Artificial Intelligence for Nano-Engineering

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Abstract
Artificial intelligence (AI) is the simulation of human-like traits such as learning, reasoning, and problem-solving via computational systems. Nano-engineering focuses on manipulating and designing materials at the nanoscale, which exhibit unique physical and chemical properties that differ from their bulk counterparts. Traditionally, analysing these properties requires resource-intensive simulations or experiments, often limited in accuracy, time and expertise. By integrating AI, we can accelerate discoveries, optimise experimental methods, and improve the analysis of large nanomaterial datasets. This review explores the future trends of machine learning in nano-engineering research, specifically on the AI-assisted characterisation of nanomaterials, by unlocking key patterns in spectroscopical analysis and rapid interpretation of datasets in microscopy image processing. Building and training an appropriate artificial neural network (ANN) has shown to be essential in displaying the mechanism involved in intracellular transport, and determining endosome type, through analysis of Raman spectra data of DNA-functionalised single-walled carbon nanotubes (DNA-SWCNTs). Additionally, using ANNs can help determine the particle size distribution of agglomerated nanoparticles from TEM images. Using real and synthetic datasets as training, a model has been shown to produce similar relative errors compared to a manual operator, dramatically decreasing time and cost.

1 Introduction

Many modern technological advancements and applications used in our daily lives are fundamentally based on nanomaterials. With the ever-growing demand for technology, nanoscience has previously never become as prominent. Nano-engineering, an interdisciplinary field in nanoscience, focuses on manipulating and designing materials at the nanoscale (<100 nm in one dimension). At this scale, materials display unique chemical and physical properties which differ from their bulk counterparts, such as enhanced mechanical, electrical, chemical, and optical properties.[1] These properties stem from the effects of quantum size and the high surface-area-to-volume ratio that nanomaterials demonstrate. Nano-engineering investigates these phenomena to introduce new functionalities, advancing scientific progress in various industries such as medicine, energy, and electronics.[2]

This driven demand for nano-engineering has pushed for rapid advancements and throughputs in nanomaterials science discoveries, leading to an overwhelming abundance of data that must be characterised. Spectroscopic techniques such as scanning electron microscopy (SEM), transmission electron microscopy (TEM), and X-ray diffraction (XRD) are typical analytical tools for characterising nanomaterials.[3] Traditional techniques, such as quantum computational chemistry methods, for simulating these properties are inefficient, requiring substantial time, computational power, and expertise to accurately analyse and interpret results**.** Therefore, a new optimisation method is required to further accelerate the development and application of nanomaterials in nano-engineering.

This challenge can be addressed by integrating artificial intelligence (AI) and machine learning (ML) into nanomaterials research.[4] AI and ML models can analyse a vast amount of experimental or computational simulation data to establish predictive algorithms, thereby quickly and accurately predicting the properties of nanomaterials. With the aid of AI, nano-engineering can continue to play a pivotal role in addressing global challenges and shaping the future of technology and healthcare.

1.1 Artificial intelligence

Artificial intelligence is a technology that empowers computers and machines to replicate human capabilities such as learning, understanding, problem-solving, decision-making, creativity, and autonomy.[4] Machine learning is a branch of artificial intelligence that enables systems to learn from data, identify patterns, and make predictions or decisions independently. It works by training algorithms on datasets to create models that improve over time as they encounter more information. Choosing the appropriate model for the specific problem is a crucial step in advancing nano-engineering. Different ML algorithms correspond to different scopes of application, and there is currently no single algorithm that can address all problems. Although there are a variety of algorithms involved in ML, the commonly used models in the field of nanomaterials can be broadly categorised as supervised learning, unsupervised learning, and its subset: neural networks and deep learning.

Supervised learning is a type of ML where a model is trained on a labelled dataset. Meaning that for each input in the training data, the corresponding correct output is provided. The goal of the model is to learn a mapping from inputs to outputs so that it can predict the correct labels for new, unseen data. Unsupervised learning is where the algorithm is provided with unlabelled data and tasked with discovering patterns, structures, or relationships within the dataset.[5] However, what has sparked the latest talks and made the furthest advancements in recent years is in the realm of artificial and deep neural networks.

1.1.1 Artificial and Deep Neural Networks

Neural networks (NN) and deep learning algorithms are subsets of machine learning algorithms, which are directly inspired by the structure of the human brain. The network is organised into three main layers: an input layer, hidden layers and an output layer. Artificial neural networks (ANN) typically only contain none or a few hidden layers, whereas deep neural networks (DNN) contain several hidden layers, enabling them to calculate more complex relationships such as non-linear patterns.[6]

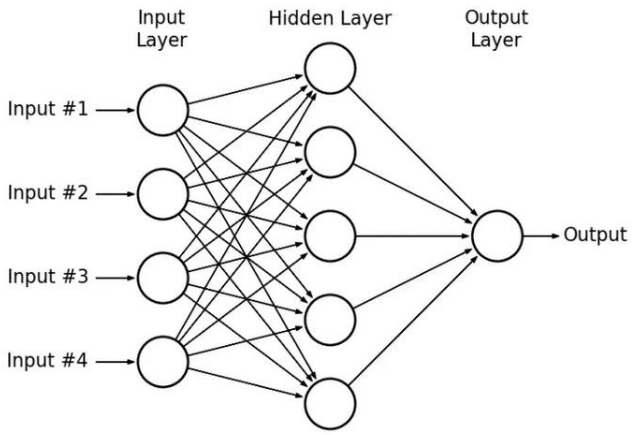

Fig.1: Schematic of the typical structure of an artificial neural network (ANN)[7]

The input layer receives raw data where the number of nodes in this layer corresponds to the number of elements being examined (features, dimensions, variables etc.) The outer layer produces a final classification, where the nature of the task is based on the number of nodes the layer contains. The hidden layers consist of one or several layers of interconnected nodes which do not have direct contact

with the outside, hence the name. Each neuron in each hidden layer calculates a weighted sum of its inputs, adds a bias term, and applies an activation function:

$$z_i = \sum_{i=0}^{n} x_i w_i + b \qquad \text{Eq. [1]}$$

Where x_i are the inputs, w_i are the weighted coefficients (strength of the connection between nodes), b is the bias in the system and z_i is the net input which determines whether the node is activated or not, this activation depends on the activation function $g(z_i)$ (ReLU, Sigmoid, etc)

$$ReLU(z_i) = \frac{z_i + |z_i|}{2} \qquad Sigmoid(z_i) = \frac{1}{1 + e^{-z_i}} \qquad \text{Eq. [2]}$$

To create an algorithm to output accurate values, the model must be trained with large samples of labelled data. ANNs typically undergo supervised machine learning using these datasets. Considering all training data, a cost function, such as the mean squared error (eq.3), is established which calculates an error between all actual and predicted values. The goal is to optimise the neural network so that the weights and biases correspond to a minimum of the cost function (eq.4), using a method such as stochastic gradient descent.[8] The step towards this minimisation in the hyper-dimensional space is defined as the learning rate, y_n (eq.5).[9] Over each training generation, the error decreases and the weighted coefficients between nodes increase, hence the accuracy of the model improves.[6]

$$MSE\ (\vec{w}, \vec{b}) = \frac{1}{N} \sum_{i=1}^{N} (o_i + \hat{o_i})^2 \qquad \text{Eq. [3]}$$

Where N is the number of training samples, o_i is the ground truth value, and $\hat{o_i}$ is the predicted value outputted from the ANN.

$$\nabla_{\vec{w},\vec{b}}\ MSE\ (\vec{w}, \vec{b}) = 0 \qquad \text{Eq. [4]}$$

$$\vec{w}_{n+1} = \vec{w}_n - y_n \nabla_{\vec{w}}\ MSE(\vec{w}, \vec{b}\,)$$

$$\vec{b}_{n+1} = \vec{b}_n - y_n \nabla_{\vec{b}}\ MSE(\vec{w}, \vec{b}\,) \qquad \text{Eq. [5]}$$

Based on how the nodes are interconnected, different architectures of ANNs and DNNs can be modified specifically for the intended application. ANNs such as Feed-forward neural networks (FFNN) send data in one direction, from the input layer to the output layer. They typically have few hidden layers and are usually used for basic linear tasks. Convolutional neural networks (CNN) are a form of deep neural networks containing convolutional layers that extract hierarchical features such as edges, shapes, and textures, and they are typically used for complex image analysis.[10] In this review, we will see how ML models such as ANNs can be used in nano-engineering to further accelerate scientific discoveries.

2 Application of AI for Nano-Engineering

AI can be combined along with traditional experimental and theoretical approaches in the field of nano-engineering to enable the acceleration of nanomaterial science discoveries, large-scale screening of datasets, material property prediction, synthesis process optimisation and much more. In this review, I will focus on one aspect, the integration of AI for the rapid characterisation of nanomaterials in nano-engineering.[11]

2.1 AI-assisted characterisation of nanomaterials

In science, characterisation techniques and establishing the properties of your product are vital for understanding your product. In nano-engineering, the structure, composition and properties of materials at the nanoscale are essential in understanding their function and performance. Using AI, rapid and accurate characterisation of spectroscopic data and nanoscale image processing can be accomplished. In this review, I will explore the research strategies of ML algorithms on spectroscopic analysis and image processing in nano-engineering.

2.1.1 Spectroscopic Analysis

Spectroscopic analysis is the most common technique used for materials characterisation in nano-engineering. Depending on the desired property, different types of spectroscopies are performed. Optical spectroscopy reveals properties of the sample material via optical analysis, for example, Infrared spectroscopy (IR) determines the functional groups in molecules from the vibrations of atoms.[12] Conventional analysis of spectroscopic data often relies on the experience and expertise of a sole operator, for which larger datasets become tedious and inefficient to handle. Results are often inconsistent and subjective to the operator. The use of machine learning algorithms can resolve these issues by producing consistent and accurate properties of nanomaterials from large spectra datasets.

Intracellular vesicular transport plays an important role in the uptake, transport, and degradation of engineered nanomaterials (ENMs) within biological cells.[13] The ENMs enter cells via endocytosis, following trafficking pathways within lysosomal vesicles in the cell, where they are sorted recycled or degraded. Understanding this mechanism assesses the effectiveness of ENMs in applications such as drug delivery and toxicity within cells. This behaviour can be analysed by the interactions of ENMs with specific types of endosomes, typically examined through spectroscopic analysis.[14] Although progress has been made in understanding the uptake and localisation of ENMs, the knowledge of the effects on the transport in intracellular pathways is limited.

A recent study involves the use of DNA-functionalised SWCNTs (DNA-SWCNTs) for intracellular processing, functioning as the signal transduction element, which gives the ability to track the processing of nanomaterials within cells.[15] Due to their unique properties, such as electrical conductivity, high surface energy and ease of functionalisation, Single-Walled Carbon Nanotubes (SWCNT) have great potential to impact intracellular pathways.[16] A key technique to measure these interactions is Raman spectroscopy, which, based on the vibrational modes of the molecules in the sample, can provide information about molecular structures and chemical bonds. Characterising the complex behaviour of ENMs within cells requires classifying the different types of endosomes which contain DNA-SWCNTs. This is done by training an appropriate ANN model.

A training dataset of compiled DNA-SWCNT Raman spectra, where only regions of interest (ROI) were considered, was used to create an ANN model. The ROIs only contained spectra segments which marked early endosome, late endosome or lysosome features, at 0,6 and 24h time points respectively. Degenerate spectra were omitted from the training set. Principal component analysis was used as a preprocessing step to avoid overfitting and reduce the dimensionality of the system. The final number of Raman spectra input for the algorithm was reduced to 44 which represented 95% of the variation of

the full training dataset. The input layer was followed by two hidden layers each with 25 nodes, which were activated using the Rectified Linear Unit (ReLU, eq.2), often used to determine non-linear relationships, whereby if the input x is greater than 0, the output is x, otherwise the output is 0. The output layer used a SoftMax function to convert the previous hidden layers' output into a class probability distribution.

$$Softmax(z_i) = \frac{e^{z_i}}{\sum_{j=1}^{n} e^{z_j}} \qquad \text{Eq. [6]}$$

The model was trained and validated on 10-fold cross-validation, where the model splits into ten segments, is trained on nine and tested on one at a time. The trained ANN model is then applied to ROIs on non-labelled Raman spectra of the DNA-SWCNTs. The model predicts the class of endosomes that each spectrum corresponds to, with high accuracy and consistency. Hence, this ANN model provides an effective way to understand the mechanisms involved in the intracellular transport and processing of nanomaterials.

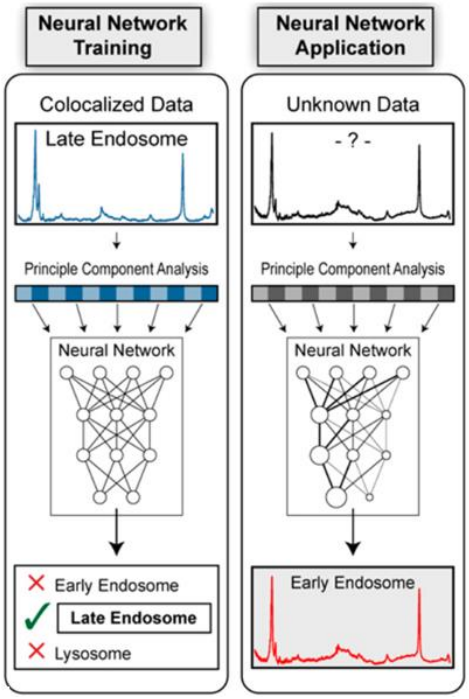

Fig.2: Schematic depicting the processing of producing an ANN model for detecting endosomal type, training the ANN with labelled data (left) and classification of unlabelled data on a trained ANN (right).[15]

2.1.2 Image processing

The characteristics of nanomaterials can also be assessed based on their typical length and size. Electron microscopy techniques like Transmission Electron Microscopes (TEM)[17] and Scanning Electron Microscopes (SEM)[18] output images that illustrate the structure of nanomaterials. Conventional image processing techniques heavily rely on experience and professional knowledge for feature extraction. Image noise and difficulties with segmentation are often challenges involved with the analysis of TEM and SEM images, as a result, it is often strenuous to produce accurate and consistent evaluations of nanomaterial properties.[19] Integrating ML models on large volumes of microscopic image datasets can create automation of feature extraction, increase accuracy and accelerate nanomaterial property predictions.[20]

Determining particle sizes for non-agglomerated particles has been performed for many decades either fully or partially autonomously in TEM. However, by contrast, determining particle sizes for an agglomerated segment heavily depends on the human operator, hence this process is expensive, laborious and inconsistent. This study shows that with the aid of an ANN, particle size analysis for agglomerated species can be autonomously implemented and determined. [21]

To train such an appropriate model, an ANN requires hundreds of thousands of labelled TEM images, however, there is no public source containing a vast amount of labelled agglomerated TEM data. Hence, synthesised TEM images with known parameters can be generated from existing images and used as a training dataset to create a suitable ANN algorithm. It is important to synthesise images which are similar to experimental TEM images, or else the model will fail.

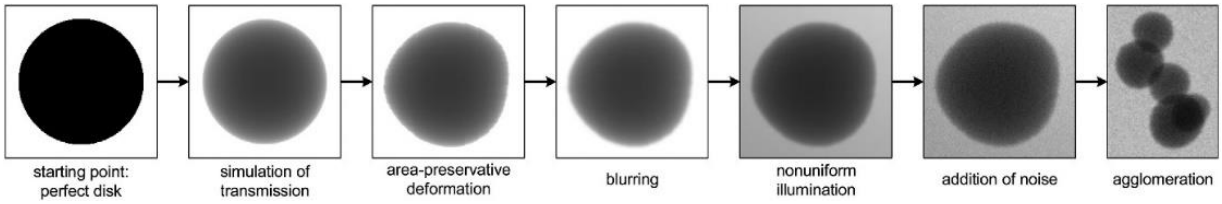

Fig.3: Elementary steps of the image synthesis of agglomerated nanoparticles for TEM images[21]

The full algorithm incorporates two different types of ANNs for determining particle sizes for agglomerated nanoparticles. The first model is a classification ANN which determines the number of particles in the agglomerate. The second model contains several regression ANNs used to analyse the regression of primary particle regions within an agglomerate, based on the count of primary particles it incorporates. This means that for an agglomerate containing five particles, five regression ANNs are used. However, since the algorithm uses a two-step process, it limits the number of particles an agglomerate contains when being analysed, meaning an agglomerate with a higher number of particles becomes excluded, hence, in this paper, the number of trained regression ANNs is limited to five and below.

After preprocessing, a total of 13 features were used to describe the agglomerate. Hence for both ANN types, the input layer contained 13 nodes. Each model also included one hidden layer and an output layer. The particle number classification ANN (PNC-ANN) consisted of 39 nodes, and the particle area regression ANN (PAR-ANN) contained a range of 11 to 124 nodes in their hidden layers, depending on the number of particles in the agglomerate. Both used a hyperbolic tangent as the activation function and a SoftMax (eq.6) function for the output. 70% of the dataset was used as training data whereas 15% was used for both validation and testing.

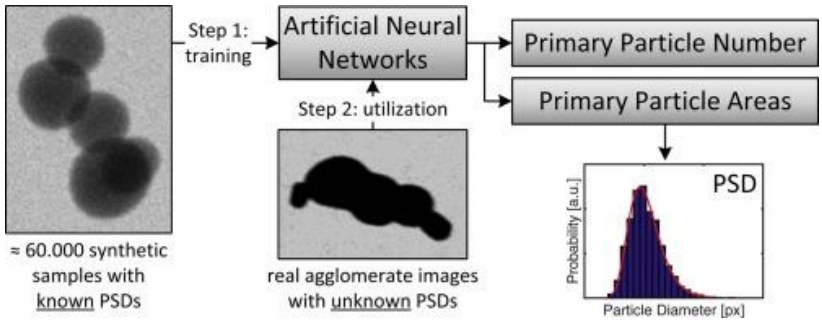

Fig.4: Simplified workflow schematic to find the size distributions of agglomerated nanoparticles in TEM images using an ANN algorithm.

With the trained algorithm, a real set of 500 TEM images of agglomerated nanoparticles was used for assessment. The results of the ANN were tested against a ground truth to calculate the relative errors of the geometric mean diameter (GMD) and geometric standard deviation (GSD), which can be shown in the table below. Although the proposed method does not match that of a manual evaluation, an acceptable level of accuracy is reached while achieving significantly shorter measurement times. Here AI can be shown to be paving a path for a higher throughput of nanomaterials discoveries and hence accelerating advancements in nano-engineering.

Table 1. Comparing errors of the GMD and GSD of analysis of 500 TEM images for the ANN algorithm, an established automated method and manual evaluation, against a ground truth[21]

Method	***GMD Error***	***GSD Error***
Proposed ANN ML Model	4.1%	5.1%
Watershed transformation	-11.6%	6.1%
Hough transformation	-20.1%	8.7%
Test person	-4.3%	-1.0%

3 Conclusions

In summary, this review emphasises the significance of incorporating AI into nano-engineering, which revolutionises the use and characterisation of nanomaterials. Two of many possible examples are shown, AI can be used for spectroscopic analysis and image processing to enhance accuracy and deliver a higher throughput of discoveries when compared to resource-extensive conventional feature extraction techniques. In the case studies reviewed, an ANN was successfully created with the ability to characterise the behaviour of nanomaterials within cells by estimating and classifying the type of endosomes which contain DNA-SWCNTs. This was done via training and evaluation of relevant Raman spectra datasets of DNA-SWCNTs. Rapid analysis of particle size distributions of agglomerated nanoparticles from TEM images was successfully carried out by using a ML algorithm comprised of classification and regression ANNs. AI proves essential, increasing discovery throughput and revealing new trends, establishing nano-engineering as a leading field for technological and scientific progress.

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