REVIEW ARTICLE
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Technology readiness and overcoming barriers to sustainably implement nanotechnology-enabled plant agriculture

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Nanotechnology offers potential solutions for sustainable agriculture, including increasing nutrient utilization efficiency, improving the efficacy of pest management, mitigating the impacts of climate change, and reducing adverse environmental impacts of agricultural food production. Many promising nanotechnologies have been proposed and evaluated at different scales, but several barriers to implementation must be addressed for technology to be adopted, including efficient delivery at field scale, regulatory and safety concerns, and consumer acceptance. Here we explore these barriers, and rank technology readiness and potential impacts of a wide range of agricultural applications of nanotechnology. We propose pathways to overcome these barriers and develop effective, safe and acceptable nanotechnologies for agriculture.

Agriculture exerts one of the largest pressures on the Earth's environment and is a major driver for biodiversity loss[1,2]. Although all of the United Nations Sustainable Development Goals are tightly linked to agriculture and food production (Fig. 1), current agricultural practices are not poised to meet these goals[1]. Crop yield curves are flattening, and competition is increasing for critical resources such as water, energy and arable land. New technologies are needed to improve the sustainability, resilience and efficiency of agricultural systems[3].

Nanotechnology, according to most definitions, is the production and manipulation of matter at length scales with at least one dimension between 1 nm and 100 nm. The definition varies across technology sectors and between countries, thus complicating regulation and market penetration[4]. For example, some definitions focus on the emergence of unique properties rather than size. The opportunity to engineer the physicochemical properties of the materials for desired purposes is advantageous[5]. At this point in time, nanotechnology has already enhanced a diverse range of products. In the field of agriculture, markets that are linked to the development of these new materials are rapidly growing and versatile, and have untapped potential[6] (Fig. 2).

Nanotechnologies have been developed to promote plant growth and protection, including smart nanocarriers for fertilizers, macro- and micronutrients and pesticides, the genetic engineering of plants with increased photosynthetic capacity, and sensors for real-time plant health monitoring[4]. Laboratory studies of these technologies indicate tremendous promise to make agriculture more sustainable, efficient and resilient[7]. However, although the potential of nanotechnology for agriculture has been discussed for more than a decade, its use in practice is limited, with only a few examples that have moved from the laboratory to the field that will be discussed in this Review Article. Importantly, the use of nanotechnology in plant agriculture will result in the release of engineered nanomaterials into the environment and may introduce nanomaterials into food. Nano-enabled plant agriculture is expected to come under public and regulatory scrutiny in which the benefits and risks of nanotechnology will be debated[8]. As such, the success or failure of nano-enabled agriculture will be intimately linked to consumer perception and acceptance.

Barriers to deployment of potentially disruptive technologies in established and conservative industries are not new; similar challenges were encountered in nanomedicine, one of the first fields

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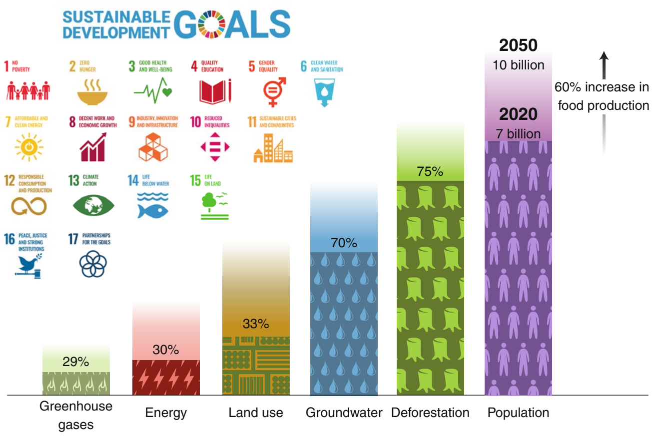

Fig. 1 | Agricultural production will need to increase to meet the United Nations Sustainable Development Goals. Agriculture represents one of the largest pressures on Earth's resources, responsible for 29% of greenhouse gas emissions, 30% of energy consumption, 33% of land use, 70% of groundwater withdrawals and 75% of deforestation[3]. Columns are not to scale. Sustainable Development Goals icons courtesy of the UN. Credit: A. Desaulniers, Orcéine, Montreal, Canada

to evaluate the potential of nanotechnology, where so far limited clinical translation has occurred[9]. Parallels between nanomedicine and nano-enabled plant agriculture include a high degree of regulatory scrutiny, the complexity of the biological target, the consideration of human exposure, overly complex technologies that limit reproducibility, difficulties in scaling up production and cost, and the limited predictive nature of the laboratory-scale experimental models, which may over-simplify in vivo systems. Lessons learned from nanomedicine have therefore been used to develop a roadmap for nano-enabled plant agriculture to responsibly move laboratory successes to the field[10].

This Review Article identifies the technological readiness of different nanotechnology-based opportunities, addresses the primary barriers to adopting nano-enabled technologies for agriculture and proposes a roadmap to advance nanotechnology-enabled plant agriculture.

Barriers to overcome in nanotechnology-enabled plant agriculture

We identify three major barriers to realization of the full potential of nanotechnology-enabled plant agriculture and propose strategies to overcome each of these barriers (Fig. 3).

Scale up to delivery at field scale. Limited information exists about delivery methods at field scale. Current soil and foliar application methods for conventional agrochemicals result in less than half of agrochemicals reaching their target (that is, the root, leaf or target pest). Tuning charge and size, or coating nanomaterials with guiding biomolecules, may increase uptake efficiency and enable targeting to specific plant cell compartments and organelles, such as chloroplasts, mitochondria or the nucleus. Achieving this will enhance plant protection and nutrient delivery while simultaneously preserving the embodied resources (for example, raw materials, processing energy and water) that are currently lost in the agrochemicals that do not reach their target. Furthermore, it may be possible to decrease emissions of ammonia, nitrogen dioxide and the greenhouse gas N_2O, and increase nitrogen delivery efficiency to crops[4]. Formulations that promote leaf adhesion and precision spraying could provide highly efficient foliar delivery and retention. Nanomaterials designed for soil applications have been studied in the laboratory, but further resolution of the concentrations necessary for a beneficial response are required. At current soil application rates, as used for conventional agrochemicals, the economic and embodied resource costs of most nanomaterials for crop growth are too high to be viable in the field.

The foliar uptake of nanomaterials is better understood. A recent paper demonstrated nearly 100% uptake of foliar-applied gold nanoparticles into wheat leaves when using an amphiphilic polyvinylpyrrolidone coating, suggesting that foliar uptake may prove to be an economically viable option. A better mechanistic understanding of how applied nanoparticles are taken up from a leaf-applied suspension would speed the development and market penetration of nano-enabled pesticides and fertilizers. High material production costs may still impede implementation of foliar application. Kocide 3000 is an example of a widely used copper-based nanomaterial fungicide that is sprayed onto plant leaves as an aqueous suspension[11]. Presently, there are few other field-scale trials in which experimental nanomaterials are sprayed onto plants[12,13].

Nanomaterials can also be applied through aerosol-mediated foliar spray, whereby applied aerosolized nanoparticles could enter leaves through stomata[14]. However, aerosol applications may result in unacceptable amounts of off-target drift, raising regulatory concerns.

A potentially efficient nanomaterials application approach is through leaf dipping of seedlings prior to planting, which is an established method to apply plant protection products in greenhouses. This would obviate the need to spray over large areas or to control leaf drip, and has been used to treat plant cuttings of *Aglaonema modestum* (Chinese evergreen) and *Gardenia augusta* (creeping gardenia), resulting in significant protection against pathogens and higher productivity using only milligrams of nanomaterials per plant[15]. The leaf-dipping application is well suited for crops planted as seedlings, such as vegetable and herbaceous fruit crops. In contrast, it is not applicable for cereal grains, fruit trees and other crops with seeds directly planted in the field.

Sustained research focused on the delivery of formulated nanomaterials under varied environmental conditions would enhance the performance and reduce the cost to move these technologies towards the market. Notably, the amount of materials required for seed treatments will inherently be lower compared to field applications, potentially shifting the economic scale for feasibility. The question of how to deliver these nanoparticles at field scale needs to be addressed at an early stage.

Regulation and safety concerns. Agriculture is highly regulated to ensure the safety of food and feed supplies. Nanotechnology further complicates regulatory review, given the potential for human exposure and widespread release into the environment. The regulatory community has not, however, arrived at a consensus[4] on the definition of nanomaterials, and inconsistencies in regulatory approaches between countries can further precipitate trade conflicts. Nanotechnology approaches in market segments with lower regulatory thresholds will probably experience an easier path to market. For example, in many countries, soil conditioning additives, fertilizers and nutrients would encounter lower regulatory hurdles compared to pesticides or genetically manipulated food crops. For instance, for ribonucleic acid interference (RNAi), adoption of nanoscale delivery platforms is expected to depend not only on the cost of producing the double-stranded RNA (dsRNA), but also on the development of regulatory frameworks for both RNAi and nanomaterials[16].

Material selection during process design can strongly impact the potential regulatory path[17]. Biologically benign, naturally sourced Generally Recognized as Safe (GRAS) materials are typically subjected to lower regulatory scrutiny, and this will probably be the case with nanotechnology-based use of such materials. In addition, a clear understanding of the transformations and fate of nanomaterials

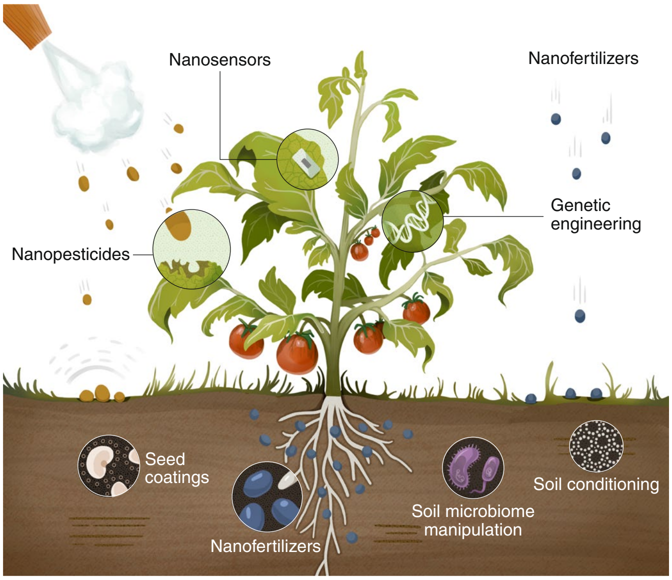

Fig. 2 | Potential application of nanotechnology in plant agriculture. Nanopesticides potentially have higher efficacy and may help to prevent runoff to surface water and groundwater. Nanotechnology-based genetic engineering may offer tremendous advantages. Plants could be used as sensors to report their nutritional or health status. Nanotechnology might be used to modify the soil microbiome or in soil conditioning, and nanocarrier-bound fertilizers may exhibit higher delivery efficiencies than conventional products. Nano-enabled seed coatings may improve seed quality. Credit: A. Desaulniers, Orcéine, Montreal, Canada

in the environment is needed for a proper assessment of potential risk. For example, some nanomaterials that transform after release into the environment may cease to be at nanoscale during their lifecycle. Selection of such technologies or materials will most certainly face lower regulatory scrutiny, as long as the transformation products are well understood or are safer. In addition, efforts can be made to control the exposure time and/or space. For example, if nanoscale amendments occur at the seed or seedling stage, exposure to on-farm workers and consumers could be minimized[18]. Similarly, if platforms can be confined to a greenhouse, environmental exposure can be minimized. Both approaches could significantly lower regulatory concerns.

Data and models for nano-enabled plant agriculture must be acquired at a systems level and include the use of sensitive endpoints[19]. Nanosafety is neither new nor unique for agriculture, whereby exposure and risks to both human and ecological receptors need to be assessed jointly[20]. The safety advancements of the last two decades have been achieved by incorporating key nanomaterial behaviours into mathematical models, including emission, transport, aggregation, dissolution, transformation and interaction with multiphase environmental matrices[21]. Nonetheless, gaps remain due to the complexity of the natural environment. Hazards specific to agricultural applications and their potential effects need to be known, and exposures must be quantified and reliably controlled[22]. Both direct and obvious endpoints (for example, crop yield and nutritional content, soil quality data) and sensitive and subtler endpoints (for example, changes in the (meta-)transcriptome, proteome, metabolome or exposome of both the plant and the soil) could be included for a more holistic understanding of system benefits and impacts[23]. Effects on pollinators or other non-target species should also be tracked. Such an assessment approach will require more research but will also ensure a thorough understanding of efficacy and limitations for successful and safe deployment in the field.

Several knowledge gaps exist in the mechanisms by which nano-enabled approaches achieve their results[4,9,24]. In particular, understanding of the influence of nanomaterial properties (for example, size, shape, charge, hydrophobicity) on interactions with plants (for example, uptake, transport, toxicity) remains limited. The ability for biorecognition approaches to guide nanomaterials to intended targets inside plants remains poorly understood or explored. The propensity to accumulate in fruits and grains is not well documented, preventing assessment of both safety and efficacy.

Multiyear experimental (sentinel) field plots would facilitate data collection but require long-term funding mechanisms that do not currently exist. By conducting studies at multiple, geographically diverse sites, environmental factors such as soil characteristics and climate could be factored into assessment. Importantly, the data generated from such studies could inform the redesign of nanomaterials or formulations to provide a thorough understanding of the dynamic transformation processes in complex natural matrices. Understanding the ultimate mechanisms of action could subsequently be used to lower regulatory barriers and inform material redesign.

Methods are needed to detect and characterize nanomaterials in complex matrices such as soil, plant biomass and food to understand their mode of action, track their fate and assess the risks[25]. Advanced analytical tools are also essential to develop and enforce regulations[26]. However, several major limitations exist. Methods are needed to measure particle-number-based concentrations and size distributions down to a few nanometres, which has not been possible to date[4]. There is also a need to distinguish engineered organic and inorganic nanoparticles from natural particles that are present in much higher concentrations — the proverbial needle in a haystack problem[27] — which is especially true for crops, soils and food. For nanomaterials containing metals, new techniques based on mass spectrometry can measure low concentrations (down to parts per trillion) and could be used to measure many nanomaterials in crops and food[28]. Multi-element measurements of single particles can help to trace the source of the nanoparticles via their elemental or isotopic ratios[29]. Currently, techniques to distinguish low concentrations of carbon-based engineered nanomaterials from either natural organic matter in soils or biomacromolecules, microorganisms and crop biomass, are mainly laborious and microscopy based. For nanoplastics, advances are being made to isolate particle-specific signals, pre-concentrate samples and automate signal collection[30]. Single-particle spectroscopy and the detection of labelled particles are also promising techniques[31].

Consumer acceptance. The rejection and scepticism of many consumers to genetically modified foods have led to more careful introduction of new technologies, such as nanotechnology, in the food sector. Both the public knowledge base and the public itself are dynamic entities, so engagement of those stakeholders who are most affected by the advancement of nano-enabled agriculture (that is, agrochemical product developers, farmers, consumers)[4] must be frequent[32]. Education and trust thus play a pivotal role in dealing with concerns associated with new technologies[33]. Trust in institutions and regulation is paramount given the high scrutiny of most consumers to their food.

Consumer acceptance of foods produced using nano-enabled technologies is essential for widespread adoption, and it is likely that public attitudes towards nano-enabled agriculture will vary by area of application. Importantly, consumer perception and acceptance will decide the success or failure of nano-enabled plant agriculture.

Technology readiness of nano-enabled plant agriculture to be moved from the laboratory to the field

We identified important areas of opportunity for engineered nanomaterials in plant agriculture by assessing the technological

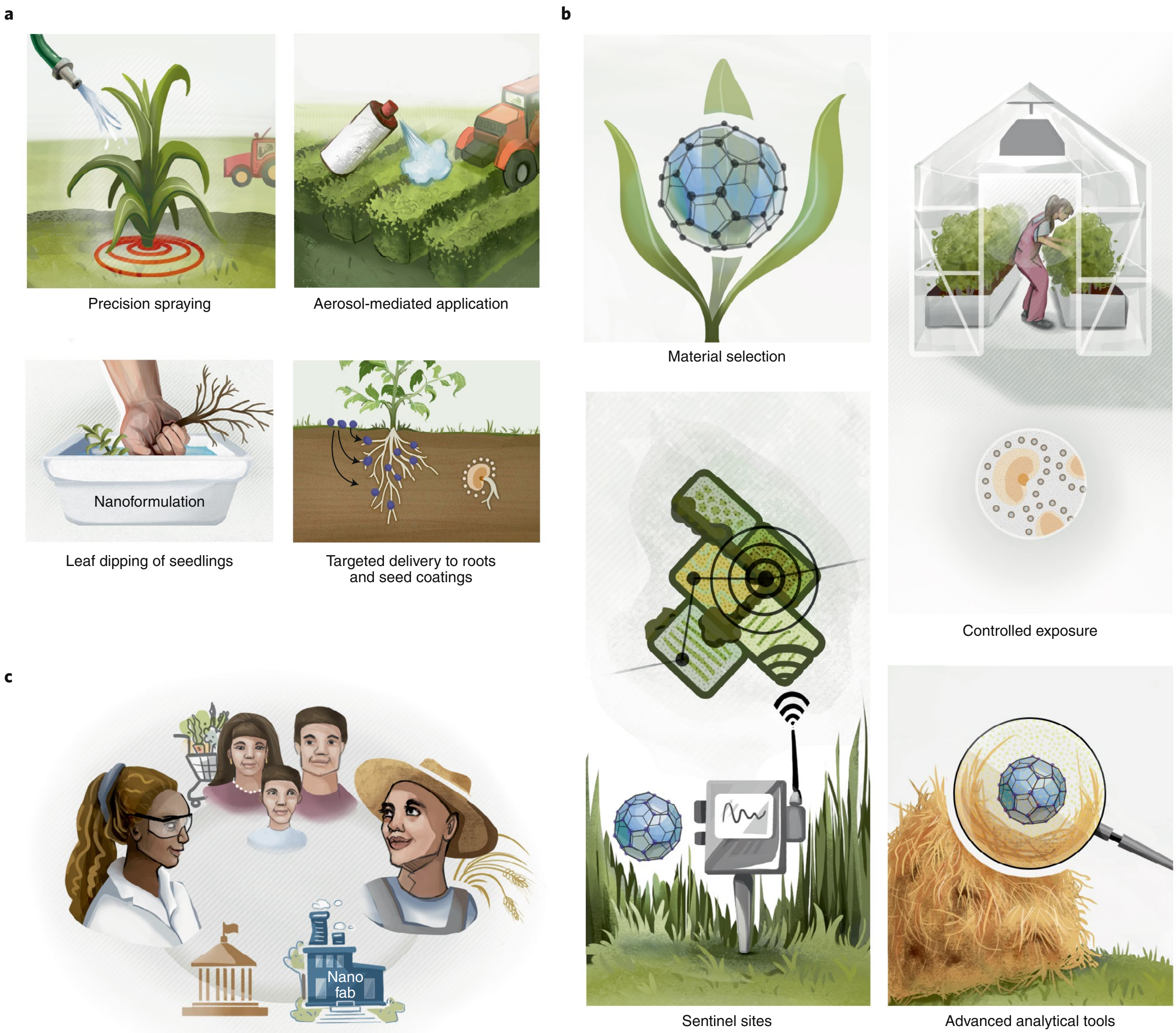

Fig. 3 | Strategies to overcome major barriers to nanotechnology deployment in agriculture. a, Nanomaterial delivery at field scale. Nanomaterial delivery to crops needs to be more sustainable. Nanomaterial delivery can be implemented as precision spraying, aerosol-mediated application methods, leaf dipping of seedlings using formulations that promote surface adhesion, and targeted delivery to roots or seed coatings. **b**, Regulatory and safety concerns. Overcoming regulatory barriers to the use of nanotechnology in agriculture will require informed and careful selection of starting materials, as well as a comprehensive and holistic analysis of the associated risks, fate and impacts. Approaches that control exposure (for example, coated seeds or greenhouse-confined treatment) could lower regulatory barriers. A network of sentinel sites can be used to generate the data needed to understand any associated risks. Advanced analytical tools are needed to detect, identify and quantify nanomaterials in complex natural environments, crops and foods. **c**, Consumer acceptance. Obtaining consumer acceptance for the use of nanotechnology in agriculture will require engagement of all stakeholders (that is, government regulators, researchers, manufacturers, farmers, consumers and retailers) in the development process. Credit: A. Desaulniers, Orcéine, Montreal, Canada

readiness and performance based on the number of studies consistently demonstrating the efficacy of selected nanomaterials, and the scale at which the technology has been evaluated to date (Fig. 4). Nanotechnologies demonstrated to be effective only at the laboratory scale on a few model crops received lower scores on the technology-readiness-level (TRL) axis. TRL was considered higher when the scale increased to more realistic conditions, such as greenhouses with multiple types of plants, or to a field scale. Commercially available approaches were given the highest TRL. The potential of the proposed nanotechnologies to promote sustainability was a subjective determination by the authors based on the magnitude of the outcomes (technology performance level (TPL)), for example, increasing nitrogen use efficiency, lowering pesticide use and lowering risk of crop failure, and on the available performance data. Such outcomes could include the potential for successful and sustainable implementation of nanotechnologies to improve nutrient use efficiency and reduce water demand, greenhouse gas emissions, energy demand, increase intensification via shorter growth cycles and higher yields with reductions in resource inputs. Making nanocarriers that are responsive to environmental conditions could also

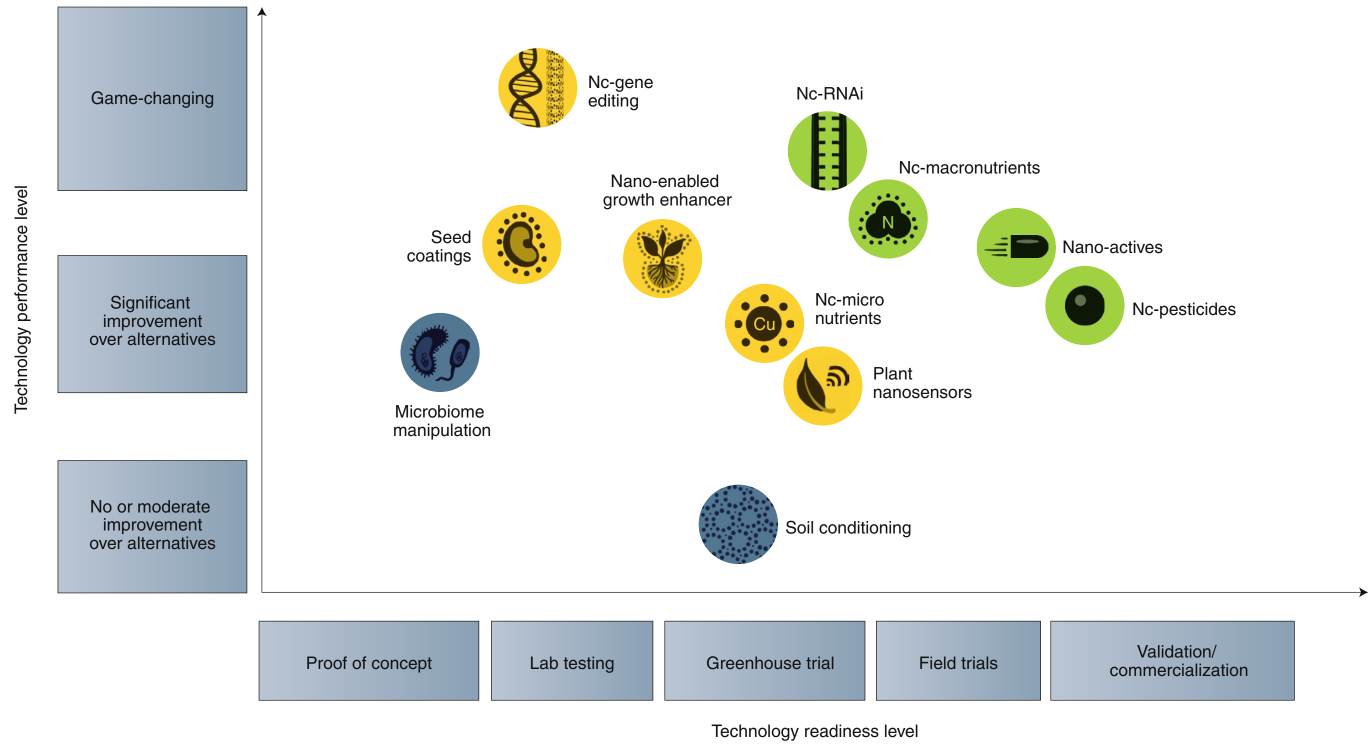

Fig. 4 | TRL for proposed applications or approaches for nano-enabled technologies that can benefit agriculture. TRL was determined based on the data available on the maturity of the technology, including the scale at which the materials or approach have been applied, the number of studies that provide evidence of efficacy, and the number of commercially available products. TPL was determined based on expert judgment of the potential magnitude of the impacts that each technology may provide to improve agricultural sustainability. Colours indicate the level of opportunity as high (green), medium (yellow) or low (blue). Nc, nanocarrier. Credit: A. Desaulniers, Orcéine, Montreal, Canada

transform the way that agrochemicals are delivered to plants and decrease material inputs.

We grouped these opportunities into four application areas: plant protection, improved fertilizers and seed, healthy soils and genetic engineering.

Plant protection. Minimizing crop losses to pests, pathogens or environmental stresses is needed to improve crop production efficiency and to mitigate environmental impacts. Nanotechnology can meet these needs in the near future through nano-enabled pesticides and by transforming plants into sensors.

Pesticides. The global market in pesticides is estimated to grow from US$75 billion in 2013 to US$90 billion by 2023 (ref. [24]). As little as 0.1% of pesticides applied to the field reach their target, that is, the exact location of the desired impact[34]. Therefore, nanocarriers and nano-formulations have the potential to improve the efficacy of existing pesticides by improving the accuracy of delivery. The concept of slow release of an active ingredient from a nanocarrier has existed since the 1960s; however, nanotechnology can provide smart and tuneable pesticides that are designed to deliver the active ingredient at the time and place needed in response to plant stress indicators, including water, pathogens, temperature, pH, redox conditions, light and plant biochemicals[34].

A diverse range of materials has been used to fabricate nanocarriers for more efficient pesticide delivery, including polymer-based structures[35] and inorganic porous materials[36]. For example, mesoporous silica nanoparticles and porous hollow silica nanoparticles have high loading rates, and their mesoporous structures aid the controlled diffusion of the active ingredient[36]. Furthermore, silica surfaces can be readily functionalized to enable targeting or to promote efficient uptake. Viruses (for example, cowpea mosaic virus) offer nanoscale biological alternatives for delivering plant protection products[37]. Several natural polymers have been proposed as nanocarriers. For example, zein — the main storage protein in maize — has been shown to be a safe, biocompatible and effective nanocarrier for botanical pest repellents[38]. While a variety of nanocarriers has been synthesized, relatively few have been registered for commercial use. AZteroid FC and Bifender FC (Vive Crop Protection) use lightly cross-linked polyacrylate polymeric nanoparticles to efficiently deliver hydrophobic pesticides (for example, bifenthrin) to plants (US patent 8,741,808)[39]. A nano-enabled version of the herbicide 2,4-dichlorophenoxyacetic acid has been tested at the field-scale with some success by AgIdea[40]. Commercial virus-based nanocarriers are also available (for example, Solvinix). Commercial or market-ready nanopesticides and nanocarriers suggests a high TRL and high potential for increasing sustainability (Fig. 4). However, limited characterization of new materials and their relatively low level of sophistication (for example, absence of environmental responsiveness or target selectivity) and lack of quantitative field trials reduce the certainty of their potential relative to traditional formulations. An important consideration for nanomaterial delivery at the field scale, regardless of whether the nanomaterial is a carrier or the active ingredient, is the suitability of currently used application practices. For products in use at present, such as Kocide 3000, this is not an issue. However, for formulations and materials for which factors such as in-tank pressurization could alter material structure or function, these potential confounding factors need consideration.

Growth enhancer. Environmental stresses such as drought, heat, salinity and frost can result in large economic losses. The increase in the frequency and intensity of stress events due to climate change pose a significant challenge to the transition to more sustainable plant agriculture[41]. Multiple nanomaterials have been reported to increase photosynthetic efficiency and growth under normal or stressed conditions[42–46]. These nanomaterials have demonstrated significant advantages over other alternatives in the laboratory or greenhouse, but the effects have not yet been tested in the field.

For example, cerium oxide nanoparticles can reduce the accumulation of reactive oxygen species, thereby enhancing photosynthetic performance in plants under abiotic stresses[42,43]. Mesoporous silica nanoparticles, delivered through soil-free nutrient media to wheat, translocate from root to shoot and localize to chloroplasts where they promote photosynthesis seedling growth[44]. Carbon nanotubes interfaced directly with leaves can promote plant photosynthesis[45]. When applied hydroponically, they increase plant growth and yield in tomato plants[46]. Concerns about the potential toxic effects of carbon nanotubes on humans or other organisms could limit their application in the field. However, recent studies indicate that carbon nanotube translocation from root to shoot in tomato could be minimal, and that the low concentrations found in products for human consumption would have no effect on human intestinal cells and microbiota[47].

The delivery of plant growth regulators represents a relatively unexplored opportunity for protecting plants against stresses. Nanomaterials can act as carriers for plant hormones. Alginate and chitosan nanoparticle complexes effectively deliver gibberellic acid leading to increased leaf area and chlorophyll content in common bean plants[48]. Mesoporous silica nanoparticles with redox-responsive gate keepers acting as controlled delivery systems for salicylic acid and abscisic acid improves plant stress responses[49].

Sensors. Nanotechnology-based plant sensors have the potential to revolutionize plant protection by enabling plants to communicate with farmers[50]. For example, nanomaterials integrated into plants can report aqueous and volatile plant signalling molecules associated with the onset of stress or resource deficiencies to agricultural and phenotyping devices via optical, wireless and electrical signals[50]. Monitoring plant health in real time with nanosensors enables fine-tuning of resource inputs before symptoms and therefore has significant potential to enhance agricultural sustainability. To date, most plant nanosensors that communicate with fixed or portable electronic devices have been demonstrated in the laboratory[51] under controlled conditions[52] Recently, a non-invasive method was developed to diagnose plant disease using plasmonic nanomaterials and smartphone-based fingerprinting of leaf volatiles. This approach has been tested in the laboratory and in greenhouses[52]. Turning plants into sensors can significantly improve the efficiency, reliance and sustainability of agriculture. However, their performance has yet to be validated in phenotyping facilities and under relevant agricultural conditions where performance and durability could be affected by weather, plant growth and developmental stage[50]. Because nanosensor technology has been tested in greenhouses, its TRL is in the mid-tier.

Fertilization and seeds. Opportunity exists in fertilization and efficient seed germination. Proposed strategies include slow-release mechanisms for both macronutrients and micronutrients using nanocarriers, and targeted applications of nutrients, including direct uptake of nanomaterials made from micronutrient metals.

Nutrients. Nanomaterials can provide slow, sustained fertilizer release to mitigate losses in runoff and infiltration. For example, a urea–hydroxyapatite nanohybrid reduced the dissolution rate of urea and extended nitrogen release time tenfold compared to free urea in sand[53] and water[54]. Mixing urea with a modified natural nanoclay (attapulgite) formed three-dimensional nanonetworks that are better retained by soil and can mitigate losses to infiltration and runoff. A large-scale field trial using this fertilizer saved 20% more than traditional application rates without affecting the yields. Moreover, when equal amounts of each fertilizer were applied, yield increased by more than 10% (ref. [55]). Synthetic apatite nanoparticles reduced the phosphorus mobility in soil, while maintaining bioavailability and increasing the growth rate and seed yield of soybean (*Glycine max*) by 32.6% and 20.4%, respectively, compared to a conventional water-soluble phosphorus fertilizer[56]. Surfactant-modified zeolites provided slow release of phosphate, increasing both longevity[57] and availability[58] in laboratory trials. Carbon nanomaterials, including nanotubes and graphene oxide, have also been proposed as nanocarriers for micronutrients[59,60]. While promising, most of these proposed nanotechnologies for micronutrient delivery have been tested only in the laboratory.

Rather than using nanomaterials as carriers, a nanoscale form of the nutrient (for example, $CuO_{(s)}$ for copper, $Fe(OOH)_{3(s)}$ for Fe) can be delivered directly to the plant. The benefits of these nanoscale fertilizers have been well documented[40,61]. Nanoscale micronutrients can also introduce indirect positive effects by altering or enhancing macronutrient uptake[62,63]. Some field studies have demonstrated that applications of low doses of nanoscale micronutrients boost crop growth under diseased conditions[64,65], and that nanoscale micronutrients can promote tolerance to abiotic stress[65]. Applications of nanoscale fertilizers using either aqueous suspensions or aerosols have been demonstrated in laboratory studies[15,66]. The application of low doses of nanoscale fertilizers for improving plant productivity have been tested at the laboratory, greenhouse and field scales. Thus, nanoscale fertilizers are given a relatively high TRL. Because micronutrients are required in smaller amounts, improving their utilization efficiency has a slightly lower impact compared to macronutrient utilization efficiency.

Seed coatings. Little public information is available on the TRL of nano-enabled seed-coating technologies in the agrochemical industry. Likewise, very few rigorous studies of the beneficial effects have been reported in the scientific literature, so a comprehensive assessment of the benefits is not possible. Recent innovations — such as electrospun seed coatings incorporating cobalt nanoparticles[67], or coatings of biosynthesized silver nanoparticles for germination enhancement[68] — show promise, but their impact on germination, and on subsequent plant survival and yield, has not been validated in transplant facilities or in the field. Dextran-coated ZnO-nanoparticle seed treatments have been shown to enhance growth and Zn content of wheat (*Triticum aestivum*) seedlings when compared to the currently used form of Zn supplement[69].

There is great potential for nano-enabled seed coatings to promote germination and growth and to increase pathogen resistance, leading to a relatively high placement on the sustainability potential scale. However, TRL for nano-enabled seed coatings is deemed low based on the lack of comprehensive studies to show the efficacy of this strategy in greenhouse field conditions. Nanotechnology could improve nutrient use efficiency through fertilization and enhance seed germination rates. Therefore, the TPL of nanotechnology-based approaches for macronutrients and seed coatings is relatively high.

Healthy soils. Nanotechnologies that can improve soil properties and promote efficient nutrient and water use, as well as mitigate plant pathogens, have significant potential to improve the efficacy and sustainability of agriculture.

Soil microbiome. The importance of the soil–plant microbiome to soil and plant health and to crop production is broadly recognized[70]. For example, controlling the assembly of the phytobiome and plant–soil microbiome can increase tolerance to saline irrigation waters[71] and improve disease suppression[72]. Several studies have demonstrated the ability of some nanomaterials (for example, Ag, CuO, TiO_2) to alter the soil microbiome, affecting important soil functions such as nitrogen cycling[73,74]. In biosolid-amended agricultural soils, addition of nanoCuO, nanoAg and nanoZnO altered the microbial community composition, but only at high doses (100 mg kg^{-1}). No effects were seen at 1 mg kg^{-1} or 10 mg kg^{-1}. NanoTiO_2 did not influence microbial community composition at doses between 1 mg kg^{-1} and 100 mg kg^{-1}, signifying that soil microbiomes are impacted differently by different nanomaterials[75]. So far, there are few reports on using nanomaterials to engineer the phytobiome or soil microbiome. The complexity of soils and the dynamic nature of the soil and plant microbiome will further challenge the application of this approach. Therefore, while the potential of these methods to improve agriculture sustainability is deemed high, the TRL is low.

Soil conditioning. Soil conditioning can improve yield and crop quality by changing soil properties, especially in regions with environmental stress and soil degradation. Most common amendments used to condition agricultural soils are not based on nanotechnology[76,77], although some nano-based soil conditioners have been proposed[78]. A nano mineral-based soil conditioner produced hydrothermally from a potassium-rich feldspar showed a slight increase in pH, soil bulk density, reduced aluminium toxicity and diminished crop cadmium concentration[78]. Biodegradable cross-linkers have been proposed for enhancing soil water retention capacity[79]. Chitosan nanoparticles can improve soil properties and increase wheat production[80]. Most work in this area has been on laboratory studies, and none have shown that the amounts needed at field scale can be produced economically and sustainably. While conventional soil amendments have been used for decades, the potential of nano-enabled soil conditioning to improve agriculture sustainability is expected to be low due to the large amounts of material needed and lack of precision agriculture opportunities[81], as is the TRL given the lack of larger-scale efficacy testing.

Genetic engineering. Nanotechnology can help to deliver genetic material into plants to promote gene editing, and to stabilize genetic materials such as dsRNA to increase efficacy as pest-control agents.

Gene editing. Genome engineering with CRISPR–Cas9 has the potential to increase crop yields and resilience. However, deployment of genome-editing applications in agricultural biotechnology is slow due to the difficulty of delivering exogenous biomolecules into plant cells through cell walls. Nanomaterials can be leveraged for grafting and subsequent delivery of relevant biomolecules for genome editing[82]. Non-pathogenic and non-biolistic delivery of DNA plasmids coding for CRISPR could also enable transient and controlled expression of Cas9 without incorporation of foreign DNA into the plant genome[83]. These nano-enabled non-genetically-modified-organism (GMO) approaches are desirable because regulatory bodies may regulate genome-edited plants as GMOs. Therefore, the use of nanocarriers in gene editing represents one of the highest potentials for making agriculture more sustainable[84]. However, investigations of nanoparticle delivery across the plant cell wall are scarce. Many outstanding questions remain, including how shape, size, aspect ratios, tensile strengths and other such physicochemical parameters affect the ability of nanoparticles to internalize into plant cells[85]. In addition, in-depth analysis of the effects of engineered nanomaterials on plant physiology must be conducted to assess the effects on plants. As such, the TRL is relatively low.

Delivery of dsRNA for RNAi. Transgenic crops can be developed to produce dsRNA to confer resistance against specific pathogens and insects in many, but not all, plant species[86]. In plants, dsRNA precursors are enzymatically processed into single-stranded small interfering RNA (siRNA) molecules that silence high-sequence-complementarity RNA transcripts[87]. As noted above, genetically modified crops encounter considerable regulatory hurdles and problems with consumer acceptance. Topical application of dsRNA to leaves to induce RNAi against viruses, fungi and insect pests represents an alternative to transgenic RNAi[86,88,89]. The instability of dsRNA on leaf surfaces results in short pathogen protection windows, limiting the efficacy of exogenously applied naked dsRNA[90]. This environmental instability can be overcome by binding exogenous dsRNA to nanoscale delivery vehicles that protect the nucleic acid from degradation and enable sustained release. Positively charged layered-double-hydroxide (LDH) clay nanosheets have been shown to be effective as a nanoscale carrier of dsRNA[91]. LDH nanosheets can carry large dsRNA loads and facilitate adhesion to leaf surfaces[91]. Formation of carbonic acid on leaf surfaces from atmospheric CO_2 and humidity promotes LDH nanosheet decomposition, enabling sustained release of dsRNA[91]. Topical delivery of dsRNA via LDH results in systemic virus protection, which lasts at least three times longer than delivery of naked dsRNA[91].

In addition, dsRNA can silence genes in certain taxa, particularly in coleopterans (beetles) and nematodes, but is less effective in other important taxonomic groups, especially lepidopterans (butterflies and moths). This is because many taxonomic groups lack the cellular machinery that allows dsRNA to escape endosomes and enter the cytoplasm, where dsRNA is processed into siRNA. One approach is to utilize nanocarriers functionalized with positively charged polymers, which both bind dsRNA and confer the ability to penetrate cell membranes to allow dsRNA to directly enter the cytoplasm. This has been shown for chitosan-nanoparticle-mediated dsRNA delivery for gene silencing in the mosquito *Aedes aegypti*, where nanoformulated dsRNA was effective at gene knockdown in contrast to naked dsRNA[92]. Another approach uses nanomaterials to carry dsRNA-loaded particles into endosomes that then rupture, releasing the dsRNA–particle complex to the cytoplasm.

Given the efficacy of the nanodelivery vehicles in enhancing RNAi from exogenously applied dsRNA, the TRL of this approach is considered to be high. In this particular instance, where the cost for dsRNA is high, the use of nanocarriers can dramatically lower the amount of dsRNA required and reduce the cost of treatment. In the case of biopolymers such as chitosan, the cost of the carrier is far lower than the active ingredient, with the additional benefit of being biodegradable. Considering the potential of this technology in plant protection without genetic engineering, and its ability to offset or replace pesticide use with low probability of adverse effects in non-target species and humans, the potential for RNAi to improve the sustainability of agriculture is also high. The environmental fate and toxicity of the nanocarriers is likely to be the primary concern. Nanotechnology-based genetic engineering has, therefore, the potential to be a game changer in plant agriculture.

Beyond the examples discussed above, many nanocarriers used for DNA, RNA and protein delivery have relied on synthetic nanoparticles that do not biodegrade[93]. In contrast, many nanocarriers used for delivery of nano-actives, macronutrients and pesticides are biocompatible and biodegradable. The 'field readiness' of these technologies must consider the fate, biotransformation and environmental impact of both the carrier and the cargo. Biodegradable carriers potentially avoid the issue of bioaccumulation in the environment and is therefore closer to being field-ready than their non-biodegradable counterparts.

Safely moving from the laboratory to the field

Our framework suggests that the applications of nanotechnology in plant agriculture with the largest potential for impact and TRL are for pesticides (especially stimuli-responsive smart delivery), fertilizer use efficiency and RNA interference for pest management. These applications should be the first to be tested in the field, at scale, collecting all of the necessary data to accurately quantify the benefits and risks that they may afford. A critical assessment of the market potential and scalability are needed for successful deployment.

The results from field trials must be conveyed to all stakeholders in an unbiased way to initiate dialogue about approaches that truly enhance agricultural sustainability, the safety of these approaches and the knowledge gaps that remain to be addressed.

Regulation and its harmonization across jurisdictions will advance nano-enabled plant agriculture. Engagement of international organizations such as the International Organization for Standardization, Organization for Economic Cooperation and Development, World Trade Organization Food and Agriculture Organization and World Health Organization is required to encourage standardized approaches to nanomaterial regulation. The US–EU Nanotechnology Communities of Research can be used as a vehicle to simultaneously interact with both regulatory bodies and policy makers in multiple countries[94]. The currently regulated system is to be compared to these alternatives, which includes the risk of doing nothing[22] and missing the opportunities that nanotechnology offers. Systems-level evaluations (for example, lifecycle assessment) can play important roles in informing material choices and designs, and in defining the optimal design spaces for nano-enabled plant agriculture.

Moving from the laboratory to the field cannot happen without the agriculture industry. Various segments of the industry will be involved in the scale up of nanoproducts, development of application protocols, training farmers on nanoproduct utilization and negotiating the regulatory landscape. The fragmented nature of this sector, constituting large fertilizer and pesticide producers, speciality chemical and formulation companies, and large and small farmers, is a challenge. Unlike the pharmaceutical, aerospace or automotive industries, the agricultural industry lacks a unified voice and organized frameworks and the resources to develop academic–industry collaborations[95,96].

Humanity must make serious efforts to ensure food and nutrition security using more efficient and resilient agricultural systems, and to address the conservation and restoration of biodiversity. Furthermore, increases in aridity and the incidence and severity of extreme weather events associated with climate change are expected to negatively impact agriculture. Nano-enabled plant agriculture holds promise as part of the solution to improve food security and crop yields while mitigating the environmental and climate impacts of food production.

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Author contributions

T.H., G.V.L., S.G. and N.T. planned and organized the workshop. All authors, except J.P.G., L.M.G. and J.M.U. participated in the workshop. T.H. and G.V.L. conceived of and led the manuscript writing and editing. The sections of this manuscript are based on the written input from all authors, which were the basis of the final manuscript. All authors carefully revised the manuscript and approved the submission.

Competing interests

W.L. is an employee of Vive Crop Protection Inc., a company that produces products for agricultural markets. All other authors declare no competing interests.

Additional information

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