2016; Ben, et al. 2017; Karkman, et al. 2016).
308 Effluents also contain significant concentrations of selective agents, thus promoting
309 the survival of resistant organisms, potentially at the expense of endemic species
310 (Borruso, et al. 2016; Caucci, et al. 2016; Koczura, et al. 2016; Lehmann, et al. 2016).
311 Application of sewage sludge, or antibiotics alone, increases the abundance of
312 resistance genes, and changes the microbial community in soils (Chen, et al. 2016;
313 Cleary, et al. 2016).

314

315 Agricultural activities also strongly promote the environmental spread of resistance
316 through disposal of wastes and application of manure (Heuer, et al. 2011; Sandberg
317 and LaPara 2016). Similarly, aquaculture is increasingly being recognized as a focal
318 point for enhancing and dispersing resistance in the environment (Muziasari, et al.
319 2016). In both of these cases, the simultaneous release of antibiotics and other
320 selective agents promotes selection of organisms containing resistance genes (He, et
321 al. 2016; Liu, et al. 2017; Wang, et al. 2016). This generates opportunities for co-

322 selection and fixation of chemical (toxic metals) and resistance determinants in
323 species, and within individual DNA molecules (Johnson, et al. 2016; Zhou, et al.
324 2016).

325

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

331

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

337

338 **Modeling of the dynamics of resistance genes in the Critical Zone**

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

346

347 However, developing realistic and flexible models that operate on an environmental
348 scale is a significant challenge. AMR encompasses a broad range of organisms, genes
349 and antimicrobial agents, and mobile genetic elements. Sensitive and resistant
350 organisms live in complex, heterogeneous communities. The processes that drive
351 fixation of resistance occur at microscopic scales. Selection and spread within the

352 Critical Zone can involve slurry tanks (Baker, et al. 2016), the animal gut (Volkova, et
353 al. 2012), wastewater treatment plants (Sharifi, et al. 2014) and industrial effluents,
354 while broader dissemination might be driven by soil movement, water percolation,
355 rivers, domestic animals and wildlife.

356

357 Mathematical modelling of resistance spread has been applied at a range of scales.
358 Models for laboratory-scale experiments have been valuable for establishing rates of
359 mutation, selection and the spread of resistance (Bootsma, et al. 2012; De Gelder, et
360 al. 2004). However, while these models are useful for characterizing key processes,
361 they do not scale up to the required complexity for whole environments.

362 Consideration of the spatial structure of microbial communities, for example biofilms,
363 gives a more accurate representation of the spread resistance in a community (Lardon,
364 et al. 2011). Models of farms or sewage treatment plants have shown that it is possible
365 for resistant organisms or pathogens to persist even in the absence of antibiotic
366 treatment (Sharifi, et al. 2014), and can also make predictions about the duration of
367 persistence (Volkova, et al. 2013). However, these models have been limited to
368 considering a single type of bacterium or antimicrobial agent.

369

370 Therefore, three developments are needed to move forward with environmental scale
371 models that can be effective in understanding and predicting spread or reduction in
372 resistance in the Critical Zone: inclusion of heterogeneity; multi-scaling in space and
373 time; and effective global data sharing.

374

375 First, models will need to consider a fuller range of organisms, resistance genes,
376 mobile genetic elements and antimicrobials, that reflect the complexity of the
377 observed system (Chen, et al. 2016; Perron, et al. 2015) and the importance of co-
378 selection of antibiotic and metal resistance genes (Gullberg, et al. 2014; Pal, et al.
379 2015). Importantly, different organisms, genes and mobile genetic elements will
380 behave differently, leading to heterogeneity in growth, transmission and selection.

381 However, their inclusion will be essential to determine the pace and range of spread or

382 elimination of resistance, and the relative contributions of resistance genes to the
383 emergence of potentially resistant pathogens. This is a considerable modeling
384 challenge, because the number of possible genetic and resistance combinations
385 increases exponentially with the degree of biological complexity to be included. For
386 example, even within a mass action ordinary differential equation framework, to
387 model populations of a single bacterial species in an environment with two different
388 antimicrobials, two respective resistance genes, that each might be carried on one of
389 two different mobile genetic elements, requires many differential equations, and such
390 models are difficult to parameterize or analyze.

391

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

404

405 Third, such models will require considerable calibration against real data. Researchers
406 carrying out environmental and field studies will need to share data in a way that is
407 useful for embedding into predictive models. To do this, we will require agreed
408 standards for data capture and sharing, and the development of an international
409 database for resistance in the critical zone. Such data could include observations from
410 a wide range of experimental techniques, and data on taxa, species, phenotypes,
411 genomes, resistance genes, mobile genetic elements, antibiotics, heavy metals and

412 other antimicrobials. Ideally, the data would also include geospatial coordinates so
413 that they can be used in geospatially explicit models. While this challenge alone is
414 considerable, there is considerable precedent for agreed data standards in other areas
415 of high throughput biology, which this development can draw upon.

416

417 **Dispersal of resistance genes in the Critical Zone – A planetary view**

418 Understanding movement of antibiotic resistance through the Critical Zone is
419 complex, and difficult to model (Figure XX). Quantifying ARG movement requires
420 the coupling between the transport of bacterial cells (and resistance genes they carry)
421 and materials (and associated selective agents) and their interactions within the
422 Critical Zone. We can then infer more general principles about the movement and
423 transformation of genes and microorganisms. These principles might then be tested
424 and applied to even more complex, multi-gene phenotypes of central importance to
425 global biogeochemistry.

426

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

439

440 The fact that biomass of humans and domestic animals now comprise 35 times that of
441 wild terrestrial mammals (Smil 2011) may have consequences for the microbial

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

454

455 Humans disperse microorganisms by mass movement of materials (Table 1).
456 Transport of ballast water in ships is estimated to move 10^{19} bacteria each day
457 (Endresen, et al. 2004; Ruiz, et al. 2000), spreading diverse microorganisms around
458 the globe and thus reshaping microbial biogeography (Brinkmeyer 2016; Lohan, et al.
459 2016). It has been suggested that anthropogenic movement of soil, sand and rock now
460 surpasses all natural processes combined (Wilkinson and McElroy 2007), incidentally
461 transporting huge numbers of microbial cells. Wastewater also transports
462 microorganisms and their cargo genes into the environment. With increasing human
463 populations, the volume of wastewater is increasing, but global data on the treatment,
464 reuse, or volumes of waste water is difficult to assemble (Sato, et al. 2013). As an
465 example, antibiotic resistance genes now pollute over 4,000 kilometers of the Chinese
466 coastline at levels up to 100 million genes per gram of sediment (Zhu, et al. 2017b).
467 None of these genes would have been present in this sediment 50 years ago.

468

469 Human activities increase the numbers of microorganisms being transported within
470 the Critical Zone and around the Earth ecosystem, thus increasing the chances for
471 successful recruitment (Table 1). Furthermore, during transport, microorganisms are

472 often exposed to pollutants, particularly during discharge of manure and waste water.
473 Exposure to antibiotics and other co-selective agents, even at low doses, can enhance
474 the rate at which bacteria generate diversity via mutation (Kohanski, et al. 2010),
475 recombination (Guerin, et al. 2009) and lateral gene transfer (Prudhomme, et al.
476 2006). The simultaneous dispersal of microorganisms and various selective agents
477 increases the genetic variation being generated in those microbial populations,
478 enhancing their potential to evolve (Gillings and Stokes 2012). Consequently a subset
479 of the cells dispersed to new locations are adapted to the co-dispersed pollutants,
480 increasing their probability of recruitment at these new locations. Further, because
481 genes for metal, disinfectant and antibiotic resistance are often closely linked
482 (Johnson, et al. 2016), exposure to any one selective agent drives their co-selection,
483 and maintains mosaic clusters of resistance determinants (Di Cesare, et al. 2016;
484 Gaze, et al. 2005; Skurnik, et al. 2010). Possession of diverse resistance determinants
485 significantly increases the probability of recruitment at novel destinations by
486 providing a selective advantage over endemic microorganisms (Table 1).

487

488 **Concluding remarks**

489 It is becoming more and more important to understand how human activities cause
490 systematic changes in ecosystems (Alberti, et al. 2017), and especially the effects on
491 the emergence and spread of ARGs in urbanizing Earth's Critical Zone (Zhu, et al.
492 2017a). To better understand the dynamics of ARGs in the Critical Zone, future
493 studies should emphasize linkages between biogeochemical cycling of nutrients and
494 contaminants with the movement of microorganisms. Under the framework of Critical
495 Zone science, tracking the dynamics of ARGs should give us insights into the
496 interconnections between multiple environmental compartments within the entire
497 Critical Zone. Due to the extreme heterogeneity of the Critical Zone, we should also
498 focus on hot spots for ARG dissemination such as locations receiving high loads of
499 wastewater or manure. Understanding the complex feedbacks between the dynamics
500 of ARGs and interactions with physical, chemical and biological processes in the
501 Critical Zone is a grand challenge. Progress can only be made by forging

502 interdisciplinary research teams that can manage and interpret the enormous datasets
503 of genomics and biogeochemistry, and by developing predictive models based on
504 these datasets.

505

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847 **Table 1: Dissemination of genes and microorganisms in Earth's Critical Zone.**

848 Three phenomena, or drivers, affect microbial/gene spread. These are: opportunity for
849 dispersal; stochasticity (the number of foreign cells landing at a particular location,
850 processes that generate local variation such as mutation and drift); and recruitment
851 (the persistence of cells at the new location, often driven by local selection).

852 Historically, these forces generate biogeographic patterns for microorganisms that are
853 similar to those of animals and plants. Human impacts have changed the dynamics of
854 these phenomena, and are altering microbial biogeography in the process.

855