

Review

# Potential Benefits and Risks for Soil Health Derived From the Use of Organic Amendments in Agriculture

Julen Urrea <sup>1</sup>, Itziar Alkorta <sup>2</sup> and Carlos Garbisu <sup>1,\*</sup>

<sup>1</sup> NEIKER-Tecnalia, Department of Conservation of Natural Resources, Soil Microbial Ecology Group, c/ Berreaga 1, E-48160 Derio, Spain; jurra@neiker.eus

<sup>2</sup> Instituto BIOFISIKA (CSIC, UPV/EHU), Department of Biochemistry and Molecular Biology, University of the Basque Country, P.O. Box 644, 48080 Bilbao, Spain; itzi.alkorta@ehu.es

\* Correspondence: cgarbisu@neiker.eus; Tel.: +34-94-403-43-00

Received: 15 July 2019; Accepted: 10 September 2019; Published: 12 September 2019



**Abstract:** The use of organic amendments in agriculture is a common practice due to their potential to increase crop productivity and enhance soil health. Indeed, organic amendments of different origin and composition (e.g., animal slurry, manure, compost, sewage sludge, etc.) can supply valuable nutrients to the soil, as well as increase its organic matter content, with concomitant benefits for soil health. However, the application of organic amendments to agricultural soil entails a variety of risks for environmental and human health. Organic amendments often contain a range of pollutants, including heavy metals, persistent organic pollutants, potential human pathogens, and emerging pollutants. Regarding emerging pollutants, the presence of antibiotic residues, antibiotic-resistant bacteria, and antibiotic-resistance genes in agricultural amendments is currently a matter of much concern, due to the concomitant risks for human health. Similarly, currently, the introduction of microplastics to agricultural soil, via the application of organic amendments (mainly, sewage sludge), is a topic of much relevance, owing to its magnitude and potential adverse effects for environmental health. There is, currently, much interest in the development of efficient strategies to mitigate the risks associated to the application of organic amendments to agricultural soil, while benefiting from their numerous advantages.

**Keywords:** agricultural systems; food security; sustainable intensification; soil health; antibiotic resistance; soil conservation

## 1. Ecological Intensification

In order to feed the constantly growing human population, it was estimated that food production will have to be doubled within the next few decades [1]. The Green Revolution, which introduced new crop varieties and livestock breeds along with the extensive use of irrigation, machinery, and synthetic agrochemicals (fertilizers, pesticides), led to sharp increases in food production from agricultural systems since the beginning of the 1960s. This global increase in food production was underpinned by intensification rather than spread of agricultural land [2]. Seeking for enhanced crop productivity, agricultural intensification was sustained by indiscriminate inputs of synthetic agrochemicals, an overuse of water, and the alteration of the soil ecosystem, at great expense to the environment. Indeed, replacing soil internal processes with external inputs resulted in the progressive deterioration of the fundamental properties of those soils, including the potential for self-regulation [3].

Soil is a multi-functional, extremely complex, and highly dynamic three-dimensional system in which solid, liquid, and gaseous components interact in multiple physical, chemical, and biological processes. On the other hand, soil is a non-renewable resource at the human scale [4]. Healthy soils support a multitude of functions [5] and the delivery of key ecosystem services. Soil health/soil quality

is recurrently defined as the capacity of a given soil to perform its functions. Although both terms are often used interchangeably, *soil quality* is normally associated with a soil's fitness for a specific use, whereas *soil health* is frequently used in a broader sense to indicate "the capacity of soil to function as a vital living system to sustain biological productivity, promote environmental quality, and maintain plant and animal health" [6]. The recovery and conservation of soil health is, thus, of utmost importance for the preservation of life on earth, justifying the concerns of the European Commission in developing a soil legislation framework [7], which was unfortunately withdrawn in 2014.

Developing strategies and tools to promote agricultural sustainability whilst maximizing crop yields will be a major challenge for the next decades, in an attempt to meet the abovementioned goal of food production while protecting the integrity of our environment. In this context, *ecological intensification* was advocated as a suitable approach to integrate ecological processes into agricultural practices, in order to simultaneously enhance the delivery of ecosystem services and reduce, or even replace, the external anthropogenic inputs [8]. This innovative approach does not display a consolidated set of guidelines, but rather a suite of alternative models for sustainable intensification, based on a greater reliance on ecological processes and ecosystem services, so as to minimize external anthropogenic inputs without adversely affecting crop productivity. Promising ecological intensification models combine technological advances in agricultural science, such as precision agriculture [9], the use of sensors [10], and state-of-the-art technologies for agricultural waste reduction and reutilization, with sustainable practices and methodologies aimed at protecting the integrity of the soil ecosystem and, specifically, its valuable biodiversity. Relying on minimum soil disturbance, a permanent soil organic cover, and crop diversification, *conservation agriculture* was shown to deliver a variety of essential ecosystem services, such as soil carbon (C) storage and sequestration, water regulation, soil erosion control, etc. [11]. However, in certain cases and situations, conservation agriculture was shown to result in a reduction in crop productivity, as compared to conventional agriculture [12]. *Organic farming* relies on natural ecological processes to maintain the integrity of the soil ecosystem and, concomitantly, the provision of ecosystem services, and it is particularly focused on long-term agricultural productivity [13]. Furthermore, organic farming aims to exclude the use of synthetic fertilizers and claims for their systematic substitution by organic amendments, thus contributing to the valorization of organic waste [14]. Nevertheless, in many cases, organic amendments may harbor traditional and emerging pollutants and, therefore, cause toxicity problems [15–17], thus entailing a potential risk to human and ecosystem health.

The aim of this review article (focusing, but not exclusively, on research papers published in the last 10 years) is to highlight the potential benefits and drawbacks associated to the use of organic amendments as agricultural fertilizers, while addressing the existing strategies and technologies to mitigate the potential downsides.

## 2. Organic Amendments

Our current production systems and transformation processes, designed to create useful goods and services, usually entail the continuous generation and disposal of massive amounts of waste. The required transition toward more ecological and sustainable production systems demands changing the current linear production model, where resources are converted into products and waste, to a circular model which, in a way, attempts to mimic the principles and functioning of natural ecological processes and cycles [18]. The paradigm of circular economy is based on closed-loop models, in which waste and by-products are effectively integrated into the system as valuable assets, thereby reducing natural resource utilization and waste production [19]. This transition was advocated by the European Commission in several documents, such as the *Roadmap to a Resource-Efficient Europe*, which appeals for sustainable production and an efficient use of resources [20], and the *European Union (EU) Action Plan for the Circular Economy*, which establishes actions covering the whole lifecycle of products and encourages to "close the loop" through greater recycling and re-use [21].

Within this circular economy paradigm, the reutilization of organic waste and by-products as soil amendments is gaining much interest, since it poses a realistic, cost-effective, and environmentally sound alternative to landfill disposal (the least preferred option for waste management) [22]. Organic amendments, such as composts, animal manures, slurries, crop residues, digestates from the anaerobic treatment of waste, biosolids, etc., are extensively applied to agricultural soil as fertilizers [23,24] or, alternatively, as amendments in soil remediation and reclamation initiatives [25–28]. Biofertilizers, defined as “mixtures of selected beneficial microorganisms and/or other organic substances (plant growth hormones, vitamins, etc.) for sustainable soil management and plant productivity” [29], are broadly applied worldwide given their promising potential [30]. Recently, “biofertilization techniques” were included within the group of “organic residues most commonly used as soil amendments” [31]. Nonetheless, other authors [23,32] differentiated “microbial inoculants” from organic waste-derived “organic amendments” or “organic fertilizers”. Undeniably, microbial inoculants are of an organic nature and may potentially exert beneficial effects on plant growth and health. However, it is not the purpose of this review article to debate whether or not microbial inoculants should be categorized as “organic amendments”, nor to discuss their potential beneficial or adverse effects.

Given that organic amendments may be (i) originated from different sources (agriculture, urban, industry), (ii) subjected or not to treatments (composting, anaerobic digestion, etc.), and (iii) presented in different stages of matter (solid, liquid), it is not surprising that they can have a wide variety of different properties and agronomic potentialities. The most common organic amendments belong to the categories below.

### 2.1. Crop Residues and Green Manures

*Crop residues* are defined as the “non-edible part of the plant that is left in the field after harvest” [33], while the term *green manure* refers to “specific forage or crop varieties that are incorporated into the soil while green or soon after maturing” [34]. These plant-based amendments are a valuable source of organic matter (OM) and are considered “the greatest source of soil organic matter (SOM)” for agricultural soils [35]. Moreover, they can provide protection against soil erosion, suppress weeds [36], improve soil physicochemical and biological properties, and enhance soil fertility [37].

### 2.2. Animal manures

Composed of feces, urine, and animal bedding, animal manure was long used as soil organic amendment since it can enhance soil fertility through the supply of essential macro- and micronutrients, as well as OM [34,38]. The application of animal manure can improve soil structure by reducing bulk density and increasing soil porosity, water infiltration/percolation rate, and aggregate stability [38,39]. Furthermore, manure-based amendments can stimulate soil microbial activity and biomass, as well as alter the composition and diversity of soil microbial communities [40,41].

### 2.3. Biosolids

Biosolids (also referred to as *sewage sludge*) are solid organic residues originated in wastewater treatment plants [42]. Given the load of macro- and micronutrients that these organic amendments contain, their application to agricultural soil can be highly beneficial for soil fertility [43]. Indeed, the application of biosolids to soil was shown to enhance its physicochemical and biological properties [44,45], and was proposed as a suitable practice for C sequestration in agricultural soil [46].

### 2.4. Compost

The decomposition of OM under controlled aerobic conditions can lead to a stable, humus-like end product known as *compost* [47]. Compost can be produced from a wide array of organic materials, including agrarian (crop residues, animal manures) and municipal solid waste and sewage sludge. In fact, compost constitutes the most commonly used organic amendment for agricultural

fertilization [48]. Composted amendments incorporate OM into agricultural soil, thereby improving soil porosity, aeration, water holding capacity, aggregate stability, and nutrient availability [39], as well as stimulating soil microbial activity and biomass [49,50]. Composted amendments contain more recalcitrant organic fractions than the raw components themselves, leading to longer-term positive effects on soil health [51].

### 2.5. Anaerobic Digestion

Anaerobic digestion is a biological process via which organic waste is stabilized in the absence of oxygen, resulting in the formation of biogas and an organic by-product known as digestate [52,53]. A broad range of organic waste can be subjected to the process of anaerobic digestion, which entails the degradation and mineralization of the labile organic constituents, thereby increasing the stability of the resulting by-product [53,54]. Given their nutrient-rich composition, digestates, which may then be separated into a liquid and solid fraction, can be used as organic amendments and agricultural fertilizers [55]. Moreover, the anaerobic digestion of organic waste was reported to effectively reduce the load of potential human pathogens and pollutants within the digested organic material [56,57].

Regardless of the specific category of amendment, the beneficial or adverse effects that any given organic amendment exert on the (agricultural) soil ecosystem depend on many different factors, ranging from intrinsic characteristics of the amendment (composition, stability, maturity, etc.) to application times and rates, soil type and properties (both physicochemical and biological), cropping system, climatic conditions, etc. [25,37]. Hence, in order to properly assess the suitability of a given organic amendment for specific agricultural purposes, an exhaustive characterization of the amendment itself and the agricultural soil and crop needs should be carried out prior to its application.

In any event, it is important to emphasize that, in many rural areas of the world (e.g., regions in southeast Asia, sub-Saharan Africa, etc.), there is a dearth of adequate sources of OM for application to agricultural soil [58]. As an example, agricultural soils in Bangladesh and Nepal are in great need of larger amounts of OM to maintain and improve their fertility, which was for decades driven by chemical fertilizers; however, regrettably, the organic fertilizer subsector in these countries is still at a very early stage of development [58]. Similarly, in sub-Saharan Africa, where agricultural soils often present a high level of degradation and poor fertility, organic inputs are customarily in short supply in smallholder farming systems due to limited affordability and/or accessibility [59]. One of the principles of integrated soil fertility management (ISFM)—the combined application of fertilizer and organic resources—can contribute to minimize this limitation and, in general, to the sustainable intensification needed in sub-Saharan Africa to address rural poverty and natural resource degradation [59]. ISFM is defined as “a set of soil fertility management practices that necessarily include the use of fertilizer, organic inputs, and improved germplasm combined with the knowledge on how to adapt these practices to local conditions, aiming at maximizing agronomic use efficiency of the applied nutrients and improving crop productivity” [60]. Within the ISFM framework, emphasis is placed on the suitable combination of agronomic practices with mineral and organic inputs and other amendments that are tailored for specific cropping systems and socioeconomic profiles [59]. Finally, in impoverished rural areas of developing countries, it is imperative to urgently emphasize the critical importance of paying much more attention to SOM, agroecological practices, and the value chains that can provide organic fertilizer in large enough quantities.

Finally, when applying organic amendments to increase the content of SOM, it must always be remembered that SOM is a complex, dynamic, and highly variable soil constituent. In any case, the persistence of OM in soil clearly indicates the existence of protective mechanisms that slow or prevent their decomposition by soil microorganisms. Thus, some OM inputs are accessed easily by soil microorganisms, and mineralized within minutes, hours, or days. In contrast, OM that becomes protected from microbial activity can remain in soils for years, decades, centuries, or even millennia. There are three main mechanisms that stabilize soil organic C (SOC): (i) *physical protection* via aggregation, which decreases the accessibility of organics to microorganisms and enzymes; (ii)

*chemical protection*, through the formation of organo-mineral complexes; and (iii) *biochemical protection*, through the chemical recalcitrance of organic molecules [61]. From these mechanisms, four soil C pools are often considered during the quantification of the soil C sequestration capacity: unprotected (free particulate OM), physically protected (microaggregate-associated C), chemically protected (silt- and clay-associated C), and biochemically protected (nonhydrolyzable C) [61,62]. This latter pool, the biochemically protected SOC pool, is also known as the passive or recalcitrant pool in SOM models. These SOM stabilization mechanisms are of great relevance in studies on soil C-saturation [62].

### 3. Beneficial Effects of Organic Amendments

Aiming to increase crop productivity while protecting agroecosystem health, organic farming was shown, through the proper application of organic amendments, to enhance soil health, as compared to conventional farming which relies on the extensive use of synthetic fertilizers and pesticides [13,38,63–65].

The beneficial or adverse effects of any given agricultural practice on soil health are usually evaluated and monitored through a wide array of indicators, which include physical (e.g., structure, bulk density, porosity, aggregate stability, water holding capacity), chemical (e.g., contents of plant macro- and micronutrients, OM, pH, cation exchange capacity), and biological (e.g., enzyme activities, respiration, potentially mineralizable nitrogen, microbial biomass C and nitrogen, microbial functional and structural diversity, diversity of macro- and mesofauna) soil properties. The latter group (biological properties) and, in particular, soil microbial indicators gained much attention lately, owing to their sensitivity, fast response, integrative characteristic, and ecological relevance [66–69]. Indeed, soil microorganisms, which comprise a major fraction of the soil total living biomass, play a key role in soil functioning and the delivery of crucial ecosystem services [70–72]. In this sense, belowground soil biodiversity was recognized as the main driver of many critical soil processes [3,73–75], as well as being responsible, to a great extent, for the stability (resistance and resilience) of the soil ecosystem [76]. The soil ecosystem is known to harbor an overwhelmingly high biodiversity and is then characterized by a high level of functional redundancy. Accordingly, it was suggested [77] that shifts in microbial community composition might not entail relevant changes in soil ecosystem functioning. This assumption can certainly be true for some natural soils, but may nonetheless fall short at low levels of soil biodiversity, as is the case for many agricultural soils [78], where increasing species diversity and a higher number of functional groups were reported to improve soil ecosystem functioning [79]. Assessing belowground soil biodiversity is, thus, imperative when measuring soil ecosystem functionality and, concomitantly, soil health. Unfortunately, the assessment of structural and functional biodiversity in such a complex ecosystem can be an extremely difficult and daunting task [80,81]. Aiming to facilitate this somewhat overwhelming task, the use of molecular and, particularly, “omics” methods and techniques is currently being increasingly promoted. Nevertheless, many of these molecular biology tools still have many technical limitations and constraints, which points out the need to be very cautious when drawing conclusions about the responses of soil microbial communities to the application of agricultural practices, including, of course, the application of organic amendments [81,82].

One of the main benefits of the application of exogenous OM to agricultural soil is the restoration and maintenance of the SOM content, which greatly contributes to long-term soil fertility and functioning [83,84]. SOM is, possibly, the most important soil property, as it sustains the physical, chemical, and biological dimensions of soil fertility and health [85]. Moreover, given that SOM simultaneously contributes to both soil fertility and soil C sequestration (and, hence, climate change mitigation), its enhancement was strongly promoted in international food security and climate forums [86].

Regarding the potential benefits of organic amendments for the biological properties of agricultural soils, it is a well-known fact that organic amendments may directly stimulate microbial growth by providing energy and essential nutrients, or indirectly by promoting plant growth and, consequently,

the amount of root exudates in the rhizosphere [23,87]. Apart from increasing microbial growth and biomass, the presence of diverse substrates susceptible to enzymatic hydrolysis within the amendments themselves leads to the stimulation of soil microbial activities [88]. A higher availability of nutrients and growth substrates may also affect soil microbial diversity and composition, by increasing the number of ecological niches and promoting a variety of ecological interactions such as competition and/or antagonism between organisms [26,89]. Biodiversity shifts may then lead to functional changes related, for instance, to plant growth promotion and disease suppression [49,90]. Moreover, increasing structural and functional soil diversity may strengthen the stability of the soil ecosystem, promoting its resistance and resilience against natural and anthropogenic stresses and disturbances [91,92]. These beneficial effects of organic amendments on the biomass, activity, and diversity of soil organisms, in turn, exert a long-term beneficial impact on soil health [93] and also contribute to the provision of key ecosystem services (C and nutrient cycling, disease suppression, etc.). Yet, it is important to highlight that microbial responses to the application of organic amendments vary greatly depending on the nature and lability of the OM present in the amendments themselves [94].

Positive effects on soil biological properties following the application of organic amendments were substantially evidenced in many studies. A great deal of investigations on the use of organic amendments [41,49,50,82,95–105] reported increases in soil microbial activity and biomass, as well as changes in microbial community composition (with potential concomitant effects on soil functioning) and, to a lesser extent, in microbial diversity. In this sense, a 10-year field experiment was conducted [106] to study the effects of replacing a mineral nitrogen fertilizer by an organic amendment (fermented pig manure), at different substitution ratios (0, 25, 50, 75, and 100%), on agricultural soil properties. Interestingly, the authors [106] reported an increase in soil bacterial diversity at increasing ratios of chemical fertilizer substitution. In another study [107], the long-term effects of organic versus conventional fertilization on soil microbial communities were investigated, finding out that the former modulated microbial community composition while increasing microbial richness and diversity. Similarly, other authors [108] reported that organic farming promotes soil microbial diversity and the abundance of beneficial soil microorganisms, with concomitant beneficial effects on the stability of the soil ecosystem. An improvement in soil microbial structural and functional diversity, as well as an increase in bacterial richness and evenness, was reported [109] after the application of organic amendments to agricultural soil. These authors [109] concluded that organic manures can “engineer” the soil ecosystem by selectively modifying the environment, thus enhancing ecosystem sustainability. The beneficial impact of increasing microbial diversity and activity, through the continuous application of organic amendments, on the restoration of saline soils was recently highlighted [110]. The effect of 10 and 20 years of continuous organic farming versus conventional farming practices on agricultural soil health was studied [111], reporting a stimulation of soil ecosystem functioning under organic management which was driven by the alteration of the soil microbial composition rather than by changes in species richness. A lack of long-term impact of organic amendments on soil microbial alpha-diversity, in the presence of significant shifts in soil microbial community structure, was observed by other authors [82,112].

Notably, changes in soil microbial structural and functional diversity were reported after the incorporation of a wide variety of organic amendments, including crop residues [113,114], manures [110,115], biosolids [103,116], composted waste [112,117], and digestates [106,118]. These changes were identified through the utilization of different techniques: community-level physiological profiling [64,115,119], phospholipid fatty-acid analysis [89,100,115], Sanger sequencing [109], and next-generation sequencing [64,111,117,120].

In addition to improving soil biological properties, organic amendments are also known to positively influence soil chemical properties. In fact, the abovementioned positive effects of organic amendments on soil microbial communities are often linked to changes in soil chemical characteristics driven by the application of amendments [45,108,120]. Several authors [121,122] evidenced the key role of soil pH for both microbial community structure and function. Indeed, as described above,

organic amendments can have a direct effect on soil fertility by supplying a wide variety of macro- and micronutrients, which support plant and microbial growth [38]. In addition, organic amendments may affect soil pH and alter cation exchange capacity, thus indirectly influencing nutrient availability, microbial activity, and, hence, soil fertility [23]. Variations in the composition and maturity of the organic amendments may alter their impact on soil pH. Some amendments contain high quantities of calcium and/or magnesium, which may then cause a kind of “liming effect” on acidic soils, increasing their pH [123]. Liming was shown to significantly increase soil microbial activity (as reflected by the values of soil dehydrogenase activity) in acid soils [124]. On the other hand, the application of organic amendments can also result in a decrease in soil pH, owing to the release of humic acids derived from the degradation of the organic C pool provided by the amendment [88], and/or due to the nitrification of the ammonium present in the amendment [96]. The addition of organic amendments may enhance the soil cation exchange capacity, mainly through the increase of the soil C pool, leading to enhanced nutrient availability and reduced nutrient leaching [125]. Nutrient availability can be affected by the biochemical composition of the amendment. In particular, its carbon-to-nitrogen (C/N) ratio can limit soil microbial growth and activity and, thus, influence the rate of OM decomposition and the patterns of nutrient release [126].

Another beneficial aspect of organic amendments is their ability to immobilize heavy metals through the formation of chemically stable metallo-humic complexes and aggregates [127], or by increasing soil pH (metal bioavailability in soil is commonly reduced at higher pH values) [128]. This beneficial effect was evidenced in many studies [42,96,129]. Also, organic amendments were shown to stimulate the degradation and/or mineralization of organic pollutants by providing nutrients and energy to soil degrading microbial populations [130].

The soil physical characteristics can also be positively influenced by the application of organic amendments. In this sense, the incorporation of exogenous OM to soil was shown to improve soil structure (better porosity and aggregate stability) [131,132] and water retention capacity, with concomitant positive effects for soil functioning and crop productivity [133]. Likewise, the stimulation of soil microbial communities through the application of organic amendments may indirectly improve soil structure, since microbial activity (through, for instance, the secretion of exopolysaccharides) and, particularly, hyphal growth can markedly influence soil aggregation and aggregate stability [134,135]. On the other hand, an increase in soil porosity often reduces soil crusting and bulk density, which could restrict the movement of water and air through the soil matrix [136,137]. In turn, this facilitates the development of the rooting matrix and improves the quality of the habitable space for soil biological communities. Furthermore, organic amendments can affect particle size distribution and the total surface area within the soil, increasing the number and types of available niches for biological colonization.

## 4. Adverse Effects of Organic Amendments

### 4.1. Traditional Risks

In spite of all the aforementioned benefits, the application of organic amendments to agricultural soil may also exert some detrimental effects on soil ecosystem health. For instance, organic amendments can harbor potentially harmful constituents such as human pathogens, heavy metal(loid)s, organic pollutants, emerging contaminants (antibiotic-resistance genes, endocrine disruptors, microplastics), etc. [103,129,138,139]. Moreover, the inappropriate application and/or overuse of organic amendments may result in other undesired environmental risks, including an excess of nutrients (eutrophication), immobilization of essential nutrients, contamination of underground water, emission of greenhouse gases, and soil acidification or salinization [25,39,140]. Altogether, these adverse side-effects threaten the safe usage of organic amendments for agricultural purposes and pose a potential risk to environmental and human health [34].

Aiming to prevent these potential drawbacks, several legislative tools arose in Europe, including, among others, the Waste Directive (EU) 2018/851, the Directive on the Landfill of Waste (1999/31/EC), the Animal Waste Directive (90/667/EEC), and the Sewage Sludge Directive (86/278/EEC) [26]. These regulations provide guidelines on waste disposal and, interestingly, set threshold values for the contaminants present in organic waste. Nevertheless, there still exist concerns about the quality of these legislations, specifically regarding the lack of data and regulation for most emerging contaminants. On the other hand, it is widely accepted that bioavailable contaminant concentrations are more significant for environmental risk assessment than total contaminant concentrations. The potential negative effects exerted by, for instance, toxic heavy metals on soil health are known to depend upon their bioavailable concentrations [141], which, in many cases, are not correlated with total concentration values [72]. In spite of this well-known fact, in most countries, the existing legislation on soil contamination still relies on the values of total contaminant concentration.

Owing to their lack of biodegradability, heavy metals have an extremely long persistence in the soil environment [142]. Therefore, the regular application of organic amendments may lead to metal accumulation in soil, with concomitant risks of metal bioaccumulation and biomagnification along the trophic chain [143]. As previously addressed, the application of organic amendments can enhance the formation of soil aggregates and metallo-humic complexes, which can then reduce the bioavailability of heavy metals. In contrast, the decomposition and mineralization of OM may increase metal bioavailability due to the disintegration of soil aggregates and the formation of soluble organic metal carriers [144,145]. In this regard, a disruption of nutrient cycling processes derived from the metal toxicity caused by the repeated application of biosolids was reported [88]. Reductions in soil microbial biomass were also observed by several authors [146,147], following the application of organic amendments.

In addition to inorganic contaminants, organic amendments can incorporate organic pollutants into the soil ecosystem which, in some cases, may also show a high level of persistence and recalcitrance [129,148,149]. Moreover, the breakdown products and secondary metabolites produced during the degradation of these organic pollutants may happen to be even more toxic and persistent than the parent compounds themselves [148]. Furthermore, little is known regarding the breakdown rates of many of these organic pollutants and their transformation products in the soil ecosystem, as well as concerning their potential toxic effects on the soil biota. Therefore, there is an urgent need to determine the potential ecotoxicity of those organic pollutants present in organic amendments, in order to ensure the long-term sustainability and safety of this agronomic practice [150].

Some organic amendments, particularly those derived from raw, unstable animal by-products or biosolids, can contain potentially pathogenic organisms [151,152], including enteric bacteria, parasites, viruses, and fungi [149]. In this regard, it was suggested that *Bacillus anthracis* and *Bordetella pertussis* may be dominant human pathogens in animal manure [153], and *Escherichia coli* and *Klebsiella pneumoniae* in biosolids [154]. The possibility of pathogen incorporation to agricultural soil through the application of organic amendments is a risk that must be thoroughly prevented given its serious implications for human health. An exhaustive biological characterization of the organic amendments is, thus, imperative in order to minimize, or better avoid, this potential biohazard. As an example, Bibby and Peccia [155] investigated the viral pathogen load of different biosolids, identifying >40 different human viruses.

An excessive and inappropriate application of organic amendments may also result in an excess of nutrients (e.g., phosphorus, nitrogen), which can eventually cause negative environmental consequences such as contamination of watercourses and eutrophication [140,156,157]. On the other hand, organic amendments with a high C/N ratio can entail the immobilization of mineral nitrogen within the soil microbial biomass, since microorganisms are generally more effective than plants at competing for nutrients [158]. In addition, the application of organic amendments to soil may trigger the release of gases to the atmosphere, including ammonia and greenhouse gases, most relevantly methane and nitrous oxides [39,140,159,160]. The emission of these gases depends upon (i) the type of



organic waste, (ii) the applied treatments (composting, anaerobic digestion), (iii) the timing, dose, and method of application, etc.

Finally, soil acidification and salinization may occur following the application of organic amendments to agricultural soil which can, in turn, affect soil structure, as well as nutrient availability, and, importantly, the mobility and bioavailability of pollutants, thus threatening agricultural productivity and ecosystem health. Some organic amendments can indeed increase the soil's electrical conductivity (higher salinity and sodicity), with concomitant detrimental effects for crop yield and soil biological activity [161]. Conversely, the use of acid organic amendments or the generation of humic acids (or the activity of some biological processes such as nitrification) may result in soil acidification, often resulting in increased solubility, mobility and bioavailability of soil contaminants [88,96].

#### 4.2. Emerging Contaminants

Microplastics (<5 mm in size) arise from the weathering and fragmentation of plastics into smaller particles [162]. Microplastics are extremely or completely resistant to biodegradation, and may cause potential detrimental effects on soil ecosystem functioning and, in particular, on soil organisms via their ingestion and accumulation [163]. Furthermore, microplastics can interact with soil contaminants, altering their ecotoxicity and mobility/bioavailability (many contaminants can become adsorbed onto microplastics) [164,165]. Domestic and industrial wastewaters can carry substantial loads of potentially harmful microplastics [163], which eventually end up in the corresponding wastewater treatment plant. Wastewater treatment plants are very effective at removing microplastics from the treated water [166], resulting in the accumulation of microplastics in the biosolids themselves [167]. The application of different rates of biosolids, as drivers of microplastic contamination, into agricultural soil was studied [168], finding detectable levels of these potentially harmful emerging contaminants in the amended soils. Nevertheless, existing data on the impact of microplastics on the soil ecosystem are still very scarce [169].

On the other hand, in the last few decades, the amount of antibiotic-resistant bacteria (ARB) and antibiotic-resistance genes (ARGs) in the environment increased substantially due to anthropogenic activities, resulting in their current identification as emerging environmental contaminants [170]. Indeed, the overuse and misuse of antibiotics for human and veterinary applications resulted in a proliferation of clinically relevant ARB and ARGs in the environment. Actually, antibiotic resistance is increasingly being recognized as one of the greatest threats for global health, as evidenced by the high-level policy initiatives that recently arose, e.g., the *Transatlantic Taskforce on Antimicrobial Resistance*, the *Global Antibiotic Resistance Partnership*, the *Joint Programming Initiative on Antimicrobial Resistance* [171], endorsed by the World Health Organization [172], and the *Political Declaration on AMR of the United Nations* [173]. In Europe, the European Commission published the *Action Plan Against the Rising Threats from Antimicrobial Resistance* [174], which contains 12 actions seeking to palliate the detrimental effects of antimicrobial resistance. This Action Plan was later updated by the publication of the *EU One Health Action Plan against Antimicrobial Resistance* [175]. Guidelines, actions, restrictions, and objectives are urgently needed, since it was estimated that antibiotic-resistant infections could cause 10 million deaths per year by 2050 [176].

Antibiotics are known to be poorly metabolized in the human and animal body. Hence, a considerable amount of these emerging contaminants are excreted unchanged or as active metabolites of the parent species [177], resulting in the presence of a high amount of antibiotics in many wastewaters [178]. Not surprisingly, both livestock manure and wastewater treatment plants are acknowledged as important reservoirs for ARB and ARGs [179,180]. In this sense, the long-term application of animal manure and biosolids to agricultural soil may lead to the introduction, proliferation, and dissemination of these emerging contaminants in the environment [181–185]. It was reported that the repeated exposure of the soil environment to amendment-borne ARGs correlates with the emergence and proliferation of ARGs in indigenous soil bacteria [186,187].

The dissemination of ARGs among bacteria is mainly driven by horizontal gene transfer (HGT). Indeed, HGT is the main mechanism for genetic variation in prokaryotic organisms, allowing their adaptation to changing environmental conditions and disturbances. HGT facilitates the colonization of ecological niches [188,189] through the acquisition of genes via mobile genetic elements (MGEs), such as plasmids, integrons, and transposons. Although there are three main mechanisms of intercellular DNA movement (transformation, conjugation, transduction) [190], conjugative plasmid-mediated HGT is considered the most relevant mechanism for the dissemination of ARGs among bacteria [191]. MGEs often carry integrons, which act as natural cloning systems and expression vectors of gene cassettes encoding functions of potential adaptive significance, e.g., antibiotic resistance [192]. Relevantly, integrons have a key role in the dissemination of ARGs in manure- and biosolid-amended soils [193,194].

In this regard, the rhizosphere was addressed as a major hotspot for HGT [195]. Interestingly, the phyllosphere was also shown to be conducive to conjugative plasmid transfer [196]. Consequently, crops harvested from manure- or biosolid-amended soils can potentially carry ARGs, representing a potential route of exposure to ARB for animals and humans [170,183]. The abundance and diversity of ARGs in organically versus conventionally produced lettuce was investigated by high-throughput quantitative PCR [197], detecting 134 ARGs in the phyllosphere and leaf endophytes of lettuce samples, which were significantly enriched in the organically produced lettuces. The same research group conducted an analogous study [183] with lettuce and endive crops in manure-amended soils, obtaining similar results. Other authors [181] detected ARGs and MGEs in vegetables grown in both manured and inorganically fertilized soils. Some antibiotic determinants were exclusively detected in the manured soils. These authors [181] highlighted the importance of pretreating the raw organic waste and/or establishing offset times between amendment incorporation and crop harvest for safe consumption. Dolliver et al. [198] found that corn, lettuce, and potato crops were able to accumulate sulfamethazine from manured soils, pointing out the concerns about the consumption of low levels of antibiotics from crops grown in manured soils.

Interestingly, antibiotic resistance is frequently associated with metal resistance [199], as the molecular mechanisms underpinning resistance to both antibiotics and heavy metals are often similar [199]. This phenomenon is due to the evolutionary mechanism of *co-selection*, which drives the simultaneous resistance to different pollutants (e.g., metals, antibiotics, biocides) through *co-resistance* (when different genes encoding for metal and antibiotic resistance are allocated in the same genetic determinant) or *cross-resistance* (when the same gene provides resistance to both antibiotics and metals) mechanisms [200]. Co-selection is a most relevant mechanism for the abovementioned risk of the appearance and dissemination of ARGs associated with the application of organic amendments to agricultural soil, since the presence of heavy metals in the amendments may enhance antibiotic resistance or select for ARB [201].

## 5. Overcoming the Drawbacks

In addition to stabilizing nutrients and OM, which results in a longer-term availability of essential nutrients and a positive effect on soil microbial activity and biomass [51], composting is a well-known mechanism for minimizing or eliminating many unwanted effects of the application of raw organic waste to agricultural soil [25]. Composting, through the hygienization of organic waste, can significantly mitigate the risk of incorporation of potential human pathogens into the soil ecosystem, although it may not entirely prevent the regrowth of pathogenic strains [152,202,203]. Moreover, composting is acknowledged to be an effective measure to alleviate antimicrobial resistance during the application of organic amendments to agricultural soil [204,205]. In this sense, total or partial degradation of antibiotic residues through composting processes was widely reported [206–208]. Moreover, as composting processes entail changes in the physicochemical characteristics of the organic waste, the bioavailability of the antimicrobial compounds may be reduced [209]. A reduction in the amount of antibiotics or their bioavailability may eventually lead to a decrease in the load of ARGs. The relatively high temperatures reached during many composting processes may also decrease the load of ARB and ARGs [205,207].

The anaerobic digestion of organic waste was also proposed as an effective mechanism to reduce the negative consequences of the application of organic waste to agricultural soil. Indeed, the anaerobic digestion of organic waste was often reported to effectively reduce the levels of organic pollutants and potential human pathogens present in organic amendments [57,210]. Furthermore, many authors [211–213] reported the potential of the anaerobic digestion for the removal of antibiotic residues and antibiotic determinants in organic waste. As with composting, this process entails the stabilization of the OM and may then influence the bioavailability of organic pollutants by promoting sorption processes [56]. Relevantly, physical adsorption was identified as a key mechanism for the removal of antibiotic residues from organic materials [214]. The anaerobic digestion of organic waste may be carried out under mesophilic or thermophilic conditions, the former being the most widely applied process [215]. However, under thermophilic conditions, better results are obtained regarding the removal of antibiotic-resistance determinants [216,217]. However, the anaerobic digestion of organic waste was repeatedly reported to inefficiently remove ARGs [218]. A previous treatment, consisting of applying a thermal hydrolysis prior to the process of anaerobic digestion, was proposed to reduce more efficiently the load of ARB and ARGs [215], since the high pressure and thermal conditions yielded by this process promote cell lysis and, thus, the release of degradable components [219].

In any event, both composting and anaerobic digestion recurrently showed their potential for the removal of antibiotic-resistance determinants. Masse et al. [220] concluded that composting was more effective than anaerobic digestion for reducing antibiotic residues from organic waste. Other authors [221] also found that composted manure contained up to seven orders of magnitude less antibiotic-resistance determinants than the one treated with other aerobic and anaerobic treatments. According to these results, composting appears the best option for reducing the reservoir of antibiotic resistance present in raw organic waste. Nonetheless, some authors showed inconsistent results regarding the positive effect of composting on the reduction of ARGs. For example, Peng et al. [222] compared the abundance and diversity of tetracycline (*tet*) resistance genes in agricultural soils after six years of continuous fresh versus composted manure application. They found nine classes of *tet* genes, and two of them were significantly more abundant in soils amended with composted manure (no reduction in the total abundance of *tet* genes after manure composting was detected).

As described above, owing to the energy and nutrient content of organic waste, many scientists traditionally investigated possible treatment options for such waste, mainly through anaerobic digestion or composting. Currently, within the fields of waste treatment and waste valorization, the utilization of organic waste as substrates for producing insects, mainly as a protein source for the livestock sector or as a source of fats for biodiesel production, appears a most promising alternative [223]. Processing of (bio)waste with larvae, such as for instance fly larvae, is becoming a promising waste treatment technology. Nonetheless, compared to more conventional waste treatment technologies such as composting or anaerobic digestion, the process performance is variable and the mechanisms driving the decomposition of the organic waste are still poorly understood [224]. The larvae grown on the (bio)waste can then be used for animal feed production, thus providing a protein source to help alleviate the rising global demand for animal feed [225] and, interestingly, revenues for financially viable waste management systems [224]. In particular, black soldier fly (*Hermetia illucens* L.; Diptera: Stratiomyidae) biowaste processing is a treatment technology that received much attention over the last few decades [226–228]. Interestingly, a recent study [225] concluded that black soldier fly biowaste treatment offers an environmentally relevant alternative, with very low direct emissions of greenhouse gases and potentially high reduction in global warming potential.

Finally, the possibility of using CRISPR/Cas (clustered regularly interspaced short palindromic repeats), a prokaryotic immune system which protects bacteria and archaea against phage attack and undesired plasmid replication [229], is being investigated to selectively remove ARGs from bacterial populations. Some studies [230,231] indeed confirmed the potential of this methodology to remove ARGs and/or the plasmids that encode those genes. Nevertheless, this technology still exhibits several important drawbacks [232]: (i) finding an appropriate delivery vector, since phages or conjugative

plasmids normally show narrow host ranges; (ii) unpredictability of the response of the microbial community following the introduction of a delivery vector, due to the inherent complexity of microbial communities; (iii) evolution of resistance to CRISPR/Cas through mutation of the target hosts and/or by exhibiting anti-CRISPR activity (selection for *arc* genes); and (iv) legislative and social barriers regarding the release of gene-editing systems to the environment, as well as a lack of unanimous acceptance by the scientific community.

## 6. Conclusions

In the search for suitable strategies to optimize agricultural environmental sustainability while maximizing crop productivity and production, the paradigm of ecological intensification recently gained much interest, in an attempt to enhance the provision of ecosystem services through the consideration of natural ecological processes during the design and implementation of agricultural practices and management systems. In this regard, the application of organic waste and by-products as agricultural soil amendments is a common practice, given their potential to increase crop productivity while enhancing the health of the soil ecosystem. Moreover, the integration of organic waste into the value chain as valuable assets meets the current circular economy paradigm.

Organic amendments can be obtained from a wide range of organic materials and origins. Their potential positive effects on soil ecosystem functioning depend upon many factors including their composition, stability, maturity, frequency and rate of utilization, soil type, cropping system, climatic conditions, etc. Therefore, an exhaustive characterization of both the organic amendment and the agroecosystem itself must be performed prior to its application, in order to identify the potentialities and limitations of any given organic amendment for soil and crop health.

Composting and anaerobic digestion are acknowledged to be efficient for overcoming some of the potential adverse impacts that organic amendments may exert on the soil ecosystem and, in general, the environment. Pertaining to the potential adverse effects that organic amendments can exert on the soil ecosystem, some emerging contaminants, such as ARB, ARGs, and MGEs, are currently causing much concern as they pose a serious risk to environmental and human health. Given that biological emerging contaminants such as these (ARGs, MGEs, ARB) can persist in the environment and, worse, make copies of themselves and be transferred by HGT to other biological receptors, there is an urgent need to develop more effective treatments of organic waste, which must go beyond the typical hygienization and bacterial disinfection and effectively destroy DNA.

**Author Contributions:** Conceptualization, C.G. and J.U.; writing—original draft preparation, J.U., I.A., and C.G.; writing—review and editing, I.A. and C.G.; supervision, C.G.

**Funding:** J.U. was the recipient of a predoctoral fellowship from the Department for Economic Development and Infrastructures of the Basque Government.

**Acknowledgments:** The authors thank the Basque Government for financial support through the URAGAN project.

**Conflicts of Interest:** The authors declare no conflicts of interest.

## References

1. Foley, J.A.; Ramankutty, N.; Brauman, K.A.; Cassidy, E.S.; Gerber, J.S.; Johnston, M.; Mueller, N.D.; O'Connell, C.; Ray, D.K.; West, P.C.; et al. Solutions for a cultivated planet. *Nature* **2011**, *478*, 337–342. [[CrossRef](#)] [[PubMed](#)]
2. Pretty, J.; Bharucha, Z.P. Sustainable intensification in agricultural systems. *Ann. Bot.* **2014**, *114*, 1571–1596. [[CrossRef](#)] [[PubMed](#)]
3. Bender, S.F.; Wagg, C.; van der Heijden, M.G.A. An underground revolution: Biodiversity and soil ecological engineering for agricultural sustainability. *Trends Ecol. Evol.* **2016**, *31*, 440–452. [[CrossRef](#)] [[PubMed](#)]
4. Hakeem, K.; Sabir, M.; Ozturk, M.; Mermut, A. *Soil Remediation and Plants—Prospects and Challenges*, 1st ed.; Academic Press & Elsevier: New York, NY, USA, 2014; p. 724.

5. Blum, W.H. Functions of soil for society and the environment. *Rev. Environ. Sci. Biotechnol.* **2005**, *4*, 75–79. [[CrossRef](#)]
6. Doran, J.W.; Zeiss, M.R. Soil health and sustainability: Managing the biotic component of soil quality. *Appl. Soil Ecol.* **2000**, *15*, 3–11. [[CrossRef](#)]
7. CEC (Commission of the European Communities). *Proposal for a Directive of the European Parliament and of the Council, Establishing a Framework for the Protection of Soil and Amending Directive 2004/35/EC*; CEC (Commission of the European Communities): Brussels, Belgium, 2006; COM (2006) 232.
8. Bommarco, R.; Kleijn, D.; Potts, S.G. Ecological intensification: Harnessing ecosystem services for food security. *Trends Ecol. Evol.* **2013**, *28*, 230–238. [[CrossRef](#)] [[PubMed](#)]
9. Capmourteres, V.; Adams, J.; Berg, A.; Fraser, E.; Swanton, C.; Anand, M. Precision conservation meets precision agriculture: A case study from southern Ontario. *Agric. Syst.* **2018**, *167*, 176–185. [[CrossRef](#)]
10. Aranguren, M.; Castellón, A.; Aizpurua, A. Crop Sensor-Based In-Season Nitrogen Management of Wheat with Manure Application. *Remote Sens.* **2019**, *11*, 1094. [[CrossRef](#)]
11. Palm, C.; Blanco-Canqui, H.; DeClerck, F.; Gatere, L.; Grace, P. Conservation agriculture and ecosystem services: An overview. *Agric. Ecosyst. Environ.* **2014**, *187*, 87–105. [[CrossRef](#)]
12. Pittelkow, C.M.; Liang, X.; Linquist, B.A.; van Groenigen, K.; Lee, J.; Lundy, M.E.; Gestel, N.; Six, J.; Venterea, R.T.; Kessel, C. Productivity limits and potentials of the principles of conservation agriculture. *Nature* **2014**, *517*, 365–368. [[CrossRef](#)] [[PubMed](#)]
13. Reganold, J.P.; Wachter, J.M. Organic agriculture in the twenty-first century. *Nat. Plants* **2016**, *2*, 15221. [[CrossRef](#)] [[PubMed](#)]
14. Misselbrook, T.H.; Menzi, H.; Cordovil, C. Preface—recycling of organic residues to agriculture: Agronomic and environmental impacts. *Agric. Ecosyst. Environ.* **2012**, *160*, 1–2. [[CrossRef](#)]
15. Kapanen, A.; Itävaara, M. Ecotoxicity tests for compost applications. *Ecotoxicol. Environ. Saf.* **2001**, *49*, 1–16. [[CrossRef](#)] [[PubMed](#)]
16. Pampuro, N.; Bisaglia, C.; Romano, E.; Brambilla, M.; Foppa Pedretti, E.; Cavallo, E. Phytotoxicity and chemical characterization of compost derived from pig slurry solid fraction for organic pellet production. *Agriculture* **2017**, *7*, 94. [[CrossRef](#)]
17. Asgharipour, M.R.; Sirousmehr, A.R. Comparison of three techniques for estimating phytotoxicity in municipal solid waste compost. *Ann. Biol. Res.* **2012**, *3*, 1094–1101.
18. Maina, S.; Kachrimanidou, V.; Koutinas, A. A roadmap towards a circular and sustainable bioeconomy through waste valorization. *Curr. Opin. Green Sustain. Chem.* **2017**, *8*, 18–23. [[CrossRef](#)]
19. Murray, M.; Skene, K.; Haynes, K. The Circular Economy: An Interdisciplinary Exploration of the Concept and Application in a Global Context. *J. Bus. Ethics* **2015**, *140*, 369–380. [[CrossRef](#)]
20. European Commission. *Roadmap to a Resource Efficient Europe*; European Commission: Brussels, Belgium, 2011; COM (2011) 571.
21. European Commission. *Closing the Loop—An EU Action Plan for the Circular Economy*; European Commission: Brussels, Belgium, 2015; COM (2015) 614.
22. Chojnacka, K.; Gorazda, K.; Witek-Krowiak, A.; Moustakas, K. Recovery of fertilizer nutrients from materials—Contradictions, mistakes and future trends. *Renew. Sust. Energ. Rev.* **2019**, *110*, 485–498. [[CrossRef](#)]
23. Abbott, L.K.; Macdonald, L.M.; Wong, M.T.F.; Webb, M.J.; Jenkins, S.N.; Farrell, M. Potential roles of biological amendments for profitable grain production—A review. *Agric. Ecosyst. Environ.* **2018**, *256*, 34–50. [[CrossRef](#)]
24. Celestina, C.; Hunt, J.R.; Sale, P.W.G.; Franks, A.E. Attribution of crop yield responses to application of organic amendments: A critical review. *Soil Tillage Res.* **2019**, *186*, 135–145. [[CrossRef](#)]
25. Larney, F.J.; Angers, D.A. The role of organic amendments in soil reclamation: A review. *Can. J. Soil Sci.* **2012**, *92*, 19–38. [[CrossRef](#)]
26. Gómez-Sagasti, M.T.; Hernández, A.; Artetxe, U.; Garbisu, C.; Becerril, J.M. How Valuable Are Organic Amendments as Tools for the Phytomanagement of Degraded Soils? The Knowns, Known Unknowns, and Unknowns. *Front. Sustain. Food Syst.* **2018**, *2*, 68. [[CrossRef](#)]
27. Galende, M.A.; Becerril, J.M.; Barrutia, O.; Artetxe, U.; Garbisu, C.; Hernández, A. Field assessment of the effectiveness of organic amendments for aided phytostabilization of a Pb-Zn contaminated mine soil. *J. Geochem. Explor.* **2014**, *145*, 181–189. [[CrossRef](#)]

28. Epelde, L.; Burges, A.; Mijangos, I.; Garbisu, C. Microbial properties and attributes of ecological relevance for soil quality monitoring during a chemical stabilization field study. *Appl. Soil Ecol.* **2014**, *75*, 1–12. [[CrossRef](#)]
29. Soil Science Society of America. *Glossary of Soil Science Terms*; Soil Science Society of America: Madison, WI, USA, 2008; ISBN 978-0-89118-851-3.
30. Schütz, L.; Gattinger, A.; Meier, M.; Müller, A.; Boller, T.; Mäder, P.; Mathimaran, N. Improving Crop Yield and Nutrient Use Efficiency via Biofertilization—A Global Meta-analysis. *Front. Plant Sci.* **2018**, *8*, 2204. [[CrossRef](#)]
31. Hueso-González, P.; Muñoz-Rojas, M.; Martínez-Murillo, J.F. The role of organic amendments in drylands restoration. *Curr. Opin. Environ. Sci. Soil Health* **2018**, *5*, 1–6. [[CrossRef](#)]
32. Malusa, E.; Vassilev, N. A contribution to set a legal framework for biofertilisers. *Appl. Microbiol. Biotechnol.* **2014**, *98*, 6599–6607. [[CrossRef](#)] [[PubMed](#)]
33. Lal, R. World crop residues production and implications of its use as a biofuel. *Environ. Int.* **2005**, *31*, 575–584. [[CrossRef](#)]
34. Goss, M.J.; Tubeileh, A.; Goorahoo, D. A review of the use of organic amendments and the risk to human health. *Adv. Agron.* **2013**, *120*, 275–379.
35. Tisdale, S.L.; Nelson, W.L.; Beaton, J.D. *Soil Fertility and Fertilizers*; Macmillan Publishing Company: New York, NY, USA, 1985.
36. Kruidhof, H.M.; Gallandt, E.R.; Haramoto, E.R.; Bastiaans, L. Selective weed suppression by cover crop residues: Effects of seed mass and timing of species sensitivity. *Weed Res.* **2011**, *51*, 177–186. [[CrossRef](#)]
37. Turmel, M.S.; Speratti, A.; Baudron, F.; Verhulst, N.; Govaerts, B. Crop residue management and soil health: A systems analysis. *Agric. Syst.* **2015**, *134*, 6–16. [[CrossRef](#)]
38. Edmeades, D.C. The long-term effects of manures and fertilisers on soil productivity and quality: A review. *Nut. Cycl. Agroecosyst.* **2003**, *66*, 165–180. [[CrossRef](#)]
39. Thangarajan, R.; Bolan, N.S.; Tian, G.; Naidu, R.; Kunhikrishnan, A. Role of organic amendment application on greenhouse gas emission from soil. *Sci. Total Environ.* **2013**, *465*, 72–96. [[CrossRef](#)] [[PubMed](#)]
40. Liu, T.; Chen, X.Y.; Hu, F.; Ran, W.; Shen, Q.R.; Li, H.X.; Whalen, J.K. Carbon-rich organic fertilizers to increase soil biodiversity: Evidence from a meta-analysis of nematode communities. *Agric. Ecosyst. Environ.* **2016**, *223*, 199–207. [[CrossRef](#)]
41. Reardon, C.; Wuest, S.B. Soil amendments yield persisting effects on the microbial communities: A 7-year study. *Appl. Soil Ecol.* **2016**, *101*, 107–116. [[CrossRef](#)]
42. Singh, R.P.; Agrawal, M. Potential benefits and risks of land application of sewage sludge. *Waste Manag.* **2008**, *28*, 347–358. [[CrossRef](#)] [[PubMed](#)]
43. Haynes, R.; Murtaza, G.; Naidu, R. Inorganic and organic constituents and contaminants of biosolids: Implications for land application. *Adv. Agron.* **2009**, *104*, 165–267.
44. Latore, A.M.; Kumar, O.; Singh, S.K.; Gupta, A. Direct and residual effect of sewage sludge on yield, heavy metals content and soil fertility under rice–wheat system. *Ecol. Eng.* **2014**, *69*, 17–24. [[CrossRef](#)]
45. Lloret, E.; Pascual, J.A.; Brodie, E.L.; Bouskill, N.J.; Insam, H.; Juárez, M.F.D.; Goberna, M. Sewage sludge addition modifies soil microbial communities and plant performance depending on the sludge stabilization process. *Appl. Soil Ecol.* **2016**, *101*, 37–46. [[CrossRef](#)]
46. Tian, G.; Chiu, C.Y.; Franzluebbers, A.J.; Oladeji, O.O.; Granato, T.C.; Cox, A.E. Biosolids amendment dramatically increases sequestration of crop residue carbon in agricultural soils in western Illinois. *Appl. Soil Ecol.* **2015**, *85*, 86–93. [[CrossRef](#)]
47. St Martin, C.C.G.; Brathwaite, R.A.I. Compost and compost tea: Principles and prospects as substrates and soil-borne disease management strategies in soil-less vegetable production. *Biol. Agric. Hortic.* **2012**, *28*, 1–33. [[CrossRef](#)]
48. Scotti, R.; Bonanomi, G.; Scelza, R.; Zoina, A.; Rao, M.A. Organic amendments as sustainable tool to recovery fertility in intensive agricultural systems. *J. Soil Sci. Plant Nutr.* **2015**, *15*, 333–352. [[CrossRef](#)]
49. Das, S.; Jeong, S.T.; Das, S.; Kim, P.J. Composted cattle manure increases microbial activity and soil fertility more than composted swine manure in a submerged rice paddy. *Front. Microbiol.* **2017**, *8*, 1702. [[CrossRef](#)] [[PubMed](#)]
50. Hernández, T.; Chocano, C.; Moreno, J.; Garcia, C. Use of compost as an alternative to conventional inorganic fertilizers in intensive lettuce (*Lactuca sativa* L.) crops—Effects on soil and plant. *Soil Tillage Res.* **2016**, *160*, 14–22. [[CrossRef](#)]

51. Diacono, M.; Montemurro, F. Long-term effects of organic amendments on soil fertility. A review. *Agron. Sustain. Dev.* **2010**, *30*, 401–422. [[CrossRef](#)]
52. Tani, M.; Sakamoto, N.; Kishimoto, T.; Umetsu, K. Utilization of anaerobically digested slurry combined with other waste following application to agricultural land. *Int. Congr. Ser.* **2006**, *1293*, 331–334. [[CrossRef](#)]
53. Tambone, F.; Genevini, P.; D'Imporzano, G.; Adani, F. Assessing amendment properties of digestate by studying the organic matter composition and the degree of biological stability during the anaerobic digestion of the organic fraction of MSW. *Bioresour. Technol.* **2009**, *100*, 3140–3142. [[CrossRef](#)] [[PubMed](#)]
54. Grigatti, M.; Di Girolamo, G.; Chincarini, R.; Ciavatta, C. Potential nitrogen mineralization, plant utilization efficiency and soil CO<sub>2</sub> emissions following the addition of anaerobic digested slurries. *Biomass Bioenergy* **2011**, *35*, 4619–4629. [[CrossRef](#)]
55. Nkoa, R. Agricultural benefits and environmental risks of soil fertilization with anaerobic digestates: A review. *Agron. Sustain. Dev.* **2014**, *34*, 473–492. [[CrossRef](#)]
56. Li, Y.B.; Park, S.Y.; Zhu, J.Y. Solid-state anaerobic digestion for methane production from organic waste. *Renew. Sustain. Energy Rev.* **2011**, *15*, 821–826. [[CrossRef](#)]
57. Martín, J.; Santos, J.L.; Aparicio, I.; Alonso, E. Pharmaceutically active compounds in sludge stabilization treatments: Anaerobic and aerobic digestion, wastewater stabilization ponds and composting. *Sci. Total Environ.* **2015**, *503*, 97–104. [[CrossRef](#)] [[PubMed](#)]
58. Cook, S.; Henderson, C.; Kharel, M.; Begum, A.; Rob, A.; Piya, S. *Collaborative Action on Soil Fertility in South Asia: Experiences from Bangladesh and Nepal*; IIED: London, UK, 2016.
59. Vanlauwe, B.; Descheemaeker, K.; Giller, K.E.; Huising, J.; Merckx, R.; Nziguheba, G.; Wendt, J.; Zingore, S. Integrated soil fertility management in sub-Saharan Africa: Unravelling local adaptation. *Soil* **2015**, *1*, 491–508. [[CrossRef](#)]
60. Vanlauwe, B.; Chianu, J.; Giller, K.E.; Merck, R.; Mokwenye, U.; Pypers, P.; Shepherd, K.; Smaling, E.; Woomer, P.L.; Sanginga, N. Integrated soil fertility management: Operational definition and consequences for implementation and dissemination. *Outlook Agric.* **2010**, *39*, 17–24. [[CrossRef](#)]
61. Stewart, C.E.; Plante, A.F.; Paustian, K.; Conant, R.T.; Six, J. Soil carbon saturation: Linking concept and measurable carbon pools. *Soil Sci. Soc. Am. J.* **2018**, *72*, 379–392. [[CrossRef](#)]
62. Six, J.; Conant, R.T.; Paul, E.A.; Paustian, K. Stabilization mechanisms of soil organic matter: Implications for C-saturation of soils. *Plant Soil* **2002**, *241*, 155–176. [[CrossRef](#)]
63. Bengtsson, J.; Ahnstrom, J.; Weibull, A.C. The effects of organic agriculture on biodiversity and abundance: A meta-analysis. *J. Appl. Ecol.* **2005**, *42*, 261–269. [[CrossRef](#)]
64. Chaudhry, V.; Rehman, A.; Mishra, A.; Chauhan, P.S.; Nautiyal, C.S. Changes in bacterial community structure of agricultural land due to long-term organic and chemical amendments. *Microb. Ecol.* **2012**, *64*, 450–460. [[CrossRef](#)]
65. Gomiero, T. Effects of Agricultural Activities on Biodiversity and Ecosystems: Organic Vs. Conventional Farming. In *Handbook on the Globalisation of Agriculture*; Robinson, G., Carson, D., Eds.; Edward Elgar: Cheltenham, UK, 2015; pp. 77–105.
66. Mijangos, I.; Pérez, R.; Albizu, I.; Garbisu, C. Effects of fertilization and tillage on soil biological parameters. *Enzyme Microb. Technol.* **2006**, *40*, 100–106. [[CrossRef](#)]
67. Epelde, L.; Becerril, J.M.; Kowalchuk, G.A.; Deng, Y.; Zhou, J.; Garbisu, C. Impact of metal pollution and *Thlaspi caerulescens* growth on soil microbial communities. *Appl. Environ. Microbiol.* **2010**, *76*, 7843–7853. [[CrossRef](#)]
68. Pardo, T.; Clemente, R.; Epelde, L.; Garbisu, C.; Bernal, M.P. Evaluation of the phytostabilisation efficiency in a trace elements contaminated soil using soil health indicators. *J. Hazard. Mater.* **2014**, *268*, 68–76. [[CrossRef](#)]
69. Garayurrebaso, O.; Garbisu, C.; Blanco, F.; Lanzén, A.; Martín, I.; Epelde, L.; Becerril, J.M.; Jechalke, S.; Smalla, K.; Grohmann, E.; et al. Long-term effects of aided phytostabilisation on microbial communities of metal-contaminated mine soil. *FEMS Microbiol. Ecol.* **2017**, *93*, fiw252. [[CrossRef](#)] [[PubMed](#)]
70. Garbisu, C.; Alkorta, I.; Epelde, L. Assessment of soil quality using microbial properties and attributes of ecological relevance. *Appl. Soil Ecol.* **2011**, *49*, 1–4. [[CrossRef](#)]
71. de Vries, F.T.; Thebault, E.; Liiri, M.; Birkhofer, K.; Tsiafouli, M.A.; Bjornlund, L.; Jorgensen, H.B.; Brady, M.V.; Christensen, S.; de Ruiter, P.C.; et al. Soil food web properties explain ecosystem services across European land use systems. *Proc. Natl. Acad. Sci. USA* **2013**, *110*, 14296–14301. [[CrossRef](#)] [[PubMed](#)]

72. Burges, A.; Epelde, L.; Garbisu, C. Impact of repeated single-metal and multi-metal pollution events on soil quality. *Chemosphere* **2015**, *120*, 8–15. [[CrossRef](#)] [[PubMed](#)]
73. Balvanera, P.; Pfisterer, A.B.; Buchmann, N.; He, J.S.; Nakashizuka, T.; Raffaelli, D.; Schmid, B. Quantifying the evidence for biodiversity effects on ecosystem functioning and services. *Ecol. Lett.* **2006**, *9*, 1146–1156. [[CrossRef](#)] [[PubMed](#)]
74. Díaz, S.; Fargione, J.; Chapin, F.S., III; Tilman, D. Biodiversity loss threatens human well-being. *PLoS Biol.* **2006**, *4*, e277. [[CrossRef](#)]
75. Harrison, P.A.; Berry, P.M.; Simpson, G.; Haslett, J.R.; Blicharska, M.; Bucur, M.; Dunford, R.W.; Egoh, B.N.; Llorente, M.G.; Geamana, N.; et al. Linkages between biodiversity attributes and ecosystem services: A systematic review. *Ecosyst. Serv.* **2014**, *9*, 191–203. [[CrossRef](#)]
76. Isbell, F.; Crave, D.; Connolly, J.; Loreau, M.; Schmid, B.; Beierkuhnlein, C.; Bezemer, T.M.; Bonin, C.; Bruehlheide, H.; de Luca, E.; et al. Biodiversity increases the resistance of ecosystem productivity to climate extremes. *Nature* **2015**, *526*, 574–577. [[CrossRef](#)]
77. Strickland, M.S.; Lauber, C.; Fierer, N.; Bradford, M.A. Testing the functional significance of microbial community composition. *Ecology* **2009**, *90*, 441–451. [[CrossRef](#)]
78. Tsiafouli, M.A.; Thébaud, E.; Sgardelis, S.P.; de Ruiter, P.C.; Van der Putten, W.H.; Birkhofer, K.; Hemerik, L.; de Vries, F.T.; Bardgett, R.D.; Brady, M.V.; et al. Intensive agriculture reduces soil biodiversity across Europe. *Glob. Change Biol.* **2015**, *21*, 973–985. [[CrossRef](#)]
79. Nielsen, U.N.; Ayres, E.; Wall, D.H.; Bardgett, R.D. Soil biodiversity and carbon cycling: A review and synthesis of studies examining diversity–function relationships. *Eur. J. Soil Sci.* **2011**, *62*, 105–116. [[CrossRef](#)]
80. O'Donnell, A.G.; Seasman, M.; Macrae, A.; Waite, I.; Davies, J.T. Plants and fertilisers as drivers of change in microbial community structure and function in soils. *Plant Soil* **2001**, *232*, 135–145. [[CrossRef](#)]
81. Hartmann, M.; Frey, B.; Mayer, J.; Mäder, P.; Widmer, F. Distinct soil microbial diversity under long-term organic and conventional farming. *ISME J.* **2015**, *9*, 1177–1194. [[CrossRef](#)] [[PubMed](#)]
82. Pershina, E.; Valkonen, J.; Kurki, P.; Ivanova, E.; Chirak, E.; Korvigo, I.; Provorov, N.; Andronov, E. Comparative analysis of prokaryotic communities associated with organic and conventional farming systems. *PLoS ONE* **2015**, *10*, e0145072. [[CrossRef](#)] [[PubMed](#)]
83. Lugato, E.; Bampa, F.; Panagos, P.; Montanarella, L.; Jones, A. Potential carbon sequestration of European arable soils estimated by modelling a comprehensive set of management practices. *Glob. Change Biol.* **2014**, *20*, 3557–3567. [[CrossRef](#)] [[PubMed](#)]
84. Lal, R. Soil health and carbon management. *Food Energy Secur.* **2016**, *5*, 212–222. [[CrossRef](#)]
85. Hijbeek, R.; van Ittersum, M.K.; ten Berge, H.F.; Gort, G.; Spiegel, H.; Whitmore, A.P. Do organic inputs matter—A meta-analysis of additional yield effects for arable crops in Europe. *Plant Soil* **2017**, *411*, 293–303. [[CrossRef](#)]
86. UNFCCC. Join the 4/1000 Initiative. In *Soils for Food Security and Climate*; UNFCCC: City, Country, 2015; Available online: <https://unfccc.int/news/join-the-41000-initiative-soils-for-food-security-and-climate> (accessed on 11 September 2019).
87. Bais, H.P.; Weir, T.L.; Perry, L.G.; Gilroy, S.; Vivanco, J.M. The role of root exudates in rhizosphere interactions with plants and other organisms. *Annu. Rev. Plant Biol.* **2006**, *57*, 233–266. [[CrossRef](#)]
88. Singh, R.P.; Singh, P.; Ibrahim, M.H.; Hashim, R. Land Application of sewage sludge: Physicochemical and microbial response. *Rev. Environ. Contam. Toxicol.* **2011**, *214*, 41–61.
89. Tian, J.H.; Pourcher, A.M.; Bureau, C.; Peu, P. Cellulose accessibility and microbial community in solid state anaerobic digestion of rape straw. *Bioresour. Technol.* **2017**, *223*, 192–201. [[CrossRef](#)]
90. Larkin, R.P. Soil health paradigms and implications for disease management. *Annu. Rev. Phytopathol.* **2015**, *53*, 199–221. [[CrossRef](#)] [[PubMed](#)]
91. Kumar, S.; Patra, A.K.; Singh, D.; Purakayastha, T.J. Long-term chemical fertilization along with farmyard manure enhances resistance and resilience of soil microbial activity against heat stress. *J. Agron. Crop Sci.* **2014**, *200*, 156–162. [[CrossRef](#)]
92. Larney, F.J.; Li, L.L.; Janzen, H.; Angers, D.A.; Olson, B.M. Soil quality attributes, soil resilience, and legacy effects following topsoil removal and one-time amendments. *Can. J. Soil Sci.* **2016**, *96*, 177–190. [[CrossRef](#)]
93. Fließbach, A.; Oberholzer, H.R.; Gunst, L.; Mäder, P. Soil organic matter and biological soil quality indicators after 21 years of organic and conventional farming. *Agric. Ecosyst. Environ.* **2007**, *118*, 273–284. [[CrossRef](#)]



94. Dijkstra, F.A.; Bader, N.E.; Johnson, D.W.; Cheng, W. Does accelerated soil organic matter decomposition in the presence of plants increase plant N availability? *Soil Biol. Biochem.* **2009**, *41*, 1080–1087. [[CrossRef](#)]
95. Marschner, P.; Kandeler, E.; Marschner, B. Structure and function of the soil microbial community in a long-term fertilizer experiment. *Soil Biol. Biochem.* **2003**, *35*, 453–461. [[CrossRef](#)]
96. Antolín, M.C.; Pascual, I.; García, C.; Polo, A.; Sánchez-Díaz, M. Growth, yield and solute content of barley in soils treated with sewage sludge under semiarid Mediterranean conditions. *Field Crop Res.* **2005**, *94*, 224–237. [[CrossRef](#)]
97. Kizilkaya, R.; Bayrakli, B. Effects of N-enriched sewage sludge on soil enzyme activities. *Appl. Soil Ecol.* **2005**, *30*, 192–202. [[CrossRef](#)]
98. Carbonell, G.; Pro, J.; Gómez, N.; Babín, M.M.; Fernández, C.; Alonso, E.; Tarazona, J.V. Sewage sludge applied to agricultural soil: Ecotoxicological effects on representative soil organisms. *Ecotox. Environ. Saf.* **2009**, *72*, 1309–1319. [[CrossRef](#)]
99. Dinesh, R.; Srinivasan, V.; Hamza, S.; Manjusha, A. Short-term incorporation of organic manures and biofertilizers influences biochemical and microbial characteristics of soils under an annual crop. *Bioresour. Technol.* **2010**, *101*, 4697–4702. [[CrossRef](#)]
100. Moeskops, B.; Buchan, D.; Sleutel, S.; Herawaty, L.; Husen, E.; Saraswati, R.; Setyorini, D.; De Neve, S. Soil microbial communities and activities under intensive organic and conventional vegetable farming in West Java, Indonesia. *Appl. Soil Ecol.* **2010**, *45*, 112–120. [[CrossRef](#)]
101. Roig, N.; Sierra, J.; Martí, E.; Nadal, M.; Schuhmacher, M.; Domingo, J.L. Long term amendment of Spanish soils with sewage sludge: Effects on soil functioning. *Agric. Ecosyst. Environ.* **2012**, *158*, 41–48. [[CrossRef](#)]
102. Xue, D.; Huang, X. The impact of sewage sludge compost on tree peony growth and soil microbiological, and biochemical properties. *Chemosphere* **2013**, *93*, 583–589. [[CrossRef](#)] [[PubMed](#)]
103. Mattana, S.; Petrovicová, B.; Landi, L.; Gelsomino, A.; Cortés, P.; Ortiz, O.; Renella, G. Sewage sludge processing determines its impact on soil microbial community structure and function. *Appl. Soil Ecol.* **2014**, *75*, 150–161. [[CrossRef](#)]
104. Insam, H.; Gómez-Brandón, M.; Ascher, J. Manure-based biogas fermentation residues—Friend or foe of soil fertility? *Soil Biol. Biochem.* **2015**, *84*, 1–14. [[CrossRef](#)]
105. Siebielec, G.; Siebielec, S.; Lipski, D. Long-term impact of sewage sludge, digestate and mineral fertilizers on plant yield and soil biological activity. *J. Clean. Prod.* **2018**, *187*, 372–379. [[CrossRef](#)]
106. Ji, L.; Wu, Z.; You, Z.; Yi, X.; Ni, K.; Guo, S.; Ruan, J. Effects of organic substitution for synthetic N fertilizer on soil bacterial diversity and community composition: A 10-year field trial in a tea plantation. *Agric. Ecosyst. Environ.* **2018**, *268*, 124–132. [[CrossRef](#)]
107. Ge, Y.; Zhang, J.B.; Zhang, L.M.; Yang, M.; He, J.Z. Long-term fertilization regimes affect bacterial community structure and diversity of an agricultural soil in northern China. *J. Soils Sediments* **2008**, *8*, 43–50. [[CrossRef](#)]
108. Liao, J.; Liang, Y.; Huang, D. Organic farming improves soil microbial abundance and diversity under greenhouse condition: A case study in Shanghai (eastern China). *Sustainability* **2018**, *10*, 3825. [[CrossRef](#)]
109. Aparna, K.; Pasha, M.A.; Rao, D.L.N.; Krishnaraj, P.U. Organic amendments as ecosystem engineers: Microbial, biochemical and genomic evidence of soil health improvement in a tropical arid zone field site. *Ecol. Eng.* **2014**, *71*, 268–277. [[CrossRef](#)]
110. Shi, S.; Tian, L.; Nasir, F.; Bahadur, A.; Batool, A.; Luo, S.; Yang, F.; Wang, Z.; Tian, C. Response of microbial communities and enzyme activities to amendments in saline-alkaline soils. *Appl. Soil Ecol.* **2019**, *135*, 16–24. [[CrossRef](#)]
111. Bonanomi, G.; De Filippis, F.; Cesarano, G.; La Storia, A.; Ercolini, D.; Scala, F. Organic farming induces changes in soil microbiota that affect agro-ecosystem functions. *Soil Biol. Biochem.* **2016**, *103*, 327–336. [[CrossRef](#)]
112. Daquiado, A.R.; Kuppusamy, S.; Kim, S.Y.; Kim, J.H.; Yoon, Y.E.; Kim, P.J.; Oh, S.H.; Kwak, Y.S.; Lee, Y.B. Pyrosequencing analysis of bacterial community diversity in long-term fertilized paddy field soil. *Appl. Soil Ecol.* **2016**, *108*, 84–91. [[CrossRef](#)]
113. Chen, Z.M.; Wang, H.Y.; Liu, X.W.; Zhao, X.L.; Lu, D.J.; Zhou, J.M.; Li, C.Z. Changes in soil microbial community and organic carbon fractions under short-term straw return in a rice-wheat cropping system. *Soil Tillage Res.* **2017**, *165*, 121–127. [[CrossRef](#)]

114. Wang, Y.; Li, C.Y.; Tu, C.; Hoyt, G.D.; DeForest, J.L.; Hu, S.J. Long-term no-tillage and organic input management enhanced the diversity and stability of soil microbial community. *Sci. Total Environ.* **2017**, *609*, 341–347. [[CrossRef](#)] [[PubMed](#)]
115. Zhong, W.; Gu, T.; Wang, W.; Zhang, B.; Lin, X.; Huang, Q.; Shen, W. The effects of mineral fertilizer and organic manure on soil microbial community and diversity. *Plant Soil* **2009**, *326*, 511–522. [[CrossRef](#)]
116. Mossa, A.W.; Dickinson, M.J.; West, H.M.; Young, S.D.; Crout, N.M. The response of soil microbial diversity and abundance to long-term application of biosolids. *Environ. Pollut.* **2017**, *224*, 16–25. [[CrossRef](#)] [[PubMed](#)]
117. Orr, C.H.; Stewart, C.J.; Leifert, C.; Cooper, J.M.; Cummings, S.P. Effect of crop management and sample year on abundance of soil bacterial communities in organic and conventional cropping systems. *J. Appl. Microbiol.* **2015**, *119*, 208–214. [[CrossRef](#)]
118. Sapp, M.; Harrison, M.; Hany, U.; Charlton, A.; Thwaites, R. Comparing the effect of digestate and chemical fertiliser on soil bacteria. *Appl. Soil Ecol.* **2015**, *86*, 1–9. [[CrossRef](#)]
119. Cesarano, G.; De Filippis, F.; La Stora, A.; Scala, F.; Bonanomi, G. Organic amendment type and application frequency affect crop yields, soil fertility and microbiome composition. *Appl. Soil Ecol.* **2017**, *120*, 254–264. [[CrossRef](#)]
120. Li, R.; Khafipour, E.; Krause, D.O.; Entz, M.H.; de Kievit, T.R.; Fernando, W.D. Pyrosequencing reveals the influence of organic and conventional farming systems on bacterial communities. *PLoS ONE* **2012**, *7*, e51897. [[CrossRef](#)] [[PubMed](#)]
121. Lauber, C.L.; Hamady, M.; Knight, R.; Fierer, N. Pyrosequencing-based assessment of soil pH as a predictor of soil bacterial community structure at the continental scale. *Appl. Environ. Microbiol.* **2009**, *75*, 5111–5120. [[CrossRef](#)] [[PubMed](#)]
122. Rousk, J.; Bååth, E.; Brookes, P.C.; Lauber, C.L.; Lozupone, C.; Caporaso, J.G.; Knight, R.; Fierer, N. Soil bacterial and fungal communities across a pH gradient in an arable soil. *ISME J.* **2010**, *4*, 1340–1351. [[CrossRef](#)] [[PubMed](#)]
123. Whalen, J.K.; Chang, C.; Clayton, G.W.; Carefoot, J.P. Cattle manure amendments can increase the pH of acid soils. *Soil Sci. Soc. Am. J.* **2000**, *64*, 962–966. [[CrossRef](#)]
124. Mijangos, I.; Albizu, I.; Epelde, L.; Amezcua, I.; Mendarte, S.; Garbisu, C. Effects of liming on soil properties and plant performance of temperate mountainous grasslands. *J. Environ. Manag.* **2010**, *91*, 2066–2074. [[CrossRef](#)] [[PubMed](#)]
125. Quilty, J.R.; Cattle, S.R. Use and understanding of organic amendments in Australian agriculture: A review. *Soil Res.* **2011**, *49*, 1–26. [[CrossRef](#)]
126. Manzoni, S.; Jackson, R.B.; Trofymow, J.A.; Porporato, A. The global stoichiometry of litter nitrogen mineralization. *Science* **2008**, *321*, 684–686. [[CrossRef](#)] [[PubMed](#)]
127. Clemente, R.; Bernal, M.P. Fractionation of heavy metals and distribution of organic carbon in two contaminated soils amended with humic substances. *Chemosphere* **2006**, *64*, 1264–1273. [[CrossRef](#)]
128. Soler-Rovira, P.; Madejon, E.; Madejón, P.; Plaza, C. In situ remediation of metal-contaminated soils with organic amendments: Role of humic acids in copper bioavailability. *Chemosphere* **2010**, *79*, 844–849. [[CrossRef](#)]
129. Mohapatra, D.P.; Cledón, M.; Brar, S.K.; Surampalli, R.Y. Application of wastewater and biosolids in soil: Occurrence and fate of emerging contaminants. *Water Air Soil Pollut.* **2016**, *227*, 1–14. [[CrossRef](#)]
130. Bastida, F.; Jehmlich, N.; Lima, K.; Morris, B.E.L.; Richnow, H.H.; Hernández, T.; von Bergen, M.; García, C. The ecological and physiological responses of the microbial community from a semiarid soil to hydrocarbon contamination and its bioremediation using compost amendment. *J. Proteom.* **2016**, *135*, 162–169. [[CrossRef](#)] [[PubMed](#)]
131. Leroy, B.L.M.; Herath, H.M.S.K.; Sleutel, S.; De Neve, S.; Gabriels, D.; Reheul, D.; Moens, M. The quality of exogenous organic matter: Short-term effects on soil physical properties and soil organic matter fractions. *Soil Use Manag.* **2008**, *24*, 139–147. [[CrossRef](#)]
132. Liu, Z.; Chen, X.; Jing, Y.; Li, Q.; Zhang, J.; Huang, Q. Effects of biochar amendment on rapeseed and sweet potato yields and water stable aggregate in upland red soil. *Catena* **2014**, *123*, 45–51. [[CrossRef](#)]
133. Young, I.M.; Ritz, K. Tillage, habitat space and function of soil microbes. *Soil Tillage Res.* **2000**, *53*, 201–203. [[CrossRef](#)]
134. Rillig, M.C.; Mummey, D.L. Mycorrhizas and soil structure. *New Phytol.* **2006**, *171*, 41–53. [[CrossRef](#)] [[PubMed](#)]

135. Six, J.; Paustian, K. Aggregate-associated soil organic matter as an ecosystem property and a measurement tool. *Soil Biol. Biochem.* **2014**, *68*, A4–A9. [[CrossRef](#)]
136. Zebarth, B.J.; Neilsen, G.H.; Hogue, E.; Neilsen, D. Influence of organic waste amendments on selected soil physical and chemical properties. *Can. J. Soil Sci.* **1999**, *79*, 501–504. [[CrossRef](#)]
137. Zhao, Y.; Wang, P.; Li, J.; Chen, Y.; Ying, X.; Liu, S. The effects of two organic manures on soil properties and crop yields on a temperate calcareous soil under a wheat-maize cropping system. *Eur. J. Agron.* **2009**, *31*, 36–42. [[CrossRef](#)]
138. Park, J.H.; Lamb, D.; Paneerselvam, P.; Choppala, G.; Bolan, N.; Chung, J.W. Role of organic amendments on enhanced bioremediation of heavy metal(loid) contaminated soils. *J. Hazard. Mater.* **2011**, *185*, 549–574. [[CrossRef](#)]
139. Petrie, B.; Barden, R.; Kasprzyk-Hordern, B. A review on emerging contaminants in wastewaters and the environment: Current knowledge, understudied areas and recommendations for future monitoring. *Water Res.* **2014**, *72*, 3–27. [[CrossRef](#)]
140. Alvarenga, P.; Mourinha, C.; Farto, M.; Santos, T.; Palma, P.; Sengo, J.; Morais, M.C.; Cunha-Queda, C. Sewage sludge, compost and other representative organic wastes as agricultural soil amendments: Benefits versus limiting factors. *Waste Manag.* **2015**, *40*, 44–52. [[CrossRef](#)] [[PubMed](#)]
141. Kumpiene, J.; Guerri, G.; Landi, L.; Pietramellara, G.; Nannipieri, P.; Renella, G. Microbial biomass, respiration and enzyme activities after in situ aided phytostabilization of a Pb- and Cu-contaminated soil. *Ecotoxicol. Environ. Saf.* **2009**, *72*, 115–119. [[CrossRef](#)] [[PubMed](#)]
142. Zhou, X.; Qiao, M.; Wang, F.H.; Zhu, Y.G. Use of commercial organic fertilizer increases the abundance of antibiotic resistance genes and antibiotics in soil. *Environ. Sci. Pollut. Res.* **2017**, *24*, 701–710. [[CrossRef](#)] [[PubMed](#)]
143. Mann, R.M.; Vijver, M.G.; Peijnenburg, W.J.G.M. Metals and metalloids in terrestrial systems: Bioaccumulation, biomagnification and subsequent adverse effects. In *Ecological Impacts of Toxic Chemicals*; Sánchez-Bayo, F., van den Brink, P.J., Mann, R., Eds.; Bentham Science Publishers: Dubai, United Arab Emirates, 2011; pp. 43–62.
144. McBride, M.B. Toxic metal accumulation from agricultural use of sludge: Are USEPA regulations prospective? *J. Environ. Qual.* **1995**, *24*, 5–18. [[CrossRef](#)]
145. Parat, C.; Denaix, L.; Lévêque, J.; Chaussod, R.; Andreux, F. The organic carbon derived from sewage sludge as a key parameter determining the fate of trace metals. *Chemosphere* **2007**, *69*, 636–643. [[CrossRef](#)]
146. Fließbach, A.; Martens, R.; Reber, H.H. Soil microbial biomass and microbial activity in soils treated with heavy metal contaminated sewage sludge. *Soil Biol. Biochem.* **1994**, *26*, 1201–1205. [[CrossRef](#)]
147. Fernández, J.M.; Plaza, C.; García-Gil, J.C.; Polo, A. Biochemical properties and barley yield in a semiarid Mediterranean soil amended with two kinds of sewage sludge. *Appl. Soil Ecol.* **2009**, *42*, 18–24. [[CrossRef](#)]
148. Semblante, G.U.; Hai, F.I.; Huang, X.; Ball, A.S.; Price, W.E.; Nghiem, L.D. Trace organic contaminants in biosolids: Impact of conventional wastewater and sludge processing technologies and emerging alternatives. *J. Hazard. Mater.* **2015**, *300*, 1–17. [[CrossRef](#)]
149. Fijalkowski, K.; Rorat, A.; Grobelak, A.; Kacprzak, M.J. The presence of contaminations in sewage sludge—The current situation. *J. Environ. Manag.* **2017**, *203*, 1126–1136. [[CrossRef](#)]
150. Clarke, B.O.; Smith, S.R. Review of ‘emerging’ organic contaminants in biosolids and assessment of international research priorities for the agricultural use of biosolids. *Environ. Int.* **2011**, *37*, 226–247. [[CrossRef](#)]
151. Chen, Q.; An, X.; Li, H.; Su, J.; Ma, Y.; Zhu, Y.G. Long-term field application of sewage sludge increases the abundance of antibiotic resistance genes in soil. *Environ. Int.* **2016**, *92–93*, 1–10. [[CrossRef](#)] [[PubMed](#)]
152. García, C.; Hernández, T.; Coll, M.D.; Ondoño, S. Organic amendments for soil restoration in arid and semiarid areas: A review. *AIMS Environ. Sci.* **2017**, *4*, 640–676. [[CrossRef](#)]
153. Fang, H.; Wang, H.F.; Cai, L.; Yu, Y.L. Prevalence of antibiotic resistance genes and bacterial pathogens in long-term manured greenhouse soils as revealed by metagenomic survey. *Environ. Sci. Technol.* **2015**, *49*, 1095–1104. [[CrossRef](#)] [[PubMed](#)]
154. Ye, L.; Zhang, T. Pathogenic bacteria in sewage treatment plants as revealed by 454 pyrosequencing. *Environ. Sci. Technol.* **2011**, *45*, 7173–7179. [[CrossRef](#)] [[PubMed](#)]
155. Bibby, K.; Peccia, J. Identification of viral pathogen diversity in sewage sludge by metagenome analysis. *Environ. Sci. Technol.* **2013**, *47*, 1945–1951. [[CrossRef](#)]

156. Aronsson, H.; Torstensson, G.; Bergstrom, L. Leaching and crop uptake of N, P and K from organic and conventional cropping systems on a clay soil. *Soil Use Manag.* **2007**, *23*, 71–81. [[CrossRef](#)]
157. Stenberg, M.; Ulen, B.; Soderstrom, M.; Roland, B.; Delin, K.; Helender, C.A. Tile drain losses of nitrogen and phosphorus from fields under integrated and organic crop rotations. A four-year study on a clay soil in southwest Sweden. *Sci. Total Environ.* **2012**, *434*, 79–89. [[CrossRef](#)]
158. Hodge, A.; Robinson, D.; Fitter, A.H. Are microorganisms more effective than plants at competing for nitrogen? *Trends Plant Sci.* **2000**, *5*, 304–308. [[CrossRef](#)]
159. Aslam, A.A.; Sattar, M.A.; Nazmul Islam, M.; Inubushi, K. Integrated effects of organic, inorganic and biological amendments on methane emission, soil quality and rice productivity in irrigated paddy ecosystem of Bangladesh: Field study of two consecutive rice growing seasons. *Plant Soil* **2014**, *378*, 239–252.
160. Bass, A.M.; Bird, M.I.; Kay, G.; Muirhead, B. Soil properties, greenhouse gas emissions and crop yield under compost, biochar and co-composted biochar in two tropical agronomic systems. *Sci. Total Environ.* **2016**, *550*, 459–470. [[CrossRef](#)]
161. Bonanomi, G.; D’Ascoli, R.; Scotti, R.; Gaglione, S.A.; González Cáceres, M.; Sultana, S.; Scelza, R.; Rao, M.A.; Zoina, A. Soil quality recovery and crop yield enhancement by combined application of compost and wood to vegetables grown under plastic tunnels. *Agric. Ecosyst. Environ.* **2014**, *192*, 1–7. [[CrossRef](#)]
162. Barnes, D.K.; Galgani, F.; Thompson, R.C.; Barlaz, M. Accumulation and fragmentation of plastic debris in global environments. *Philos. Trans. R. Soc. B* **2009**, *364*, 1985–1998. [[CrossRef](#)]
163. Horton, A.A.; Walton, A.; Spurgeon, D.J.; Lahive, E.; Svendsen, C. Microplastics in freshwater and terrestrial environments: Evaluating the current understanding to identify the knowledge gaps and future research priorities. *Sci. Total Environ.* **2017**, *586*, 127–141. [[CrossRef](#)]
164. Rochman, C.M.; Manzano, C.; Hentschel, B.T.; Simonich, S.L.; Hoh, E. Polystyrene plastic: A source and sink for polycyclic aromatic hydrocarbons in the marine environment. *Environ. Sci. Technol.* **2013**, *47*, 13976–13984. [[CrossRef](#)]
165. Wang, J.; Peng, J.; Tan, Z.; Gao, Y.; Zhan, Z.; Chen, Q.; Cai, L. Microplastics in the surface sediments from the Beijiang River littoral zone: Composition, abundance, surface textures and interaction with heavy metals. *Chemosphere* **2016**, *171*, 248–258. [[CrossRef](#)]
166. Sun, J.; Dai, X.; Wang, Q.; van Loosdrecht, M.C.; Ni, B.J. Microplastics in wastewater treatment plants: Detection, occurrence and removal. *Water Res.* **2019**, *152*, 21–37. [[CrossRef](#)]
167. Li, X.; Chen, L.; Mei, Q.; Dong, B.; Dai, X.; Ding, G.; Zeng, E.Y. Microplastics in sewage sludge from the wastewater treatment plants in China. *Water Res.* **2018**, *142*, 75–85. [[CrossRef](#)]
168. Corradini, F.; Meza, P.; Eguiluz, R.; Casado, F.; Huerta-Lwanga, E.; Geissen, V. Evidence of microplastic accumulation in agricultural soils from sewage sludge disposal. *Sci. Total Environ.* **2019**, *671*, 411–420. [[CrossRef](#)]
169. Ng, E.L.; Lwanga, E.H.; Eldridge, S.M.; Johnston, P.; Hu, H.W.; Geissen, V.; Chen, D. An overview of microplastic and nanoplastic pollution in agroecosystems. *Sci. Total Environ.* **2018**, *627*, 1377–1388. [[CrossRef](#)]
170. Pruden, A.; Pei, R.T.; Storteboom, H.; Carlson, K.H. Antibiotic resistance genes as emerging contaminants: Studies in northern Colorado. *Environ. Sci. Technol.* **2006**, *40*, 7445–7450. [[CrossRef](#)]
171. Nahrgang, S.; Nolte, E.; Rechel, B. Antimicrobial resistance. In *The Role of Public Health Organizations in Addressing Public Health Problems in Europe: The Case of Obesity, Alcohol and Antimicrobial Resistance*; Rechel, B., Maresso, A., Sagan, A., Hernández-Quevedo, C., Richardson, E., Jakubowski, E., McKee, M., Nolte, E., Eds.; European Observatory on Health Systems and Policies: Copenhagen, Denmark, 2018.
172. World Health Organization (WHO). *Global Action Plan on Antimicrobial Resistance*; World Health Organization (WHO): Geneva, Switzerland, 2015.
173. United Nations (UN). *Political Declaration of the High-Level Meeting of the General Assembly on Antimicrobial Resistance*; United Nations (UN): New York, NY, USA, 2016.
174. European Commission. *Action Plan against the Rising Threats from Antimicrobial Resistance*; European Commission: Brussels, Belgium, 2011; COM (2011) 748.
175. European Commission. *A European One Health Action Plan against Antimicrobial Resistance (AMR)*; European Commission: Brussels, Belgium, 2017.
176. O’Neill, J. *Tackling Drug-Resistant Infections Globally: Final Report and Recommendations*; The Review on Antimicrobial Resistance; Wellcome Trust: London, UK, 2016.

177. Kumar, K.; Gupta, S.C.; Chander, Y.; Singh, A.K. Antibiotic use in agriculture and their impact on the terrestrial environment. *Adv. Agron.* **2005**, *87*, 1–54.
178. Michael, I.; Rizzo, L.; McArdell, C.S.; Manaia, C.M.; Merlin, C.; Schwartz, T.; Dagot, C.; Fatta-Kassinos, D. Urban wastewater treatment plants as hotspots for the release of antibiotics in the environment: A review. *Water Res.* **2013**, *47*, 957–995. [[CrossRef](#)]
179. Rizzo, L.; Manaia, C.; Merlin, C.; Schwartz, T.; Dagot, C.; Ploy, M.C.; Michael, I.; Fatta-Kassinos, D. Urban wastewater treatment plants as hotspots for antibiotic resistant bacteria and genes spread into the environment: A review. *Sci. Total Environ.* **2013**, *447*, 345–360. [[CrossRef](#)]
180. Zhu, Y.G.; Johnson, T.A.; Su, J.Q.; Qiao, M.; Guo, G.X.; Stedtfeld, R.D.; Tiedje, J.M. Diverse and abundant antibiotic resistance genes in Chinese swine farms. *Proc. Natl. Acad. Sci. USA* **2013**, *110*, 3435–3440. [[CrossRef](#)]
181. Marti, R.; Scott, A.; Tien, Y.C.; Murray, R.; Sabourin, L.; Zhang, Y.; Topp, E. Impact of manure fertilization on the abundance of antibiotic resistant bacteria and frequency of detection of antibiotic resistance genes in soil and on vegetables at harvest. *Appl. Environ. Microbiol.* **2013**, *79*, 5701–5709. [[CrossRef](#)]
182. Mao, D.; Yu, S.; Rysz, M.; Luo, Y.; Yang, F.; Li, F.; Hou, J.; Mu, Q.; Alvarez, P.J. Prevalence and proliferation of antibiotic resistance genes in two municipal wastewater treatment plants. *Water Res.* **2015**, *85*, 458–466. [[CrossRef](#)]
183. Wang, F.H.; Qiao, M.; Chen, Z.; Su, J.Q.; Zhu, Y.G. Antibiotic resistance genes in manure-amended soil and vegetables at harvest. *J. Hazard. Mater.* **2015**, *299*, 215–221. [[CrossRef](#)]
184. Peng, S.; Feng, Y.; Wang, Y.; Guo, X.; Chu, H.; Lin, X. Prevalence of antibiotic resistance genes in soils after continually applied with different manure for 30 years. *J. Hazard. Mater.* **2017**, *340*, 16–25. [[CrossRef](#)]
185. Urra, J.; Alkorta, I.; Mijangos, I.; Epelde, L.; Garbisu, C. Application of sewage sludge to agricultural soil increases the abundance of antibiotic resistance genes without altering the composition of prokaryotic communities. *Sci. Total Environ.* **2019**, *647*, 1410–1420. [[CrossRef](#)]
186. Udikoviv-Kolic, N.; Wichmann, F.; Broderick, N.A.; Handelsman, J. Bloom of resident antibiotic-resistant bacteria in soil following manure fertilization. *Proc. Natl. Acad. Sci. USA* **2014**, *111*, 15202–15207. [[CrossRef](#)]
187. Xie, W.Y.; Shen, Q.; Zhao, F.J. Antibiotics and antibiotic resistance from animal manures to soil: A review. *Eur. J. Soil Sci.* **2018**, *69*, 181–195. [[CrossRef](#)]
188. Norman, A.; Hansen, L.H.; Sorensen, S.J. Conjugative plasmids: Vessels of the communal gene pool. *Philos. Trans. R. Soc. B Biol. Sci.* **2009**, *364*, 2275–2289. [[CrossRef](#)]
189. Vos, M.; Hesselman, M.C.; te Beek, T.A.; van Passel, M.W.J.; Eyre-Walker, A. Rates of lateral gene transfer in prokaryotes: High but why? *Trends Microbiol.* **2015**, *23*, 598–605. [[CrossRef](#)]
190. Frost, L.S.; Leplae, R.; Summers, A.O.; Toussaint, A. Mobile genetic elements: The agents of open source evolution. *Nat. Rev. Microbiol.* **2005**, *3*, 722–732. [[CrossRef](#)]
191. Garbisu, C.; Garaiyurrebaso, O.; Lanzén, A.; Álvarez-Rodríguez, I.; Arana, L.; Blanco, F.; Smalla, K.; Grohmann, E.; Alkorta, I. Mobile genetic elements and antibiotic resistance in mine soil amended with organic wastes. *Sci. Total Environ.* **2018**, *621*, 725–733. [[CrossRef](#)]
192. Gillings, M.R. Integrons: Past, present and future. *Microbiol. Mol. Biol. Rev.* **2014**, *78*, 257–277. [[CrossRef](#)]
193. Burch, T.R.; Sadowsky, M.J.; LaPara, T.M. Fate of antibiotic resistance genes and class 1 integrons in soil microcosms following the application of treated residual municipal wastewater solids. *Environ. Sci. Technol.* **2014**, *48*, 5620–5627. [[CrossRef](#)]
194. Sandberg, K.D.; LaPara, T.M. The fate of antibiotic resistance genes and class 1 integrons following the application of swine and dairy manure to soils. *FEMS Microbiol. Ecol.* **2016**, *92*, fiw001. [[CrossRef](#)]
195. Van Elsland, J.D.; Bailey, M.J. The ecology of transfer of mobile genetic elements. *FEMS Microbiol. Ecol.* **2002**, *42*, 187–197. [[CrossRef](#)]
196. Björklöf, K.; Suoniemi, A.; Hahtela, K.; Romantschuk, M. High frequency of conjugation versus plasmid segregation of RP1 in epiphytic *Pseudomonas syringae* populations. *Microbiology* **1995**, *141*, 2719–2727. [[CrossRef](#)]
197. Zhu, B.; Chen, Q.; Chen, S.; Zhu, Y.G. Does organically produced lettuce harbor higher abundance of antibiotic resistance genes than conventionally produced? *Environ. Int.* **2017**, *98*, 152–159. [[CrossRef](#)]
198. Dolliver, H.; Kumar, K.; Gupta, S. Sulfamethazine uptake by plants from manure-amended soil. *J. Environ. Qual.* **2007**, *36*, 1224–1230. [[CrossRef](#)]
199. Baker-Austin, C.; Wright, M.S.; Stepanauskas, R.; McArthur, J.V. Co-selection of antibiotic and metal resistance. *Trends Microbiol.* **2006**, *14*, 176–182. [[CrossRef](#)]

200. Chapman, J.S. Disinfectant resistance mechanisms, cross-resistance and co-resistance. *Int. Biodeterior. Biodegrad.* **2003**, *51*, 271–276. [[CrossRef](#)]
201. Bondarczuk, K.; Markowicz, A.; Piotrowska-Seget, Z. The urgent need for risk assessment on the antibiotic resistance spread via sewage sludge land application. *Environ. Int.* **2016**, *87*, 49–55. [[CrossRef](#)]
202. Marin, J.M.; Maluta, R.P.; Borges, C.A.; Beraldo, L.G.; Maesta, S.A.; Lemos, M.V.F.; Ruiz, U.S.; Ávila, F.A.; Rigobelo, E.C. Fate of non O157 Shigatoxigenic *Escherichia coli* in ovine manure composting. *Arq. Bras. Med. Vet. Zootec.* **2014**, *66*, 1771–1778. [[CrossRef](#)]
203. Masciandaro, G.; Macci, C.; Peruzzi, E.; Ceccanti, B.; Doni, S. Organic matter-microorganism-plant in soil bioremediation: A synergic approach. *Rev. Environ. Sci. Biotechnol.* **2013**, *12*, 399–419. [[CrossRef](#)]
204. Gou, M.; Hu, H.W.; Zhang, Y.J.; Wang, J.T.; Hayden, H.; Tang, Y.Q.; He, J.Z. Aerobic composting reduces antibiotic resistance genes in cattle manure and the resistome dissemination in agricultural soils. *Sci. Total Environ.* **2018**, *612*, 1300–1310. [[CrossRef](#)]
205. Qian, X.; Gu, J.; Sun, W.; Wang, X.J. Diversity, abundance, and persistence of antibiotic resistance genes in various types of animal manure following industrial composting. *J. Hazard. Mater.* **2017**, *344*, 716–722. [[CrossRef](#)]
206. Dolliver, H.; Gupta, S.; Noll, S. Antibiotic degradation during manure composting. *J. Environ. Qual.* **2008**, *37*, 1245–1253. [[CrossRef](#)]
207. Selvam, A.; Xu, D.; Zhao, Z.; Wong, J.W. Fate of tetracycline, sulphonamide and fluoroquinolone resistance genes and the changes in bacterial diversity during composting of swine manure. *Bioresour. Technol.* **2012**, *126*, 383–390. [[CrossRef](#)]
208. Wang, L.; Oda, Y.; Grewal, S.; Morrison, M.; Michel, F.C., Jr.; Wu, Z. Persistence of resistance to erythromycin and tetracycline in swine manure during simulated composting and lagoon storage. *Microb. Ecol.* **2012**, *63*, 32–40. [[CrossRef](#)] [[PubMed](#)]
209. Chessa, L.; Jechalke, S.; Ding, G.C.; Pusino, A.; Mangia, N.P.; Smalla, K. The presence of tetracycline in cow manure changes the impact of repeated manure application on soil bacterial communities. *Biol. Fertil. Soils* **2016**, *52*, 1121–1134. [[CrossRef](#)]
210. Ghattas, A.K.; Fischer, F.; Wick, A.; Ternes, T.A. Anaerobic biodegradation of (emerging) organic contaminants in the aquatic environment. *Water Res.* **2017**, *116*, 268–295. [[CrossRef](#)] [[PubMed](#)]
211. Arikian, O.A.; Sikora, L.J.; Mulbry, W.; Khan, S.U.; Rice, C.; Foster, G.D. The fate and effect of oxytetracycline during the anaerobic digestion of manure from therapeutically treated calves. *Process Biochem.* **2006**, *41*, 1637–1643. [[CrossRef](#)]
212. Mohring, S.A.I.; Strzysch, I.; Fernandes, M.R.; Kiffmeyer, T.K.; Tuerk, J.; Hamscher, G. Degradation and elimination of various sulfonamides during anaerobic fermentation: A promising step on the way to sustainable pharmacy? *Environ. Sci. Technol.* **2009**, *43*, 2569–2574. [[CrossRef](#)]
213. Munir, M.; Wong, K.; Xagorarakis, I. Release of antibiotic resistant bacteria and genes in the effluent and biosolids of five wastewater utilities in Michigan. *Water Res.* **2011**, *45*, 681–693. [[CrossRef](#)]
214. Zheng, W.; Wen, X.; Zhang, B.; Qiu, Y. Selective effect and elimination of antibiotics in membrane bioreactor of urban wastewater treatment plant. *Sci. Total Environ.* **2019**, *646*, 1293–1303. [[CrossRef](#)]
215. Ma, Y.; Wilson, C.A.; Novak, J.T.; Riffat, R.; Aynur, S.; Murthy, S.; Pruden, A. Effect of various sludge digestion conditions on sulfonamide, macrolide, and tetracycline resistance genes and class I integrons. *Environ. Sci. Technol.* **2011**, *45*, 7855–7861. [[CrossRef](#)]
216. Ghosh, S.; Ramsden, S.J.; LaPara, T.M. The role of anaerobic digestion in controlling the release of tetracycline resistance genes and class I integrons from municipal wastewater treatment plants. *Appl. Microbiol. Biotechnol.* **2009**, *84*, 791–796. [[CrossRef](#)]
217. Miller, J.H.; Novak, J.T.; Knoche, W.R.; Pruden, A. Survival of antibiotic resistant bacteria and horizontal gene transfer control antibiotic resistance gene content in anaerobic digesters. *Front. Microbiol.* **2016**, *7*, 263. [[CrossRef](#)] [[PubMed](#)]
218. Zhang, T.; Yang, Y.; Pruden, A. Effect of temperature on removal of antibiotic resistance genes by anaerobic digestion of activated sludge revealed by metagenomic approach. *Appl. Microbiol. Biotechnol.* **2015**, *99*, 7771–7779. [[CrossRef](#)] [[PubMed](#)]
219. Pei, J.; Yao, H.; Wang, H.; Ren, J.; Yu, X. Comparison of ozone and thermal hydrolysis combined with anaerobic digestion for municipal and pharmaceutical waste sludge with tetracycline resistance genes. *Water Res.* **2016**, *99*, 122–128. [[CrossRef](#)] [[PubMed](#)]

220. Masse, D.I.; Cata Saady, N.M.; Gilbert, Y. Potential of Biological Processes to Eliminate Antibiotics in Livestock Manure: An Overview. *Animals* **2014**, *4*, 146–163. [[CrossRef](#)] [[PubMed](#)]
221. Chen, J.; Michel, F.C., Jr.; Sreevatsan, S.; Morrison, M.; Yu, Z. Occurrence and persistence of erythromycin resistance genes (*erm*) and tetracycline resistance genes (*tet*) in waste treatment systems on swine farms. *Microb. Ecol.* **2010**, *60*, 479–486. [[CrossRef](#)] [[PubMed](#)]
222. Peng, S.; Wang, Y.; Zhou, B.; Lin, X. Long-term application of fresh and composted manure increase tetracycline resistance in the arable soil of eastern China. *Sci. Tot. Environ.* **2015**, *506*, 279–286. [[CrossRef](#)] [[PubMed](#)]
223. Salomone, R.; Saija, G.; Mondello, G.; Giannetto, A.; Fasulo, S.; Savastano, D. Environmental impact of food waste bioconversion by insects: Application of Life Cycle Assessment to process using *Hermetia illucens*. *J. Clean. Prod.* **2017**, *140*, 890–905. [[CrossRef](#)]
224. Gold, M.; Tomberlin, J.K.; Diener, S.; Zurbrügg, C.; Mathys, A. Decomposition of biowaste macronutrients, microbes, and chemicals in black soldier fly larval treatment: A review. *Waste Manag.* **2018**, *82*, 302–318. [[CrossRef](#)]
225. Mertenat, A.; Diener, S.; Zurbrügg, C. Black soldier fly biowaste treatment—Assessment of global warming potential. *Waste Manag.* **2019**, *84*, 173–181. [[CrossRef](#)]
226. De Smet, J.; Wynants, E.; Cos, P.; Van Campenhout, L. Microbial community dynamics during rearing of black soldier fly larvae (*Hermetia illucens*) and its impact on exploitation potential. *Appl. Environ. Microbiol.* **2018**, *84*, e02722-17. [[CrossRef](#)]
227. Zurbrügg, C.; Dortmans, B.; Fadhila, A.; Verstappen, B.; Diener, S. From pilot to full scale operation of a waste-to-protein treatment facility. *Detritus* **2018**, *1*, 18–22.
228. Makkar, H.P.S.S.; Tran, G.; Heuzé, V.; Ankers, P. State-of-the-art on use of insects as animal feed. *Anim. Feed Sci. Technol.* **2014**, *197*, 1–33. [[CrossRef](#)]
229. Marraffini, L.A.; Sontheimer, E.J. CRISPR interference: RNA-directed adaptive immunity in bacteria and archaea. *Nat. Rev. Genet.* **2010**, *11*, 181–190. [[CrossRef](#)] [[PubMed](#)]
230. Bikard, D.; Hatoum-Aslan, A.; Mucida, D.; Marraffini, L.A. CRISPR interference can prevent natural transformation and virulence acquisition during in vivo bacterial infection. *Cell Host Microbe* **2012**, *12*, 177–186. [[CrossRef](#)] [[PubMed](#)]
231. Yosef, I.; Manor, M.; Kiro, R.; Qimron, U. Temperate and lytic bacteriophages programmed to sensitize and kill antibiotic-resistant bacteria. *Proc. Natl. Acad. Sci. USA* **2015**, *112*, 7267–7272. [[CrossRef](#)] [[PubMed](#)]
232. Pursey, E.; Sünderhauf, D.; Gaze, W.H.; Westra, E.R.; van Houte, S. CRISPR-Cas antimicrobials: Challenges and future prospects. *PLoS Pathog.* **2018**, *14*, e1006990. [[CrossRef](#)] [[PubMed](#)]

