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Nanotechnology and artificial intelligence to enable sustainable and precision agriculture

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Climate change, increasing populations, competing demands on land for production of biofuels and declining soil quality are challenging global food security. Finding sustainable solutions requires bold new approaches and integration of knowledge from diverse fields, such as materials science and informatics. The convergence of precision agriculture, in which farmers respond in real time to changes in crop growth with nanotechnology and artificial intelligence, offers exciting opportunities for sustainable food production. Coupling existing models for nutrient cycling and crop productivity with nanoinformatics approaches to optimize targeting, uptake, delivery, nutrient capture and long-term impacts on soil microbial communities will enable design of nanoscale agrochemicals that combine optimal safety and functionality profiles.

The Green Revolution of the 1950s and 1960s—also known as the third Agricultural Revolution—markedly increased the production yield of global agriculture, thereby avoiding the spread of famine and malnutrition. However, the world population has grown by more than 5 billion since the beginning of the Green Revolution, which has necessitated a continuous growth in crop production. The global agriculture and food security sector is facing a wide range of challenges, such as low crop yields, declining soil health and fertility, and low use efficiency of agrochemicals mainly due to excessive use of fertilizers and pesticides, shrinking arable land per capita and diminishing freshwater availability for irrigation[1]. Moreover, climate change arising from increasing atmospheric CO_2 concentration leading to rising temperature is likely to further affect the resilience of agricultural soils and their ability to sustain productivity and ensure food security for an increasing human population. Nanotechnology offers great potential to enable precision and sustainable agriculture, the opportunities and challenges of which have been discussed in several recent reviews covering strategies to enhance crop nutrition and smart plant sensors[2–4]. With the application of nanotechnology, the delivery of fertilizer[5] can be tailored by targeting to specific tissues or organisms and delivered in a controlled manner via stimulus-responsive release, potentially improving nutrient-use efficiency (NUE) by releasing the nutrient slowly for plant uptake[6]. Nano-enabled agriculture is also expected to target pests more efficiently using smaller amounts of pesticide[7], thereby avoiding widespread effects on soil health and biodiversity, and improving soil function and nutrient cycling by enhancing the soil microbiome (optimization of nitrifying and denitrifying bacterial communities). Longer-term applications include development of smart 'sensor' plants, whereby the plant itself is adapted to sense abiotic stress using targeted delivery of nanomaterials[8]. Figure 1 summarizes four key areas in which nanotechnology is improving—and will continue to improve—the precision and sustainability of agriculture.

As with all new technologies, however, the risks must be evaluated in parallel with the benefits, and indeed several nanomaterials have been demonstrated to cause negative changes in soil community structure; for example, there were cascading negative effects on denitrification enzyme activity and substantial modifications of the bacterial community structure after just 90 days of exposure to a realistic concentration of TiO_2-containing nanoparticles (1 mg kg^{-1} dry soil)[9], and studies with silver-containing nanomaterials, which are well known for their antimicrobial activity, have shown that the impact on soil community composition over 90 days is affected by exposure time and physicochemical composition of soil, as well as the type and coating of the nanomaterials[10]. Thus, an important caveat at the outset of this Perspective is that nanomaterials represent a very broad range of chemistries, compositions and physicochemical properties, which are dynamic and evolving as the nanomaterials interact with their surroundings, and it is therefore difficult to generalize their applications in agriculture and challenging to predict any long-term effects.

However, as previous reviews have noted[2–4], the development of nanotechnology for agricultural applications is still at an early stage, although a range of first-generation products such as nanoemulsion and nano-encapsulation technologies are on the market (for example, Karate Zeon, Seltima and others) alongside commercial formulations of nanoscale silver and copper as biocides (for example, Nano Green and Kocide 3000) and nanoporous zeolites that stimulate plant growth (for example, Nano-Gro). The nanopesticide market was valued at US$410 million in 2019 and is expected to grow at a compound annual growth rate of just over 15% during the forecast period from 2020 to 2027, reaching US$940 million in 2027 (https://www.credenceresearch.com/report/nanopesticide-market). However, much of this market relates to encapsulation technologies for existing active ingredients. A recent review by Hofman et al. provides a good overview of the status of the field[11]. Notably, important differences may exist between nanotechnology-based pesticides and conventional pesticides, including altered bioavailability, sensitivity, dosimetry and pharmacokinetics[12,13]. Challenges and barriers to exploiting the full potential of nanomaterials as sensors, soil enhancers and plant growth stimulators, and to enhancing NUE, include a limited understanding of plant–nanomaterial interactions, limited methods for efficient delivery of nanomaterials to plants and soil, risks of potentially hazardous effects of nanomaterials on human health from accumulation of nanomaterials and active ingredient residues in edible portions of plants[3], and on long-term soil quality and soil health from the accumulation of nanomaterials and their

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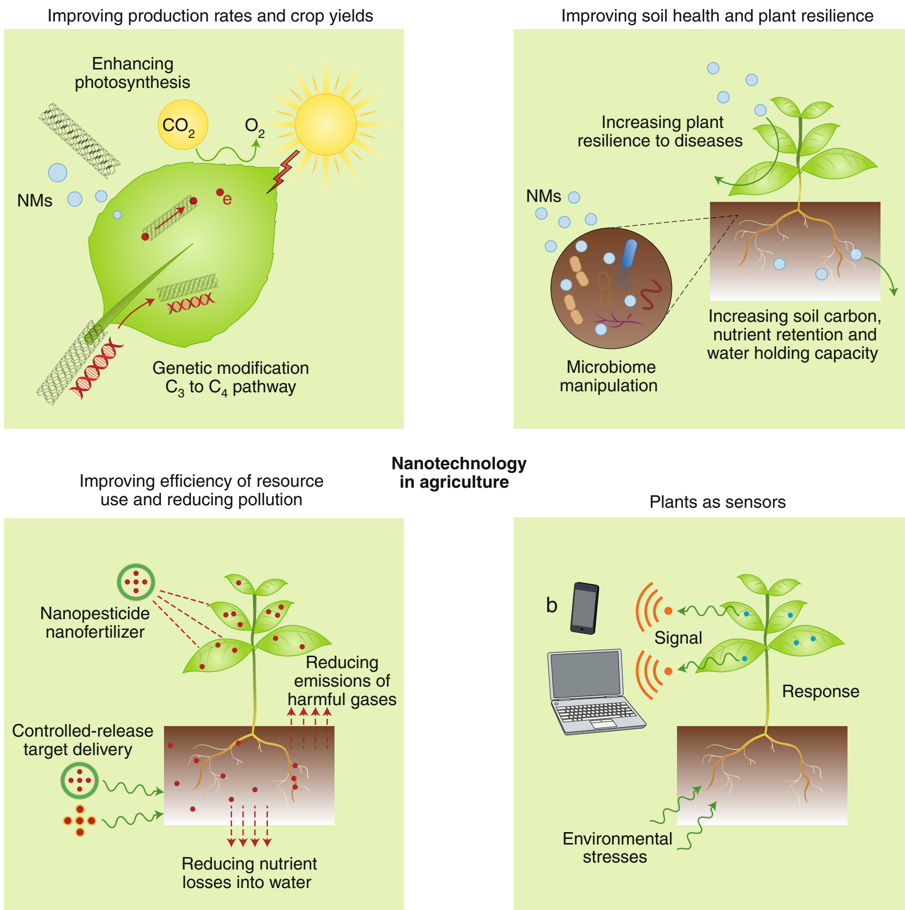

Fig. 1 | Applications of nanotechnology in agriculture, focusing specifically on crop production. Most applications are still at research stage, due to uncertainties regarding safety and complex and emerging regulatory processes for approval of agricultural chemicals, including plant-protection products, biocides and fertilizing products or plant biostimulants. NMs, nanomaterials.

degradation products in soil, and the resultant potential alterations in microbial biodiversity[14]. There is an urgent need to address these barriers and achieve a true win-win scenario, in which improved agricultural production, reduced environmental pollution from agriculture and lower costs for farmers can be achieved synergistically. A one-health approach to nano-agriculture was proposed by Lombi et al., which requires interdisciplinarity and the bridging of human and environmental health research[15]. In this Perspective, we suggest that computational approaches including artificial intelligence (AI) and machine learning modelling will have a critical role in driving the progress of nano-enabled agriculture; indeed, such approaches are already starting to gain regulatory acceptance for safety assessment of nanomaterials, facilitating safe-by-design nanomaterials for a range of consumer products and in medicine.

We also present examples of where the integration of AI and nanotechnology in precision agriculture could accelerate development and provide the insights needed to overcome the current barriers. Nanoinformatics will have a vital role in probing the design parameters of nanomaterials for use in fertilizer and pesticide delivery to ensure minimal impacts on soil health coupled with low phytotoxicity and minimal nanomaterial residues remaining in the edible tissue portions; in exploring and predicting the plant and ecosystem responses to nanomaterials across different climate and soil conditions and over multiple growing seasons; and in optimizing the interplay of nanomaterials and plant responses for safe and sustainable agriculture. By leveraging advances in cheminformatics for de novo design of drugs[16] and for multi-objective optimization[17] to simultaneously optimize numerous or competing objectives, and advances in nanoinformatics for prediction of cellular attachment, uptake, toxicity, biodistribution and safe-by-design optimization of nanomaterial properties[18–20], it is clear that, despite current limitations in data availability and harmonization, the time is ripe for application of AI and machine learning approaches to nano-enabled agriculture. For example, AI may predict nanomaterial impacts on the agricultural ecosystem and their performance in improving agricultural production (NUE and reduction in air and water pollution from key elements) by integrating experimental data from across different soil conditions and different plant species or climate conditions, and from nanomaterial physicochemical properties to develop predictive models to optimize the efficacy of delivery, while minimizing pollution and ensuring a high safety profile for the nanomaterials in soil and minimal residues in the edible plant parts, as part of an overall approach for safer-by-design development of nano-agrochemicals.

Current challenges and applications of AI in agriculture

The application of computers and AI in agriculture is not new—for example, articles addressing software for integrated resource management[21], image digitization for soil and crop science[21], and light and temperature monitoring and control for plants[22] were published 35 years ago. The rise of remote sensing and integration of remote sensing data in decision-support tools for contemporary farming systems is expected to improve yield production and management while reducing operating costs and environmental impact[23].

Models of agricultural systems have emerged over the past 50 years, spanning field, farm, landscape, regional and global spatial scales and engaging questions in past, current and future time periods. Integrated agricultural systems models combining grasslands and cropping models, livestock models, pest and disease models and risk-behaviour models are also emerging, although data gaps exist across all aspects, hampering their implementation[24]. A comparison of the capabilities of a random-forest machine-learning-based model and a physics-based model (a two-dimensional solver of Richards equation using HYDRUS 2D) to predict soil matrix potential in the root zone of a cranberry field over 72 h found that although both models can accurately forecast the soil matrix potential in the root zone, the machine-learning-based model achieved better performance compared with the physics-based model, but its forecasting accuracy decreased rapidly toward the end of the 72 h lead time[25].

The main driver for innovation in agritech is the need to optimize productivity to feed the increasing human population with the decreasing global per capita agricultural land area while ensuring the conservation of soil health and the protection of environmental quality[26]. The intensification of agriculture for enhanced productivity has resulted in extremely poor NUE globally[27,28] (less than 50%), which poses a serious threat to environmental quality as large amounts of nutrients are lost to water and air, causing eutrophication and greenhouse effects (nearly 11% of global greenhouse gas emissions are from agriculture[29]). Rockström et al. recommended a reduction of reactive nitrogen (N) use in agriculture from 150 MtN yr^{-1} to about 35 MtN yr^{-1} globally to ensure sustainability[30]. Such a reduction may be achieved through a combination of targeted nano-enabled delivery of fertilizer to match plant demands and thus avoid excessive losses, development and availability of low-cost in situ nutrient-sensing technology to help farmers plan fertilization efficiently, and identification of crop breeds that are efficient in nutrient uptake or fixation of atmospheric N_2 directly or through enhanced symbiosis[31]. Recent efforts to enhance NUE include the use of biofertilization to enhance microbial biodiversity[32] and the application of a range of N management tools across the growing season, including soil testing, plant tissue testing, spectral response, fertilizer placement and timing, and vegetative indexes (leaf area index and normalized difference vegetation index) using AI-enabled drones, handheld sensors and satellite imagery[33].

Global agricultural yields are also impacted by crop loss due to competition from weeds, insect damage and plant diseases. Weed competition causes 34% of crop loss on a global scale, and microbial diseases and pest damage cause a further 34% of crop loss[34]. The application of synthetic herbicides and pesticides thus increases yields (reducing crop loss) and, in the case of herbicides containing nitrogen, phosphorus and potassium, improves food quality through enhanced nutrient uptake and retention[35]; however, these agrochemicals, which are designed to kill, also cause severe adverse impacts on the health of human and non-targeted organisms and soil fertility, and result in contamination of water, soil and air[36]. Misuse of agrichemicals on poor-quality soils, soil degradation as a result of farming intensification, decreasing water availability and water quality, and globalization of diseases have led to low resilience of agriculture systems[37]. Moreover, climate change effects, such as increased atmospheric CO_2 levels and increasing temperatures, will also impact the future of agriculture[38].

Nanotechnology applications in the agricultural sector have great potential to improve all aspects of crop production—that is, to increase crop production yields and resource-use efficiency while reducing agriculture-related environmental pollution—thereby ensuring global food security while ensuring future agricultural sustainability. The convergence of AI approaches and nano-enabled agriculture is in its infancy and thus this Perspective aims to stimulate the development of this important area. Coupling existing models for nutrient cycling and crop productivity with AI and machine learning to optimize targeting, uptake, delivery, nutrient capture and soil microbial composition will enable design of nanoscale agrochemicals that combine optimal safety and functional profiles and implementation of nano-agrichemicals into mainstream agricultural systems management. A roadmap to achieve this, and the existing components that can be leveraged from nanosafety research more broadly, are laid out in the following sections.

Leveraging progress in nanosafety and nanoinformatics for nano-agrochemicals

Before maximizing the use of nanomaterials in agriculture and agronomy, some concerns need to be addressed, including the potential toxicity of the nanomaterials to target and non-target organisms and adverse impacts on ecosystems[39,40], their persistence and mobility in the environment and those of their breakdown or transformation products. As with all agrochemicals, concerns about potential residues in edible portions of plants also need to be addressed as part of an overall risk assessment of nano-enabled agrochemicals[41]. Since the use of nanomaterials on farmland will require large quantities of nanomaterials—the synthesis of which requires high energy input—evaluating the cost of production and the cost–benefit trade-offs should be considered in the development of nanomaterials for application in agriculture.

The rapid pace of the development of nanotechnologies, the enormous diversity of physicochemical properties of nanomaterials and their dynamic interactions with, and transformations by, their surroundings (including, for example, biomolecule corona formation, dissolution and sulfidation[42,43]) lead to a need for in silico approaches to predict and assess their safety[19]. Nanoinformatics emerged a decade ago in the context of development and implementation of nanotechnology in the real world requiring the harnessing of information at the nexus of environmental and human safety, risk assessment and management, physiochemical properties and function. Through the application of AI and machine learning for in silico risk assessment[44], nanomaterials grouping and classification[45], and safe-by-design[46] nanomaterials design, as well as for prediction of nanomaterials corona formation[47] and consequences of cellular attachment and uptake[48–50], nanoinformatics has had a notable role in the area of nanosafety and nanomedicine. Deep learning approaches have been applied, for example, to microscopic images of the aquatic indicator species *Daphnia magna* exposed to nanomaterials in a range of representative waters of different ionic strengths and natural organic matter contents, and can automatically detect possible malformations—such as effects on the length of the tail, overall size and uncommon lipid concentrations and lipid-deposit shapes, which are due to direct or parental exposure to nanomaterials—and can classify the nanomaterials as toxic or non-toxic[20]. An early application of Bayesian networks modelled the risk of silver nanomaterials exposure in aquatic environments[51], which was subsequently used for sensitivity analysis[52]. A Bayesian network combining physicochemical properties and exposure potential of nanomaterials was used to perform hazard assessment[53]. Bayesian networks can also underpin the development and quantitative analysis of the causal relationships in adverse-outcome pathways (AOPs) and AOP networks[54]. For example, the causal relationships between the building blocks of an AOP relating the reproductive failure of *Caenorhabditis elegans* through oxidative stress caused by silver nanomaterials were established using Bayesian networks[55]. This highlights an important difference between Bayesian and machine learning approaches, which is that the former requires that causal relationships are known or are assumed, whereas the latter does not require any a priori causal relationships.

A key challenge in the development of nanoinformatics models has been the accessibility of datasets, although there are considerable efforts underway currently to curate, harmonize and integrate nanosafety data and to enrich them with environmental, gene, protein, geospatial and other data. Tools and approaches to automate data mining have been developed, including workflows that simplify the handling, processing and modelling of cheminformatics and nanoinformatics data, including the Enalos toolbox of more than 25 processing modules called Enalos+ nodes, which extract useful information and analyse experimental and virtual screening results in a chemoinformatics or nanoinformatics framework via KNIME[56]. Other approaches applied in the nanosafety area to overcome the limitations of dataset size include application of read-across approaches for gap filling[57] and enrichment of datasets through image analysis[58,59] or by generation of computational descriptors[60,61], for example, which are then correlated with toxicity. The increasing availability of nanomaterials models that can make predictions without the need for any experimental input, using only knowledge of nanomaterial structure and composition (that is, physics-based models[62]) enables developers to screen nanomaterials in silico before actually producing them, thus ensuring that the properties of concern are reduced or eliminated, which should make the nanomaterials safe by design[63,64]. For nanomaterials and individual molecules, the starting level of the data is quantum chemical, and includes explicit representation of all atoms and valence electrons. To set up such simulations, input of the nanomaterial chemical composition, including impurities, as well as nanomaterial crystal structure is needed. At this level, atomistic and quantum-chemical representation can be used to evaluate the electronic structure of the nanomaterial and to parameterize a coarser representation: an atomistic model, by development of appropriate force fields and material constants. This procedure can combine physics-based multiscale modelling for calculation of advanced descriptors and properties of nanomaterials with nanoinformatics methods for evaluation of their complex properties and functionalities[63]. By scanning the main groups of engineered nanomaterials, specific properties can be identified that might be responsible for causing a particular toxic effect and lead to a particular adverse outcome, which needs to be modified or avoided. This provides a means of grouping and read-across characterization of nanomaterials and enables development of nanomaterials that are safe by design, and is currently an area of very intensive research.

As the available pool of fully validated nanoinformatics models and tools with well-defined domains of applicability grows, the nanosafety field is becoming less reliant on animal testing and more targeted towards the safe-by-design principles for early stages of nanomaterial development. Integration of models into predictive risk assessment frameworks, such as Integrated Approaches to Testing and Assessment (IATA) are the next step, combining nanomaterials exposure and hazard characterization for complete risk assessment. IATA use existing information coupled with the generation of new information in an iterative approach to answer a defined question in a specific regulatory context, and can include a combination of methodological approaches (such as quantitative structure–activity relationships (QSARs), read across in silico, in vitro, ex vivo and in vivo) or omics technologies (for example, toxicogenomics). As AI and machine learning models for nanosafety emerge, they are increasingly being incorporated into IATA. In these IATA, the output from one model can be the input for the next, and predictions from several different models can then be integrated in a final machine learning modelling and predictive analysis. The analysis can then be applied to generate, for example, development of nanomaterial fingerprints—predictive and informative physicochemical, biological and computational descriptors that describe a set functionality—that is, the minimum set of descriptors required as input to predict specific nanomaterial functionalities[63].

Standard nanoinformatics methods for modelling have thus far ignored the multi-objective nature of the problem and have focused on optimizing each biological or material property individually as they become available during the material design process. Multi-objective optimization (MOOP) methods introduce an innovative approach for optimization founded on compromises and trade-offs among the various objectives[17]. The aim of MOOP methods is to discover a set of satisfactory compromises and through them, the global optimal solution, by optimizing numerous dependent properties simultaneously. The primary benefit of MOOP methods is that local optima corresponding to one objective can be avoided by consideration of all the objectives simultaneously, thereby escaping single-objective dead ends and leading to a more efficient overall process. Several methods have been developed for the in silico optimization of small molecules that account for the multi-objective aspect of the drug-design process, enabling scientists to optimize in multiple spaces simultaneously. Although MOOP models have not yet been explored properly in the area of nanomaterials, a pool of well-validated nanoinformatics models and tools, assisted by physics-based models, is available, and efforts to integrate these and facilitate multi-factor optimization of safety and functionality as the basis of safety by design are now beginning[63]. For example, multi-perspective AI- and machine-learning-based modelling techniques can be used to optimally aggregate and integrate experimental information and outcomes of the multi-scale modelling methods and eventually increase confidence levels concerning evidence of particular hazards. The resulting commercial benefits will include improved market access for agricultural applications and reduced costs for the exposure, hazard and risk assessment of nanomaterials, including safe-by-design screening before production to optimize both functionality and safety.

The examples highlighted above demonstrate that there is ample scope to apply nanoinformatics in nano-enabled agriculture, although this has yet to be explored and is thus the rationale for the current Perspective to inspire the community to begin to apply the wealth of knowledge and existing approaches to the specific challenges of nanomaterials applied to agriculture. Areas ripe for application of nanoinformatics and modelling include prediction of nanomaterial interactions with and impacts on rhizosphere secretions (both proteins and metabolites), nanomaterials transformations before and during uptake and translocation, nanomaterials impacts on soil microbial communities and for prediction of plant uptake following foliar or soil application. Experimental data are emerging in all these areas[14,65,66], and a dedicated effort to integrate and curate these data and present them in a format suitable for modelling is currently underway within the nanoinformatics e-infrastructure projects NanoCommons and NanoSolveIT[63]. Coupling these approaches with existing models for nutrient cycling[67], NUE[68] and crop productivity[69], and the aforementioned agricultural systems models into overall IATA with MOOP capabilities, will begin to enable co-optimization of nanomaterials for use in agricultural systems that combine safety and functionality profiles (including enhancing NUE and calorific value of crops) enabling precision agriculture, as shown schematically in Fig. 2.

Experimental studies using nanomaterials for agriculture in the laboratory, mesocosms and field are expensive, time consuming and complicated, limiting the range of conditions that can be varied systematically. Conclusions may be ambiguous, because the interpretation of the results is influenced by factors such as experimental procedures, protocols, duration, nanomaterials types, doses, soil types and plant species. Integration of the existing data—albeit with gaps and limitations—and supplementation with predictive modelling and machine learning approaches—including Bayesian networks[53,70], which can be dynamically updated as new knowledge emerges—into IATA underpinned by MOOP approaches offer exciting new directions. Development of a nano-agriculture IATA case study using the Organisation for Economic Co-operation and Development IATA case study approach[71] seems to be a logical next step as shown schematically in Fig. 2.

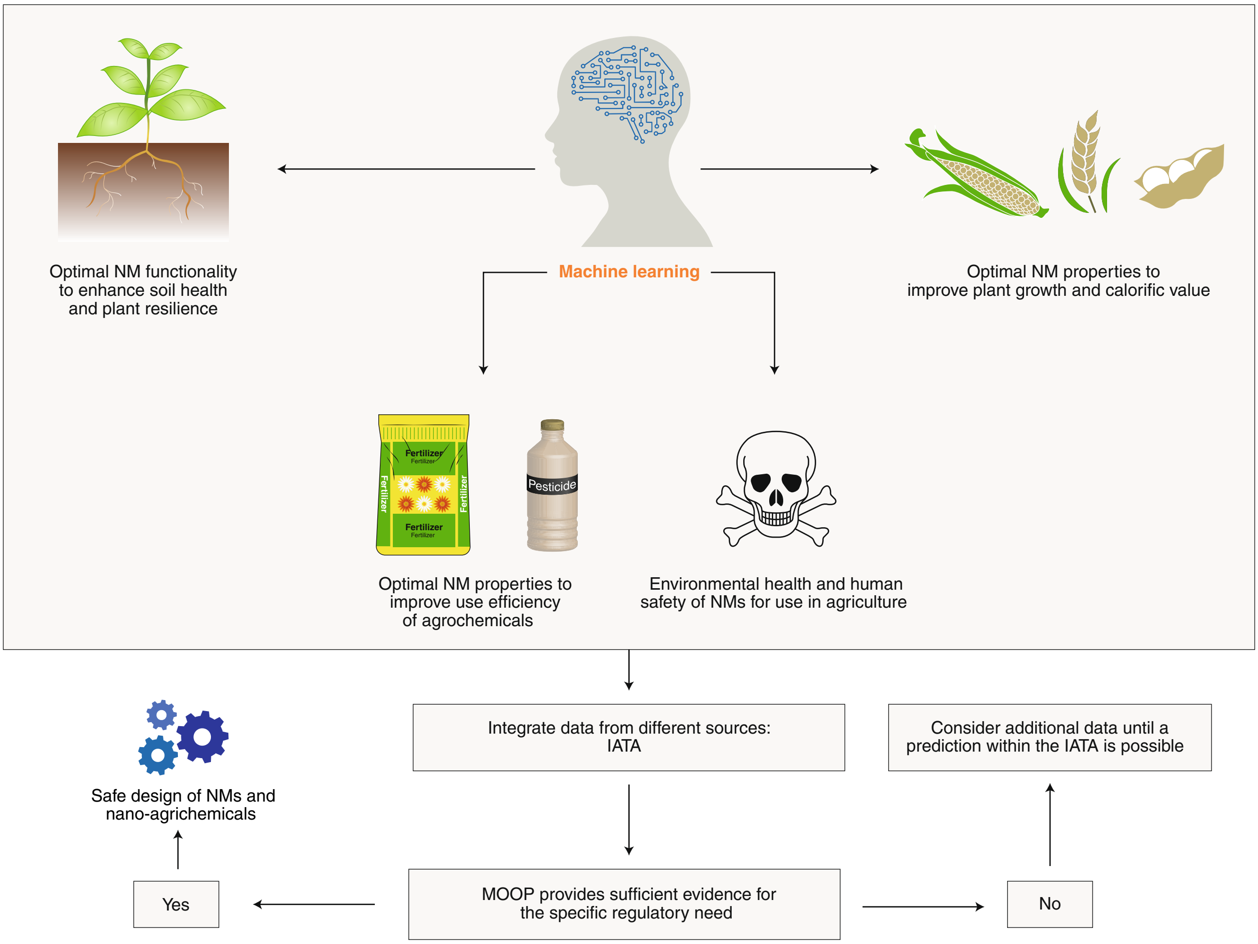

Fig. 2 | Applications of machine learning to nano-enabled agriculture. Application of machine learning in risk assessment and safe-by-design nanomaterials design and the potential for extension of machine learning approaches to support nano-enabled agriculture, building on advances in both nanoinformatics and agricultural systems modelling and emerging developments related to MOOP modelling. Integrating a range of different modelling and experimental approaches via an IATA will lead to enhanced prediction power in terms of optimal nanomaterials properties for safety and functionality across the range of potential nano-agriculture applications, and faster and safer implementation of precision nano-enabled agriculture.

AI and machine learning for nano-enabled agronomy

Here we present current and future applications of AI and machine learning applications in agriculture.

AI and machine learning approaches. As computational capabilities grow and the value of data as knowledge to be exploited is increasingly realized, AI and machine or deep learning approaches are emerging as means to identify patterns in large datasets that are predictive of future outcomes. One of the most widely used approaches involves neural network algorithms, which use an unbiased subset of the total available data as the training set to develop a model that makes predictions using the rest of the data—the validity of the predictions is evaluated to ensure that they could not arise randomly. The size and range of the dataset used to train the model provides the limits of its predictive power, or its domain of applicability—models cannot predict reliably outside the range of these data. Box 1 describes the various types of data-driven machine learning models, which include models that link structure or properties (for example, of a chemical or nanomaterial) to specific effects or impacts on the environment—QSARs or quantitative property–activity relationship models[72], and Bayesian networks, which are a powerful tool for incorporating uncertainty into decision-support systems[73]—by providing a basis for probabilistic inference and facilitating assessment of changes in probabilistic belief as new evidence is entered into the model. The larger the dataset available to train a machine learning model, the more powerful it will be—for example, in drug discovery or cheminformatics, models typically use data from thousands of different chemicals to develop a prediction. Similarly, genomics and related approaches, in which hundreds of thousands of data points are available, enable generation of strong gene-interaction networks and assessment of effects of specific genetic perturbations; these are used, for example, to understand gene-regulation networks in plants[74].

For application of AI and machine learning in nano-enabled agriculture, it will be necessary to mine the existing publicly available datasets, including those on nanomaterials safety and nanomaterials impacts on plants and soil microbial communities, existing plant omics databases such as the Plant Omics Data Center[75], an integrated web repository for interspecies gene-expression networks incorporating information on eight plant species (*Arabidopsis thaliana*, *Oryza sativa*, *Solanum lycopersicum*, *Sorghum bicolor*, *Vitis vinifera*, *Solanum tuberosum*, *Medicago truncatula* and *Glycine max*) with functional annotation of the genes to facilitate biological comprehension, the plant proteome database, the Plant Secretome and Subcellular Proteome KnowledgeBase (PlantSecKB[76]) and similar databases for soil microbiota, and integrate these with relevant agricultural databases such as the global gridded data of soil physical properties, hydroclimatic and agricultural variables,

Box 1. The main types of machine learning algorithms and examples of their application in agriculture and/or nanomaterials design and safety assessment[104]

• **Supervised learning**. This algorithm consists of a target outcome (dependent variable) to be predicted from a given set of predictors (independent variables), generating a function that maps inputs to desired outputs. The training process continues until the model achieves the desired level of accuracy on the training dataset, and the model is then tested on the test dataset, which was not involved in the training procedure.

Examples of supervised learning: regression, decision tree, random forest, *k*-nearest neighbours (KNN) and logistic regression.

Applications in agriculture and agronomy: a KNN algorithm was used to predict water retention at −33 and −1,500 kPa matric potentials using a hierarchical set of inputs (soil texture, bulk density and organic matter content)[105].

Applications in nanomaterials design, safety and interactions[106]: KNN algorithms have been applied to develop a predictive QSAR model for nanomaterials cellular association based on their physicochemical properties and adsorbed protein corona, as a means to understand the drivers of nanomaterials toxicity[84].

Potential applications in nano-enabled agriculture: these algorithms could be applied for prediction of acquired biomolecule coronas (rhizosphere secretions, foliar sections and biont) and their evolution during nanomaterials uptake into plants, and for prediction of nanomaterials transformations and impacts on soil or foliar bionts. They could be integrated into IATA with water-retention models to predict nanomaterials mobility in soil.

• **Unsupervised learning**. In this algorithm, there is no target or outcome variable to predict. It is used to cluster data into different groups.

Examples of unsupervised learning: a priori algorithm and *k*-means clustering.

Applications in agriculture and agronomy: a segmentation algorithm—inspired by an image-processing region-merging algorithm—for delineation of discrete contiguous management zones, that is applicable to high- or low-density irregular datasets such as yield data[107], has been developed and can identify coherent management units to facilitate differential crop management.

Applications in nanomaterials design, safety and interactions: *k*-means clustering has been applied to signal processing of single-particle inductively coupled plasma mass spectrometry (spICP-MS) raw data (used for characterization of nanomaterials size and to distinguish particulate versus ionic fractions for quantification of nanomaterials dissolution, uptake and other properties) to discriminate particle signals from background signals, leading to a sophisticated, statistically based method to quantitatively resolve different size groups contained within a nanomaterial suspension[108].

Potential applications in nano-enabled agriculture: could be applied to prediction of nanomaterials transformations under different soil and climate conditions for prediction and clustering of efficacy of nano-enabled agrichemicals and NUE of fertilizers. Integration with crop management approaches could be applied to determine optimal nano-agrichemical application strategies.

• **Reinforcement learning**. The machine is trained to make specific decisions. Using trial and error, the machine learns from past experience and captures the best possible knowledge to make accurate decisions.

Example of reinforcement learning: Markov decision process.

Applications in agriculture and agronomy: a smart agriculture Internet-of-Things system based on deep-reinforcement learning has been developed to increase food production using deep-reinforcement learning in the cloud layer to make immediate smart decisions such as determining the amount of water needed for irrigation to improve the crop growth environment[109].

Applications in nanomaterials design, safety and interactions: a recent example used Kohonen networks[110] (also known as self-organizing maps) to visualize sets of silver and platinum nanomaterials on the basis of structural similarity and overlay functional properties to reveal hidden patterns and structure–property relationships. Visual inspection of the self-organizing maps revealed a strong structure–property relationship between the shape of silver nanomaterials and the energy of their Fermi level, and a weaker relationship between shapes with a high fraction of surface area and the ionization potential, electron affinity and electronic band gap. Both energy levels and crystal structure or exposed crystal face are linked to nanomaterials reactivity and toxicity[111].

Potential applications in nano-enabled agriculture: initial applications in hydroponics as part of real-time responsiveness to changes in nutrient and microbial compositions; integration with nanomaterials structure–property relationships under different environmental and local conditions to optimize release rates and NUE.

socio-economic metrics, and historical pesticide usage data (for example, table 1 in Maggi et al.[77]). The utility of such an approach of integrating disparate datasets has recently been demonstrated with the establishment of PEST-CHEMGRIDS, a comprehensive database of the 20 most-used pesticide active ingredients on 6 dominant crops and 4 aggregated crop classes at 5 arcmin resolution (about 10 km at the equator) projected from 2015 to 2025. The use of automated data extraction, curation and integration via the Enalos+ KNIME tools, which has already been demonstrated for drug discovery and nanoinformatics[56], will facilitate this process, and new nodes for specific databases or data clean-up and integration will be developed for nano-agriculture datasets as needed.

Current AI and machine learning in agriculture. A 2018 review of the use of machine learning in agriculture classified the application areas into (1) crop management, including applications in yield prediction, disease detection, weed detection crop quality and species recognition; (2) livestock management, including applications in animal welfare and livestock production; (3) water management (daily, weekly or monthly evapotranspiration rates); and (4) soil management such as prediction and identification of agricultural soil properties[78]. However, application of Bayesian networks to agricultural systems has remained challenging, as there are often insufficient data to compute the prior and conditional probabilities required for the network[73]. Several other machine learning methodologies can be investigated without the need for a priori relationships, and numerous models can be linked together to fill gaps in the data and predict missing values, as demonstrated successfully for a meta-analysis of 216 published articles on cytotoxicity of metal oxide nanomaterials[79].

In terms of the key areas identified for improvements in crop production, process-based machine learning models (for example, the SPACSYS model[80]) for plant growth—incorporating assimilation, respiration, water and nitrogen uptake, partitioning of photosynthate and nitrogen, nitrogen fixation for legume plants and root growth[81]—are emerging and being constantly improved. With increased understanding of the processes and, more importantly, the variables driving them, and the availability of intervention strategies such as precision nano-agrochemicals to target specific locations or release in response to specific stimuli, the potential of machine learning for optimization of agroecosystems has never been greater. Integrating machine learning, simulation and portfolio optimization can inform decisions and support selection of optimal seed varieties (for example, soybean) to grow, with resolution at the level of a specific farm with its individual crop rotation history rather than at regional scale based on soil type and quality[82]. Incorporating such information into multi-object optimization modelling of nanomaterial safety, soil management and plant yield offers exciting new possibilities. Indeed, a recent review of the potential impacts of AI on achieving the United Nations Sustainable Development Goals (SDGs) suggested that AI will be an enabler for SDG2 ("improved nutrition and promote sustainable agriculture"), but highlights generally that the pace of development of AI may have implications in terms of a lack of regulatory oversight and insight, which could potentially result in gaps in transparency, safety and ethical standards[83].

Nanoinformatics models applicable to nano-enabled agriculture. The application of machine learning in nanomaterial risk assessment and for design of safe and environmentally friendly nanomaterials has also been an area of intensive research over the past few years. For example, nanoQSAR models linking specific nanomaterials properties to uptake by, and impacts on, cells or organisms are emerging. Models that allow determination of surface functionalizations that enhance (or decrease), for example, protein binding and/or cellular association (as a pre-requisite for internalization[84]) are also emerging, and can be applied for design of targeting strategies in precision nano-agriculture. Although to date no nanoQSARs have been developed for plants, ecotoxicities of plant-protection chemicals to target and non-target species have been predicted using QSAR[85], and as the corpus of data related to nanomaterials in plants and soil species is growing exponentially, it is only a matter of time before the first nanoQSARs for plants and soil microbiota are developed. Similarly, extending advances in nanomedicine to precision nano-agriculture will facilitate the design of optimized controlled-release agrochemicals[86,87]. For example, deep learning using an automatic data-splitting algorithm and evaluation criteria suitable for pharmaceutical formulation data has been developed for the prediction of optimal pharmaceutical formulations and doses[88]. From an agricultural perspective, understanding the factors (including nanomaterial, plant, soil and climate factors) that control the release rate of active ingredients, and the factors driving transport of the carrier can influence selection of formulation parameters and suitability of application to specific locations or climates. Such data-driven models require substantial amounts of data to train and validate them, which remains a barrier to their development. However, significant work is underway in the wider nanosafety arena to develop optimized workflows for generation of data and metadata (for example, using electronic laboratory notebooks[89] to capture experimental data as it is generated, linking them to underlying protocols and calibrations, and facilitating curation and storage of the data in databases, thereby accelerating their accessibility and re-usability), annotation with relevant ontological terms mapped to the data schema of the receiving databases and automated upload to nanosafety knowledge bases[90], which in the medium term will facilitate the aggregation, integration and reuse of nanosafety- and nano-agriculture-related datasets.

However, as noted above, there are important concerns regarding the safety and risks of nanomaterials that must be addressed before their widespread intentional application to the environment can be sanctioned, and there are tight regulatory processes for approval of agrochemicals[91]. A recent review assessed the regulation of pesticides and the potential use of computer-based chemical modelling technologies to facilitate risk assessment of nano-enabled pesticides[88], and concluded that quantum chemistry is an appropriate tool for characterization of the structure and relative stabilities of organic compounds and for studying degradation pathways. However, a re-evaluation is needed to determine its suitability for nano-enabled agriculture, using quantum nanomaterials descriptors for QSAR development. Among the quantum descriptors for nanomaterials are molecular and electronic properties such as band gap, ionization potential, atomic charge, electronegativity and adsorption energy, as well as interaction parameters for prediction of interactions of proteins and small molecules, such as binding energies, binding affinities, Hamaker constants and absorption energies, which can be used to predict biomolecule corona formation[92]. In due course as data emerges, the evolution of the adsorbed biomolecule as nanomaterials interact with, and respond to, soil and plant secretomes, and are transformed as shown in Fig. 3, will also be predictable through modelling, allowing tailoring of nanomterials to acquire the desired biomolecule corona.

Challenges and barriers to precision nano-agriculture

Although nanotechnology has potential in a wide range of applications in agriculture, there are many challenges to be overcome to move this area forward and facilitate full commercial-scale application of many of the innovative nanomaterials presented in Fig. 1. These include a lack of mechanistic understanding of the interactions at the nanomaterial–plant–soil interface and nanomaterial uptake and translocation in plant vascular structure and organelles; insufficient understanding of the environmental safety and human health risks of intentional nanomaterial application; a lack of soil and large-scale field studies to demonstrate the efficacy of nanomaterials under realistic scenarios; balancing the adoption of new technology and the low profit margins in agriculture; and the challenges in collection and harmonization of the datasets needed for development of AI models.

Long-term studies at ecosystem level under environmentally relevant conditions and at realistic nanomaterials exposure concentrations are currently lacking. For example, silver, zinc and copper-based nanomaterials have demonstrated potential to be applied as efficient pesticides or fungicides; however, the potential impact on non-target organisms (for example, beneficial plant rhizosphere bacteria and worms) and long-term impacts on soil quality are not known. While there remain challenges for the detection of nanomaterials in complex matrices, particularly at low concentrations, and access to state-of-the art facilities with sufficient resolution such as synchrotrons is limited, application of deep learning tools to plant spectral images (for example STXM. XRF etc.) is expected to enable advances in terms of determining and predicting nanomaterials localization and in situ transformations even with relatively limited datasets and against a background of naturally occurring particles. Indeed, as models are trained using existing high-resolution datasets for specific nanomaterial–plant combinations, they can be coupled with more generalized QSARs or physical models of nanomaterials transformations under specific environmental conditions, and supplemented with the development of functional assays that can provide the input data needed for models but under simplified conditions[93,94]. For example, surface affinity and dissolution rate have been identified as two critical functional assays for characterizing nanomaterial behaviour in soil systems. A range of functional assays for nanomaterials transformations, including binding of secreted proteins and small molecules or uptake using simpler hydroponic systems could be envisaged to begin parameterizing more complex predictive machine learning models.

Although nanofertilizers may enhance the NUE, effects of nanomaterials on the nutritional quality of food (for example, alteration of the content of carbohydrates and macro- or micronutrients) have

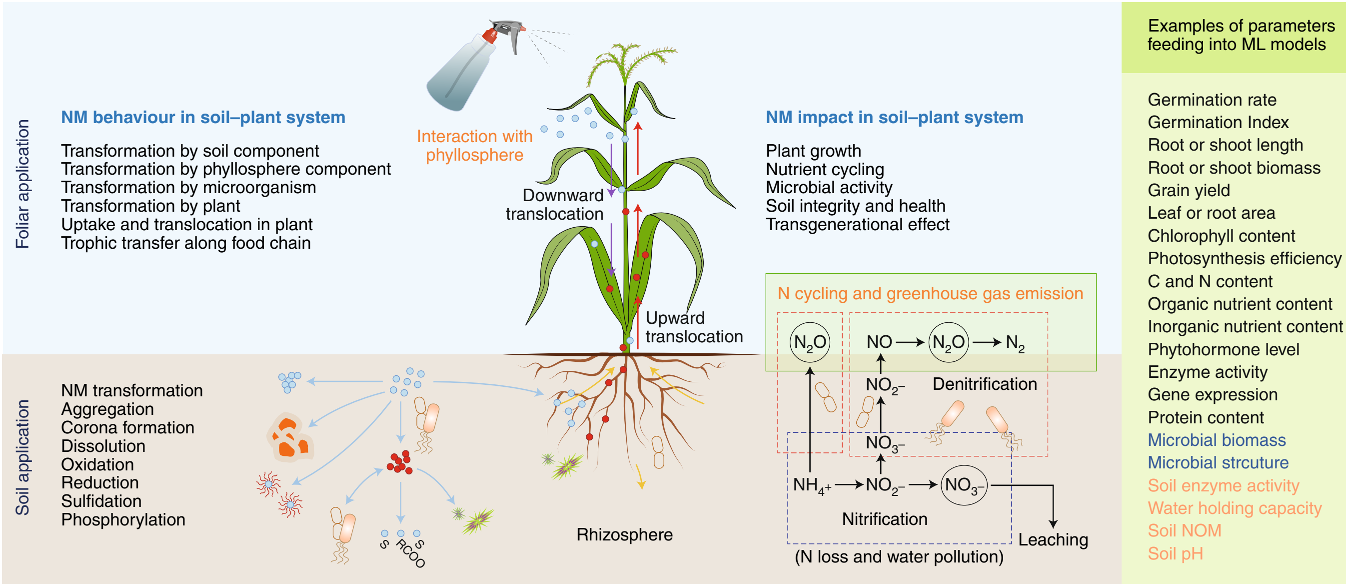

Fig. 3 | The complexity of nanomaterial behaviour in the soil–plant environment and the potential impacts in soil–plant systems. Understanding and predicting nanomaterial translocation and transformation, and identifying the optimal nanomaterial forms to retain bioavailable N species in the soil, will facilitate design of sustainably functional nanomaterials for agriculture, enhancing NUE while simultaneously reducing pollution and the need for fertilizers. Coupling this knowledge with enhanced targeting and sustained, controlled release of pesticides can be facilitated using AI to design optimal nano-agrichemicals. Among the input data for machine learning (ML) models are the nanomaterials characteristics and those of the plants and soils exposed to the nanomaterials, as indicated (a non-exhaustive list). Gene expression, proteomics and secretomics information, global soil quality and other parameters can be mined from existing databases. NOM, natural organic matter; S, sulfur-containing functional groups; RCOO, carboxylate ion.

been reported[95] and need to be assessed systematically, and predictive models need to be established. Nanomaterials may accumulate in seeds and their potential to cause transgenerational effects[96,97] are largely unknown. The presence of nanomaterials may cause enhanced uptake of contaminants by plants—for example, through binding to the nanomaterial surface and co-transport—and may amplify their adverse effects[98,99]. Such effects need to be fully understood and the use of nanoQSAR, multi-object optimization and other machine learning approaches will support this understanding and prediction.

Nanomaterials undergo numerous transformations (physical, chemical or biological) in soils and plants. For example, many nanomaterials based on metals and metal compounds such as zinc, copper and silver tend to dissolve and release metal ions, which can further react with soil and plant components such as phosphate, sulfur and chloride. These transformations may alter the original nanomaterial properties that were designed for the specific application. For example, antifungal nanomaterials such as those based on silver can be oxidized, dissolved and sulfidized in soil environments, either by interaction with the soil microbiome or within plants, and the antifungal property of the silver nanomaterials could be reduced or diminished[100]. Some transformations might release toxic components—for example, graphene oxide was reported to degrade under sunlight and release polycyclic aromatic hydrocarbon-like compounds that are likely to exhibit toxic properties and persist in the environment[101]. Development of QSAR or machine learning models that can predict the transformations of nanomaterials under a wide range of soil and temperature conditions will facilitate optimization of nanomaterials properties for specific locations. Substantial progress towards modelling of nanomaterials transformations in the environment has already been made, including environment fate models and process-based models. Combining current models with experiments will enhance next-generation nanomaterial fate and transport models in key areas, including descriptions of nanomaterial heteroaggregation, descriptions of reactive nanomaterial chemistry, increased temporal and spatial resolution and sensitivity analyses to allow simplification of model structure[102]. Efforts to develop functional assays to generate the data needed to parametrize these models are also underway[43,93,94], and can be extended to include functional assays for rhizosphere secretions in response to nanomaterials—for example, using hydroponics systems or standardized soils.

Computational tools that can predict nanomaterial transformation processes will enable manipulation or direct simulation of the transformation to maintain the nanomaterial function or modify its effects. However, the complexity of soil chemistry and the high responsiveness of plants and their secretions into the rhizosphere increase the variability and diversity of potential nanomaterial transformations (Fig. 3). Many such factors are interlinked; for example, nanomaterial transformations are affected by the soil and plant microbiome and the extracellular polymeric substances and plant root exudates around the rhizosphere. However, plant root exudate and the microbiome can affect each other and both may be altered by exposure to nanomaterials, which in turn can affect the nanomaterial transformation processes. Changes to the microbiome will affect the nitrogen-cycling processes in soil. Foliar applied nanomaterials can be translocated downwards to the roots and interact with phyllosphere components such as microorganisms and leaf exudates. All of the above areas are also subject to change and disruption as a result of climate change—for example, changes in CO_2 concentration and temperature can shift nutrient cycling, alter rates of reactions and transformations and change plant susceptibility to nanomaterials, among other effects. Therefore, the dynamic nature of the whole system needs to be considered, making this a perfect candidate for AI and machine learning solutions, by integrating existing predictive models for nanomaterials corona formation (for example, those based on binding affinities and Hamaker constants[92]) or machine learning models using biophysicochemical characteristics of proteins, nanomaterials and solution conditions via random-forest classification[47], with databases of plant and

Box 2 | Future research needs

• Determine the long-term fate of nanomaterials, including transformation, transport in soil, and uptake and translocation in plants, curate these data and the accompanying metadata into nanomaterials knowledge bases and enrich them with global soil and weather characteristics, knowledge of plant biology (including proteome, secretome and transcriptomics data), global pesticide use datasets, soil microbial community characteristics and any other relevant datasets to facilitate development of deep learning models tailored to specific nanomaterials being developed for nano-agriculture and the local environmental conditions, crop rotations and historical and future needs.

• Assess the long-term life cycle impacts of nanomaterials in agricultural ecosystems, including the trophic transfer of nanomaterials along food chains and the potential for transgenerational impacts. Integration of these datasets into the aforementioned knowledge bases will enable further iteration of the AI and machine learning models, including development of IATA and integrated agricultural systems models.

• Take a systems-levels approach (as illustrated in Fig. 3), since the whole ecosystem is interlinked with numerous co-variances, and feed this enhanced understanding into emerging regulatory frameworks. For example, regulatory frameworks for biocides in the EU do not account for impacts on soil quality or accumulation of residues in soil, which could potentially be re-mobilized by application of nanomaterials, leading to unintended consequences. A more holistic and whole-systems regulatory approach, built on whole-systems modelling approaches that can integrate a range of scenarios such as past use of pesticides into a MOOP modelling strategy including nanomaterials properties and predicted behaviours, would help to pre-empt future problems.

• Apply AI and machine learning to identify key nanospecific properties that initiate the adverse effects or beneficial function of nanomaterials from the large dataset thus obtained, thereby facilitating design of optimized (safe-by-design) nano-agrochemicals that are fully compliant with emerging regulations and achieve the desired functionality, which may include improved production rates and/or crop yields, improved soil health and resilience, improved NUE and reduced pollution from agriculture, or application of nanomaterials as sensors to tailor delivery or other interventions (Fig. 1). This will require development and implementation of MOOP modelling approaches—which have recently been applied to drug-discovery computational pipelines—to find optimal nanomaterials compositions to achieve these goals under different (and evolving) combinations of soil, climate and crop conditions.

• Integrate models addressing different aspects of the overall challenge (physics-based, process-based and data-driven) through alignment of input and output parameters and development of an IATA, as shown schematically in Fig. 2. Tailoring of the input parameters, the modelling approaches and models used with the MOOP strategy to address each of the four main application areas of nanotechnology in agriculture, and iterative development including incorporation of consensus modelling approaches as new machine learning algorithms and approaches emerge will facilitate progress and support development of commercial and open-source tools for use in regulation, and by nano-agrichemical developers, suppliers and farmers operating at different scales. To this end, in will be essential to provide user-friendly and non-expert graphical user interfaces for such models and IATA.

microbe secretomics and plant proteomes to develop corona evolution and exchange models.

Compared with prediction of small-molecule toxicity, nanoinformaticians tend to work with smaller datasets (sometimes including only a few nanomaterial variants), and typically use exposure concentrations and time points as a means to expand the dataset. Thus, evaluation of the impact of nanomaterials on NUE in a hydroponic system, for example, could assess a panel of 8–10 nanomaterials and gauge their effects alone and in combination with fertilizer at different ratios and over different timescales, and determine the nitrogen concentrations in the water and plant mass and gaseous emissions under controlled temperatures and CO_2 levels. This would provide a multi-factorial dataset for establishment of machine learning models to predict the NUE of a new nanomaterial, as long as its physicochemical characteristics fell within the domain of applicability of the model; that is, if at least one of the nanomaterials in the training and test set overlapped with the properties of the new nanomaterial. If the nanomaterials were characterized over time under different conditions—for example, in terms of their size, dissolution and acquired corona composition—further models could be built predicting corona composition and nanomaterials fate and behaviour, identifying the key nanomaterials properties and environmental factors driving the specific effect. If data on plant growth (roots and shoots) or localization of the nanomaterials in the plants were determined, increasingly complete models of NUE could be developed, taking into account the nanomaterial localization and speciation within the plant. System complexity can then be increased by moving to soils, where nanomaterial characterization is more challenging, but where models for the environmental fate of the nanomaterials—such as the NanoFASE soil–water–organism model, which predicts the fate of nanomaterials in the environment[43]—may already exist. Thus, the initial steps will be small, but as the datasets and models emerge, their integration with other models and tools into overall IATA and agricultural systems models will become feasible and achievable.

A roadmap for progress

Smart and nano-enabled agriculture combined with AI and machine learning capabilities offer an exciting convergence of technologies with the unique capability to address the overarching SDG2. The impetus for smart agriculture is therefore multi-pronged: from enhancing and sustaining productivity through nano-enabled (responsive) delivery of agrochemicals to crops, to reduction in environmental pollution and negative human health impacts from agriculture. The grand challenges in agriculture can only be solved if the power of nanomaterials can be harnessed safely, responsibly and sustainably. Nanoinformatics will have a vital role in probing the design parameters, the plant and ecosystem responses, and their co-optimization for safe and sustainable agriculture. For example, AI may predict nanomaterial impacts on the agricultural ecosystem and their performance in improving agricultural production (NUE and reduction in air and water pollution forms of key elements), by integrating experimental data from across different soil conditions, plant species, climate conditions and nanomaterial physicochemical properties to predict both the nanomaterials impacts on the agricultural system (on plants and soil) and the impacts of the agricultural system on the nanomaterials in terms of their transformations, transport and bioavailability. This will enable safer-by-design development of nano-agrichemicals and co-optimization of both safety and desired functionality of the nanomaterials. For example, the potential impact of nanomaterials for remobilization of pesticide residue contaminants of soil resulting from decades of pesticide use remains an unexplored area, and indeed monitoring of pesticide residues in soil is not currently required at the European Union

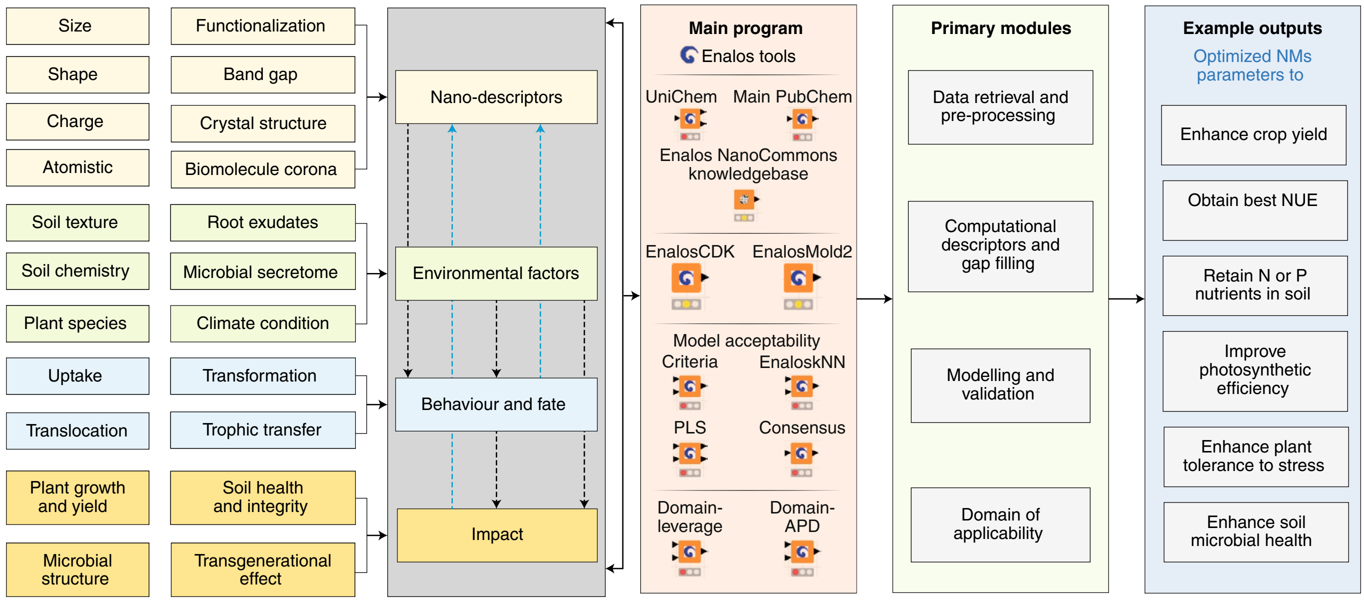

Fig. 4 | Approach to integration of AI models needed to assess nanomaterials behaviour, fate and impact in agriculture based on the interplay between nanomaterial and environmental factors including the crop type and soil characteristics. Application of automated tools for harvesting data from public databases and pre-processing and curation of the data for direct input into the AI or machine learning models—for example, using the Enalos tools[56] in KNIME—ensures that the output data from one model can serve as the input data for subsequent models, thereby facilitating model integration and development of increasingly multiplexed predictions for nano-enabled precision agriculture. A number of potential multi-object optimization machine learning modelling outputs are shown in the far right panel to inspire the development of the field.

(EU) level despite the known degradation of soil quality, in contrast to the water monitoring regulated by the EU Water Framework Directive[103]. Future research directions to address these challenges are outlined here and summarized in Box 2.

Understand the long-term fate of nanomaterials in agricultural environments. Transformation of nanomaterials will change their original designed properties, which may affect their function as fertilizers, pesticides, carriers or sensors. The transformation could occur in soil, at the plant interface (for example, root or leaf surface) or inside the plant. In soil, the transformation could be driven by soil texture and chemistry, and by interactions with soil microorganisms and animals. Plant interfaces, including the rhizosphere and phyllosphere, are critical locations for nanomaterials transformation. The transformations in these regions are driven by the dynamic and complex composition, including plant metabolites and microorganisms. Nanomaterials may also be transformed during their translocation in plant vascular structure by interacting with plant fluids. All of these areas remain largely unknown and thus generation of datasets that are deposited in open access databases is urgently required.

Another critical question is how to effectively deliver nanomaterials to target different locations in plants. This requires a clear understanding of the uptake and translocation of the nanomaterials. Both the leaf and root contain physiological barriers to prevent the entry of unwanted substances, and the structures of these two organs are very different. Nanomaterials that enter the leaf translocate downward in phloem, whereas those entering roots translocate upward in the xylem. The fluid composition and flow rate in xylem and phloem may greatly affect the translocation and accumulation of nanomaterials in plant. Data and predictive models for these questions are all required urgently.

Assess the long-term life cycle impact of nanomaterials in the agricultural ecosystem. Given the fact that repeated application of nanotechnology in agriculture will become possible in the future, long-term retention of nanomaterials in agricultural soil is inevitable. The majority of current studies regarding plant–nanomaterials interactions are phenomenological observations of nanomaterials toxicity under short-term, high-dose conditions. Long-term, low-dose effects of nanomaterials on agroecosystems therefore also need to be studied, addressing nanomaterial impacts on plant growth, microbial activity and community structure, soil health (for example, soil enzyme activity and nutrient cycling), trophic transfer of nanomaterials and transgenerational effects. Use of multiple doses, multiple sampling time points and a wide panel of nanomaterials, a range of different soil conditions or different plants under identical exposure conditions will facilitate implementation of data-hungry machine learning models, although meta-analysis and computational gap filling of smaller datasets is also helping to accelerate the pace of development of nanomaterials models.

Take a systems-level approach to nano-enabled agriculture. The behaviour, fate and impact of nanomaterials in the soil–plant system, plants and microorganisms are all interconnected. As shown in Fig. 3 and described above, change of one factor may induce a change of the whole system. Given the power of AI and the complexity of the optimization challenges facing nano-agriculture, it is clear that their convergence offers exciting new directions (Fig. 4). Using extensive existing models and datasets for soil quality, crop yield and NUE, for example, and combining these with models and datasets related to plant and microbial secretomes, nanomaterials physicochemical properties, transformations and bioavailability, and release of active ingredients, could enable important new insights into: (1) the probable transformation pathways for the nanomaterials and their resulting environmental transport and bioavailability; (2) the potential impact of the nanomaterial and its associated active ingredients (in cases where the nanomaterial is a carrier) on crop yield and NUE; and (3) potential identification of biomarkers of crop health and disease that can be used as early warning systems. Identification of data gaps can also drive the design of focused experiments to fill the gaps or to develop sub-models for gap filling or prediction of specific parameters, to be integrated into an overall model framework enabling design of combinations of nanomaterials and active ingredients that optimize NUE and minimize pollution while enhancing crop yield and potentially even nutritional (calorific) value. Integration of safe-by-design approaches and feeding forward the emerging knowledge into the updating of regulatory processes for advanced nano-enabled agricultural applications, both in fertilization and in plant protection, are also essential.

Systems-wide approaches can also support pre-emptive identification of potential challenges or solutions arising from use of nanomaterials. For example, integrating knowledge on the historical use of pesticides and the accumulation of pesticide residues in soils globally could potentially identify specific nanomaterials with high affinities for such residues, leading to their remobilization and unintended uptake into plants. Thus, the convergence of nanotechnology and AI or machine learning will also support efforts under the EU Green Deal, and could be used to identify hot spots and/or optimized nanomaterial compositions for soil remediation, for example, as well as supporting impact assessment and helping in efforts to protect soil fertility, reduce soil erosion and the overuse of nutrients, while increasing soil organic matter levels as part of an overall adoption of sustainable soil management practices, including as part of the forthcoming revision to the Common Agricultural Policy, which a recent report has suggested is only marginally consistent with the ambitions of the EU Green Deal[11]. Extensive changes to EU legislation are expected in 2021, including the EU Soil Thematic Strategy and the Zero Pollution Action Plan for Air, Water and Soil, which will encompass a range of chemicals including pesticides.

Use AI and machine learning to identify key nanospecific properties that initiate the effects or functions of nanomaterials. There are multiple physicochemical properties of nanomaterials such as size, shape, surface charge, surface area, surface reactivity and crystal structure that can influence their transformations and toxicities. AI and machine learning will enable selection of the most critical parameters that determine and predict the behaviour of nanomaterials in soil and plant systems from large datasets (Fig. 4). The use of automated data retrieval from public databases, data pre-processing and gap filling, and automated splitting of the data into test and validation sets for modelling[56] will facilitate the in silico design of NMs that can be delivered to plants efficiently. Nanomaterial transformations in different soil conditions and different rhizosphere compositions under changing climate conditions could also be predicted by integrating predictive models, enabling optimization of nanomaterials for agricultural application in a range of climatic and local conditions. Wider ecosystem effects and prediction of tripartite (nanomaterials–soil–plant) behaviours under future climate scenarios can also be predicted using, for example, Bayesian networks and deep learning approaches. Such models are especially important as they can operate under data scarcity, yet can easily incorporate new data as they emerge. Application of these emerging models to address the broader issues of food security, and to tackle SDG2—improved nutrition and promotion of sustainable agriculture—will provide important new intersectional insights and suggestions for ways forward.

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Author contributions
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