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Environmental Pollution and Cytotoxic Effects of Metallic Nanoparticles: Integrating Mechanistic Toxicology with Support Vector Regression-Based Predictive Modeling

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Abstract

The prevalent application of metallic nanoparticles (NPs) in various industries, biomedical sector, agricultural field, and products for consumers leads growing concerns regarding their environmental release and potential toxicological effects. Nanoparticles such as silver (Ag) NPs, zinc oxide (ZnO) NPs, Titanium Dioxide (TiO_2) NPs, copper (Cu) NPs, & gold (Au) NPs possess unique physicochemical properties that enhance their functionality but also increase their environmental mobility and biological reactivity. Upon entering aquatic and terrestrial ecosystems, these nanoparticles can accumulate and interact with living organisms, potentially disrupting ecological balance. Numerous studies have demonstrated that metallic nanoparticles induce cytotoxic effects through mechanisms including oxidative stress, membrane damage, mitochondrial dysfunction, inflammation, and DNA damage. *In - vitro* live cell-based assays have been extensively used to measure nanoparticle-induced toxicity. Understanding the environmental fate and cytotoxic mechanisms of metallic nanoparticles is crucial for developing safer nanomaterials and establishing effective regulatory strategies for environmental protection and public health.

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Introduction

Nanotechnology has arisen as the most transformative scientific disciplines of the 21st century, revolutionizing applications in medicine, agriculture, environmental engineering, electronics, food technology, cosmetics, and material science. Metallic and metal oxide nanoparticles, particularly silver (Ag) NPs, zinc oxide (ZnO) NPs, Titanium Dioxide (TiO_2) NPs, copper-ion nanoparticles (CuNPs/CuO NPs), and gold nanoparticles (AuNPs), have catch significant attention due to their noble physicochemical properties, including higher surface area to the volume ratio, increased catalytic activity, optical characteristics, antimicrobial potential, and tunable surface chemistry. These properties have enabled their widespread incorporation into commercial and industrial products ranging from wound dressings, drug delivery systems, biosensors, paints, textiles, food packaging materials, and agricultural formulations to products for personal use such as UV sunscreens and variety of cosmetics (Wang et al., 2024; Chandoliya et al., 2024). As global production and consumption of nanomaterials continue to increase, concerns regarding their environmental release, persistence, bioaccumulation, and toxicity have become increasingly important.

Impact of nanoparticles on environment

The extensive use of metallic nanoparticles inevitably leads to their introduction into the environment through multiple pathways. Industrial discharges, wastewater treatment plant effluents, agricultural runoff, landfill leachates, atmospheric deposition, and degradation of nanoparticle-containing consumer products represent major sources of environmental contamination. Due to their nanoscale dimensions, metallic nanoparticles exhibit high mobility and can readily disperse through aquatic, terrestrial, and atmospheric systems. Unlike bulk materials, nanoparticles possess enhanced reactivity and a greater capacity to interact with biological molecules, increasing the likelihood of unintended ecological consequences. Recent investigations have indicated that metal-based nanoparticles may accumulate in sediments, soil matrices, aquatic organisms, and food chains, thereby contributing to long-term environmental pollution and ecosystem disruption (Wang et al., 2024; Xiao et al., 2024). The risks for ecology are associated with all these nanomaterials are further amplified by their ability to undergo physicochemical changes, including aggregation, oxidation, dissolution, and interactions with organic matter available naturally, which can alter both their environmental fate & biological toxicity.

Role of NPs in cytotoxicity

Among metallic nps, Ag nanoparticles are among the most extensively produced nanomaterials (NMs) worldwide because of the remarkable antimicrobial properties. AgNPs are incorporated into medical devices, wound dressings, textiles, coatings, and water purification systems. However, environmental exposure to AgNPs has raised concerns regarding toxicity toward beneficial microorganisms, algae, aquatic invertebrates, and higher organisms. Studies have showcased that Ag nanoparticles can generate ROS (reactive oxygen species), which ultimately disrupt membrane integrity, reacting with cellular respiration, and finally oxidative stress is induced in exposed organisms (Sati et al., 2025, Singh D et. al., 2026). Similarly, titanium dioxide nanoparticles are widely utilized in paints, photocatalytic systems, self-cleaning surfaces, and sunscreens. Although TiO_2 nanoparticles are often considered relatively stable, photoactivation under ultraviolet radiation can trigger ROS formation, leading to oxidative damage in living biological systems (Chandoliya et al., 2024). Zinc oxide nanoparticles, another important class of metal oxide nanomaterials, are frequently employed in cosmetics, pharmaceuticals, food packaging, and antimicrobial applications. Their dissolution can release Zn^{2+} ions, which contribute significantly to cellular toxicity through oxidative stress and disruption of ion homeostasis. Copper-based nps are extensively used in agriculture, catalytic reactions, and antimicrobial (antibacterial, antifungal) formulations, yet their ability to release copper ions may induce severe cytotoxic and genotoxic effects. Gold nanoparticles, while generally regarded as biocompatible and valuable for biomedical applications, have also been reported to influence cellular signaling pathways, inflammatory responses, and oxidative balance depending on particle size, morphology, concentration, and surface functionalization (Kim et al., 2025).

The effects on biological system of metallic nanoparticles are closely associated with their capacity to slip in biological barriers and react with cellular structures. Following exposure through breathing, dermal contact, ingestion, or intravenous administration, nanoparticles may enter systemic circulation and accumulate in various organs. Numerous studies have flagged nanoparticle deposition in the liver, kidneys, lungs, spleen, brain, and cardiovascular tissues (Hadrup et al., 2025). Once internalized by cells, nanoparticles can localize within lysosomes, mitochondria, endoplasmic reticulum, and nuclei, where they interfere with normal cellular functions. Oxidative stress is widely recognized as the primary mechanism underlying nanoparticle-induced cytotoxicity. Excessive ROS generation swaps endogenous antioxidant defenses, which leads resulting in the protein oxidation, lipid peroxidation, mitochondrial dysfunction, DNA strand breaks, and activation of inflammatory pathways. Persistent oxidative damage may ultimately trigger apoptosis, necrosis, autophagy, or ferroptosis, depending on the nature and extent of exposure (Kim et al., 2025; Tamilselvi et al., 2025).

At the organ level, prolonged exposure to metallic nanoparticles has been seen together with a broad spectrum of worsen health outcomes. Hepatic accumulation may impair detoxification processes and induce inflammatory responses, while renal deposition can compromise filtration and excretory functions. Inhaled nanoparticles may penetrate deep into pulmonary tissues, causing inflammation, fibrosis, and respiratory dysfunction. Emerging evidence also indicates that certain nanoparticles can penetrate the BBB (blood–brain barrier) and contribute to neurotoxicity through oxidative stress and neuroinflammatory mechanisms. Furthermore, cardiovascular toxicity has become an area of increasing concern, as metal-based nanoparticles have been shown to impair endothelial function, increase vascular permeability, promote thrombosis, and induce apoptosis in cardiovascular cells (Kim et al., 2025). These findings highlight the necessity of comprehensive toxicological evaluation for both environmental and biomedical applications of nanomaterials.

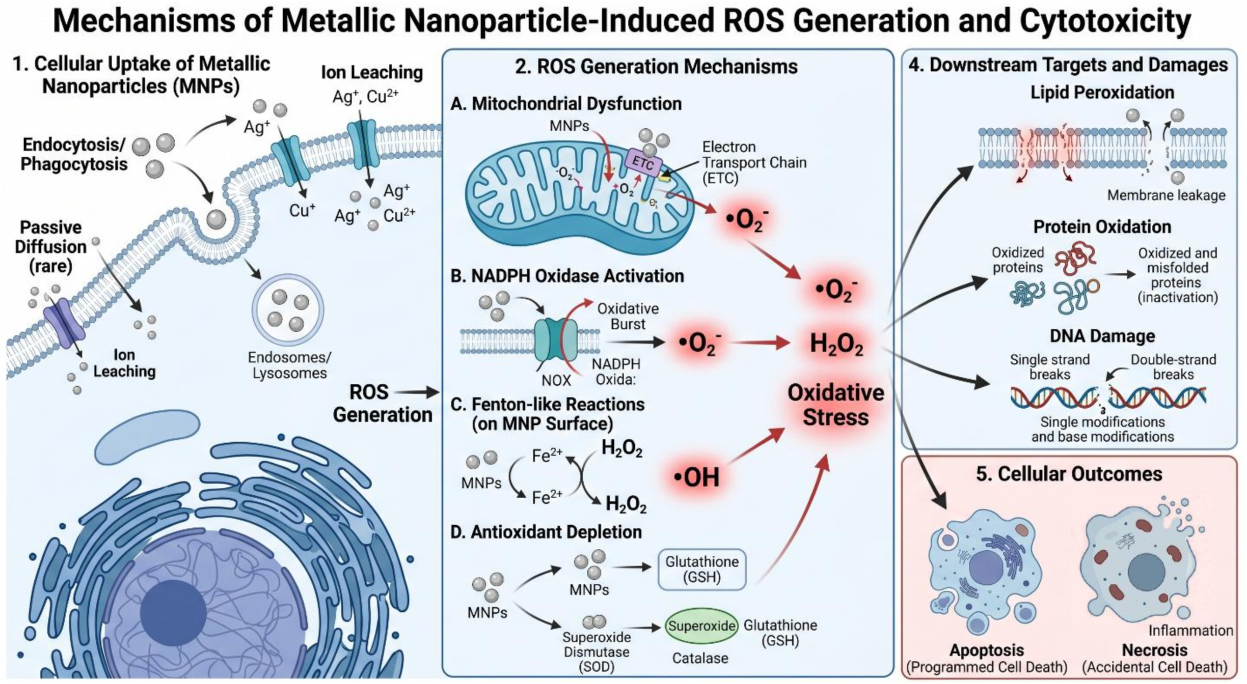


Fig. 1: Generation of ROS and mechanism of cell death

Traditional methods for evaluating nanoparticle toxicity primarily rely on experimental approaches involving cell cultures, animal models, and biochemical assays. In vitro cytotoxicity assessments commonly employ MTT, XTT, WST-1, LDH release, Alamar Blue, flow cytometry, and live/dead staining techniques to quantify changes in cell viability, membrane integrity, metabolic activity, oxidative stress, and apoptotic signaling. Although these approaches give valuable mechanistic details, they are often labor-intensive, time-consuming, expensive, and ethically challenging when extended to animal studies. Consequently, there is growing interest in computational approaches capable of predicting nanoparticle toxicity using physicochemical descriptors and biological response data.

Nanoparticles and QSAR

Understanding of nanomaterial's toxicity is central to prediction of potential of nano materials. This information will likewise play main role in improving of new nanotherapeutics. While there are numerous approaches to move toward this issue, it is quite clear that nanotoxicology is a genuinely multiscale endeavour, incorporating cellular, molecular and organismic experiences. Coupling of these examinations with the tools provided through polymer, materials and organic synthesis will give a productive field to both fundamental and applied bio nanotechnology (Kim et al., 2013). The order of NP highlights which is a concern for cytotoxicity is a difficult question. For instance, the question arise that is the size of NP more predictive than the material or surface? Very few methodologies are present which try and successfully convey a hypothesis of nanoparticles toxicity directly through either models or quantitative structure-activity relationships. Having regularly based model with a restricted informational index from a selective investigation instead of thinking about the "entire" group of distributed proofs. Basically, examination, or information mining and information extraction with writing information, can uncover associations that were somehow not clear in the first research. To these different procedures are already proposed further for determining properties and noticing of cytotoxic effects. Up till date many attempts for meta-examination of appropriated data have already been confined to two explicit sorts of nanoparticles, specifically quantum dots and carbon nanotube. (Labouta et al., 2019). After almost fifty decades, QSAR modelling has set up itself very major computational molecular demonstrating methodologies among various techniques available. QSAR modelling can be portrayed by collection of distinct set of rules and procedures that empower the expert use of the technique for investigating and exploring truly developing collection of biologically dynamic chemical compounds. Tropsha et al examined most basic QSAR modelling schedules as best practices. They talked about these systems with regards to best practices in this field. Demonstrating this work process that is centred around accomplishing models of the external predictive power and highest statistical rigor. Specific components of the work process comprise of data preparation including chemical structure (and whenever the situation allows, related biological information) curation, anomaly detection, dataset adjusting, and model validation. Particularly emphasis is given to approve models, both externally and internally, just as the necessarily to characterize model applicability areas that ought to be utilized where models are used for predicting external mixtures or compound libraries. At last, a few instances of effective uses of QSAR models for screening to distinguish experimentally confirmed hits (Tropsha, 2010). Holden et al. gave the conclusion that an important part of assessing toxicity of NPs is assumed by test procedures which includes HTS/HCS (high throughput/content screening). In any case, getting confirmation from such bioassays is tedious and regularly costly. In the special occurrence of NPs, this stems from the way that they epitomize a huge compound variety, shapes, extent of types, sizes, etc, obviously identified with a wide area having scope of different biological behaviors. Thus, it is basically hard to cover and filter the chemical-natural space with the use of test procedures or all unfeasible to adjust to the impacting of nano enabled items available. One way to deal with easing up the above issues is to involve computational strategies that could well guide in both the prioritization & danger evaluation of NPs. Among them, quantitative-structure activity (QSAR) model or quantitative structure toxicity relationship (QSTR) models are very useful in the virtual assumption for toxic levels of NPs, helping with supporting the quest for safer nanomaterials, and giving the establishments concerning the various important aspects for the toxic effects (Concu et al., 2017). A QSAR (quantitative structure activity relationship) examination of 17 MNPs (metal oxide nanoparticles), regarding their light governed toxicity to *Escherichia coli* was introduced with light induced toxicity, was created with the use of quantum compound methodologies. A straightforward, genuinely huge QSAR model having value of $F = 33.83$, and $R^2 = 0.87$ was viably made for the gathering subject to 2 descriptors, preeminent and the metal oxide and its electronegativity. Additionally, the most correct connection has $F = 20.51$ value and $R^2 = 0.804$ value) and these values are attained by use of 2 descriptors warmth limit and the energies of metal oxide namely the α and β LUMO energies to anticipate the photograph actuated poisonousness of MNPs. Divulgence of these persuasive atomic descriptors which are very important in explaining that frameworks and for prediction of the natural peril related with delivering metal oxide nanoparticles. Additionally, the already made model might be having a job in assembling and futuristic planning of safe nanomaterial (Pathakoti et al., 2014). The computational approaches developed have progressed as useful as alternatives to comprehend the opposing impact of the use of nanoparticles on the human wellbeing and the climate. The capacity of using QSAR (quantitative structure activity relationship) demonstrating to develop really basic models for anticipation of cytotoxicity examination of different metal oxide nanoparticles. For portraying nanostructure data of NPs, SMILES based ideal descriptors were incorporated by original sort of nano specific hypothetical descriptors. Escherichia coli cells and HaCaT cells were applied with some new descriptor to display MeOx NP cytotoxicity correlation reason. These two cells were further used for exploring the size variation over cytotoxicity. Further forecoming about QSAR were then completely approved, and broadly contrasted and others as of late conveyed models. The findings displayed the heartiness, legitimacy and predictivity of these QSAR models. Predominately nanostructure and its factors obligated for metal oxide nanoparticle whose cytotoxicity were perceived through QSAR model translation. These outcomes or result affirmed to have different segments for these 2 sorts of cells. The model already proposed can be needed in forecast of cytotoxicity of the original NPs only from the as of late developed descriptors, and offer direction to zeroing in on the plan and assembling of more protected nanomaterials with required properties (Yong Pan et al., 2016)

Integration of ML (machine learning)

Recent advances in AI (artificial intelligence), machine learning (ML), and nano-informatics have transformed the field of nanotoxicology by enabling predictive modeling of nanoparticle-induced biological effects. Machine learning algorithms can identify complex nonlinear relationships between nanoparticle characteristics and toxicity outcomes that may not be apparent through conventional statistical analyses. Parameters such as particle size, zeta potential, shape, surface area, concentration, dissolution rate, chemical composition, and exposure duration can be integrated into predictive models to estimate cytotoxic responses (Singh et al., 2023; Yousaf, 2024). These computational approaches significantly reduce the need for extensive experimental testing while accelerating hazard identification and risk assessment.

Among the available machine learning techniques, Support Vector Regression (SVR) has emerged as a particularly powerful method for quantitative toxicity prediction. SVR is derived from Support Vector Machine (SVM) theory and is specifically designed to model continuous response variables. The algorithm operates by identifying an optimal hyperplane that minimizes prediction errors while maintaining strong generalization performance. Unlike traditional regression methods, SVR effectively handles high-dimensional datasets and nonlinear relationships through using of kernel functions such as polynomial kernels, radial basis functions (RBF), and sigmoid kernels. These characteristics make SVR highly suitable for nanotoxicology applications, where complex interactions among physicochemical properties often govern biological responses.

In nanotoxicity prediction studies, SVR models have been successfully applied to estimate cell viability, oxidative stress levels, inflammatory responses, and dose-dependent toxicity endpoints. By integrating experimental cytotoxicity datasets with nanoparticle descriptors, SVR can identify critical determinants of toxicity and generate robust predictive frameworks. Such models enable researchers to prioritize high-risk nanomaterials, optimize nanoparticle design, and support safer-by-design strategies. Furthermore, the combination of SVR with feature selection techniques, quantitative structure–activity relationship (QSAR) modeling, and high-throughput screening data has significantly improved prediction accuracy and interpretability (Singh et al., 2023; Xiao et al., 2024).

The collaboration of environmental nanotoxicology with machine learning represents a promising approach for addressing the growing challenges associated with nanoparticle pollution. As the production by industries & utilization of metallic nanoparticles continue to enhance globally, the development of reliable predictive models is essential for evaluating potential ecological and human health risks. Therefore, understanding the environmental behavior, cellular interactions, organ-specific toxicity, and computational prediction of metallic nanoparticle-induced cytotoxicity is important for ensuring the sustainable development of nanotechnology and the protection of environmental and public health.

Methodology

Data Collection

A dataset comprising cytotoxicity information of metallic nanoparticles was compiled from peer-reviewed research articles published between 2021 and 2026. The related studies were identified through literature searches in PubMed, ScienceDirect, Google Scholar, Scopus & Web of Science using keywords like "metallic nanoparticles", "cytotoxicity", "silver nanoparticles", "titanium dioxide nanoparticles", "zinc oxide nanoparticles", "copper nanoparticles", "gold nanoparticles", "cell viability", and "nanotoxicity". Only studies reporting quantitative cytotoxicity outcomes and physicochemical characteristics of nanoparticles were included. The extracted information consisted of nanoparticle type, particle size, surface charge (zeta potential), shape, concentration, exposure duration, cell line, and percentage cell viability. Studies lacking complete experimental information were excluded from further analysis.

Dataset Construction

The extracted data were organized into a structured dataset in Microsoft Excel and subsequently imported into Python for computational analysis.

The following nanoparticle descriptors were used as independent variables:

- Nanoparticle type
- Particle size (nm)
- Surface area (m^2/g)
- Zeta potential (mV)
- Exposure time (h)
- Shape and morphology
- Concentration (µg/mL)

The target variable was: Cell viability (%)

Cell viability was selected as the primary indicator of cytotoxicity because it is one of the most commonly reported endpoints in nanotoxicological studies.

Data Preprocessing (Curation)

Data curation was done to improve dataset quality and enhance model performance.

Missing Value Treatment

Records containing excessive missing values were filtered from the dataset. Remaining missing values were imputed using median (Md) values for numerical features and mode (Z) values for categorical features.

Outlier Detection

Extreme observations were identified using the IQR (Interquartile Range) method and visualized through boxplots. Outliers resulting from experimental errors were excluded.

Categorical Encoding

Categorical variables such as nanoparticle type and cell line were changed / transformed into numerical representations / values using One-Hot Encoding.

Feature Scaling

Because machine learning algorithms are sensitive to identify differences in feature magnitude, all numerical variables were normalized using Min-Max Scaling.

The scaling procedure transformed each feature into a range between 0 and 1 according to:

[

$$X_{scaled}=\frac{X-X_{min}}{X_{max}-X_{min}}$$

]

where:

- X = original value
- Xmin = minimum value
- Xmax = maximum value

Feature scaling ensured equal contribution of all descriptors during model training and prevented dominance of variables with larger numerical ranges.

Exploratory Data Analysis

EDA (Exploratory Data Analysis) was done to understand relationships among variables and identify trends within the dataset.

The following analyses were performed:

- Summary statistics
- Distribution analysis
- Correlation matrix
- Heatmap visualization
- Pairwise feature relationships

Pearson correlation coefficients were calculated to determine the strength of association between nanoparticle descriptors and cytotoxicity outcomes.

Feature Selection

Feature selection was performed to identify the most critical physicochemical properties affecting cytotoxicity.

The process involved:

- Correlation-based feature selection
- Recursive Feature Elimination (RFE)
- Feature importance ranking

The selected features were used as inputs for model development to reduce dimensionality and improve prediction accuracy.

Selection of machine learning algorithm using IBM Watson Studio

IBM Watson studio is a web server based on cloud which provides number of services like AI, ML, Data analysis, cloud computing etc. It provides a virtual environment for development of machine learning algorithm. In ML section, it has option in which one can automatically generates the ML model or can generate model using Jupiter notebook.

It also provides an edge over other platforms. If one is not sure about which type of algorithm is suitable for the dataset made by him/her, this server can predict best and suitable algorithm by analyzing the dataset (fig. 2). It is a paid server but free trial is also available. It supports young coders to practice and learn about various technologies used by IBM company itself. It also provides spaces on virtual clouds; hence it will not use host machine for the storage of its results etc. In its trail version it only supports one service at a time. For using multiple services at a time, plan needs to be upgraded and that is paid.

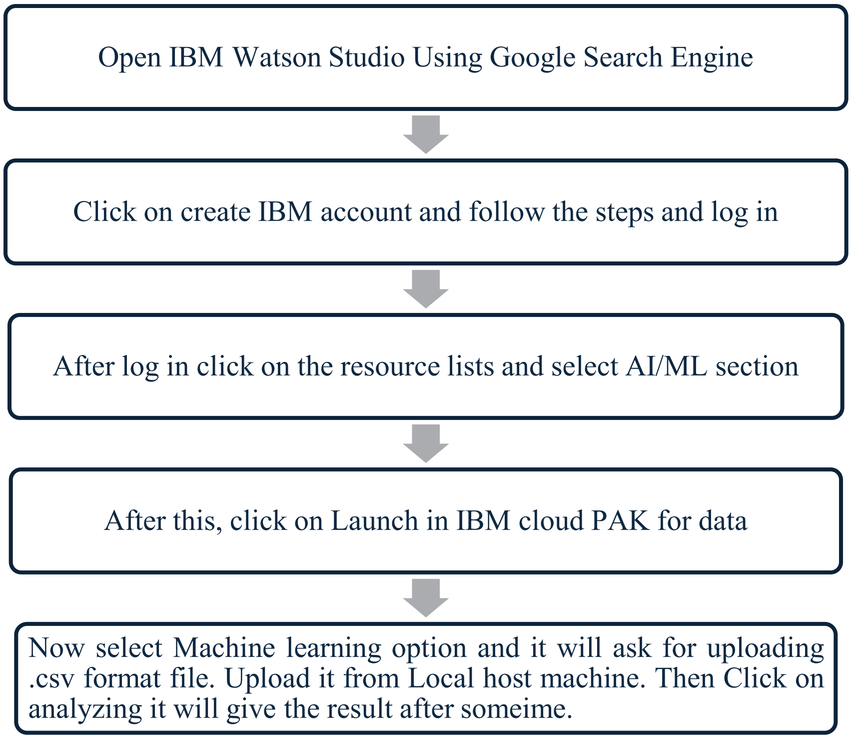


Fig 2: - Flow chart showing various steps using IBM Watson Server

Support Vector Regression

SVR is a part of Support Vector Machine. If the classification problem is the then SVM is used, while for the regression problem, SVR is used. Support Vector Regression can be used for linear as well as non-linear data.

SVR is different form SVM because SVM is used for classify the data with discrete categorical variable while SVR, a kind of regressor, used to predict continuous data. In MLR or general regression model, the focus is on to minimize the error while in SVR, the marginal lines / functions has been incorporated in the model itself. The marginal functions automatically deal with error function and give more accurate results.

SVR has following steps: -

Firstly, all the libraries will be imported in its proper format. These libraries have some in built function by which one can make its model. The libraries mainly used for reading the dataset, data visualization, splitting the data set, training and testing of the model etc.

After importing the libraries, dataset need to be read using library function.

- Once the dataset is read properly, the X and Y have to be declared. X consists all the variables which are independent in nature while Y consists dependent variable.
- After declaration of X and Y, train- test- split function is used to split the X and Y into training one and testing dataset. The model will learn from training dataset and evaluate itself. Once everything will be at its best, model will be completed.
- At the time of building model, Kernel will be selected. These Kernel will play important role in marginal lines optimization. Kernel will be selected based upon problem but sigmoid kernels are generally used.
- Once the model is generated, the prediction values are calculated using the testing dataset.

- After this correlation coefficient is calculated for both the dataset. It is to ensure that model has good accuracy or not.
- After this several others scores are all calculated like Root Mean Squared Error, Variance, Mean Squared Error etc. These all are used for evaluation of the model.

Validation of model using cross validation function

Cross validation is a method to validate and evaluate the model. In this Cross validation, the dataset given is divided into subset which is considered as testing dataset (validation dataset). For k fold cross validation, in each fold this subset will be different. Hence, it's the best way to validate model because chances are getting selected for validation are equal for all the data points. Hence k fold cross validation checks the model accuracy. As the model were trained on one fixed subset and another subset (testing) was also fixed. The model made predictions based upon this.

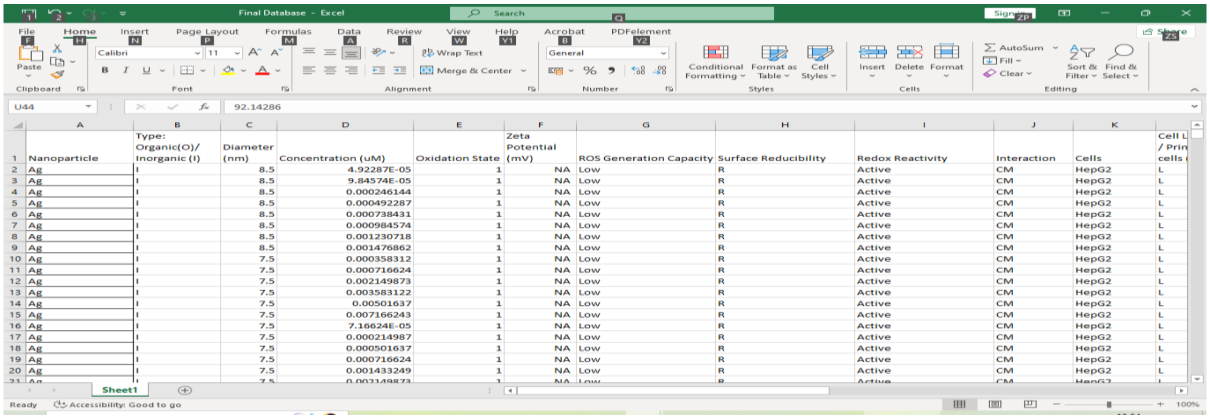
But in real, model is validated in this method where subsets of training and testing are not fixed. Now model predicted and the scores were given. In this way the model is validated. If model is not showing appropriate result, then once again model is optimized. It is an iterative process and give accuracy of the model.

Result & Discussion

Formation of Dataset

Around 100 research papers with appropriate keywords were analyzed and a dataset with 1015 x 21 was prepared. The prepared dataset has noise in it. Hence it was further optimized or curated for further study.

Fig. 3: Sample of prepared dataset



U44 92.14286

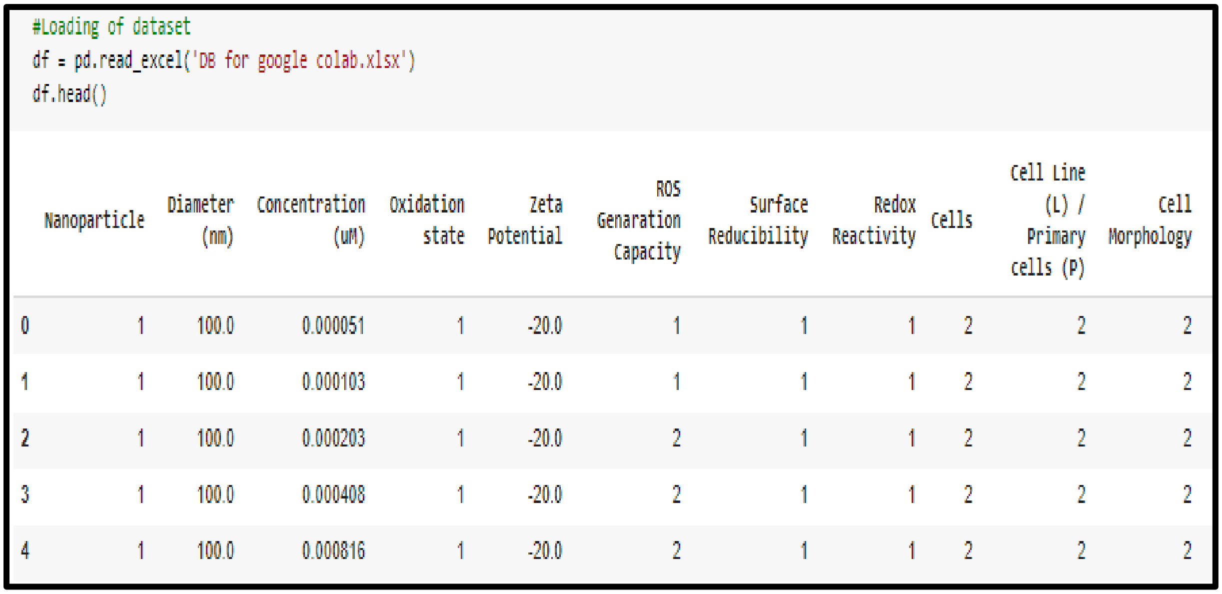
	A	B	C	D	E	F	G	H	I	J	K	
1	Nanoparticle	Type: Organic(O)/ Inorganic (I)	Diameter (nm)	Concentration (uM)	Oxidation State	Zeta Potential (mV)	ROS Generation Capacity	Surface Reducibility	Redox Reactivity	Interaction	Cells	Cell L / Prin cells
2	Ag	I	8.5	4.92287E-05	1	NA	Low	R	Active	CM	HepG2	L
3	Ag	I	8.5	9.84574E-05	1	NA	Low	R	Active	CM	HepG2	L
4	Ag	I	8.5	0.000246144	1	NA	Low	R	Active	CM	HepG2	L
5	Ag	I	8.5	0.000492287	1	NA	Low	R	Active	CM	HepG2	L
6	Ag	I	8.5	0.000738431	1	NA	Low	R	Active	CM	HepG2	L
7	Ag	I	8.5	0.000984574	1	NA	Low	R	Active	CM	HepG2	L
8	Ag	I	8.5	0.001230718	1	NA	Low	R	Active	CM	HepG2	L
9	Ag	I	8.5	0.001476862	1	NA	Low	R	Active	CM	HepG2	L
10	Ag	I	7.5	0.000358312	1	NA	Low	R	Active	CM	HepG2	L
11	Ag	I	7.5	0.000716624	1	NA	Low	R	Active	CM	HepG2	L
12	Ag	I	7.5	0.002149873	1	NA	Low	R	Active	CM	HepG2	L
13	Ag	I	7.5	0.003583122	1	NA	Low	R	Active	CM	HepG2	L
14	Ag	I	7.5	0.00501637	1	NA	Low	R	Active	CM	HepG2	L
15	Ag	I	7.5	0.007166243	1	NA	Low	R	Active	CM	HepG2	L
16	Ag	I	7.5	7.16624E-05	1	NA	Low	R	Active	CM	HepG2	L
17	Ag	I	7.5	0.000214987	1	NA	Low	R	Active	CM	HepG2	L
18	Ag	I	7.5	0.000501637	1	NA	Low	R	Active	CM	HepG2	L
19	Ag	I	7.5	0.000716624	1	NA	Low	R	Active	CM	HepG2	L
20	Ag	I	7.5	0.001433249	1	NA	Low	R	Active	CM	HepG2	L

Dataset processing

This dataset was further analyzed using python programming for data analytics using libraries like matplot, numpy, pandas etc. This dataset was further refined and made suitable for machine learning algorithm. The final dataset has 321 rows and 21 columns.

Using the feature selection method for non linear dataset, the heatplot was generated. By analyzing the fig. 6; following columns were selected as independent variable for cell viability.

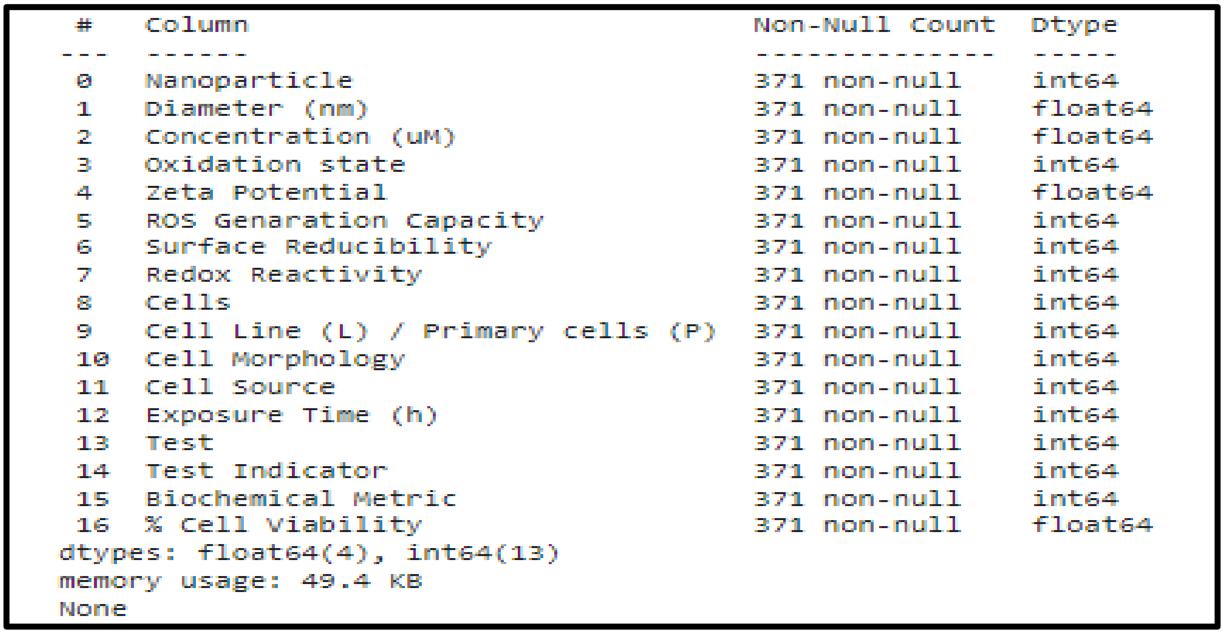
- Nanoparticle
- Concentration
- ROS Generation Capacity
- Zeta Potential (mV)
- Oxidation state
- Diameter (nm)
- Redox Reactivity
- Exposure Time (h)
- Cells
- Surface Reducibility
- Cell Morphology



```
#Loading of dataset
df = pd.read_excel('DB for google colab.xlsx')
df.head()
```

	Nanoparticle	Diameter (nm)	Concentration (uM)	Oxidation state	Zeta Potential	ROS Genaration Capacity	Surface Reducibility	Redox Reactivity	Cells	Cell Line (L) / Primary cells (P)	Cell Morphology
0	1	100.0	0.000051	1	-20.0	1	1	1	2	2	2
1	1	100.0	0.000103	1	-20.0	1	1	1	2	2	2
2	1	100.0	0.000203	1	-20.0	2	1	1	2	2	2
3	1	100.0	0.000408	1	-20.0	2	1	1	2	2	2
4	1	100.0	0.000816	1	-20.0	2	1	1	2	2	2

Fig.4: - Dataset reading using python



```
 #   Column                              Non-Null Count  Dtype  
---  ------                              --------------  -----  
 0   Nanoparticle                        371 non-null    int64  
 1   Diameter (nm)                       371 non-null    float64
 2   Concentration (uM)                  371 non-null    float64
 3   Oxidation state                     371 non-null    int64  
 4   Zeta Potential                      371 non-null    float64
 5   ROS Genaration Capacity             371 non-null    int64  
 6   Surface Reducibility                371 non-null    int64  
 7   Redox Reactivity                    371 non-null    int64  
 8   Cells                               371 non-null    int64  
 9   Cell Line (L) / Primary cells (P)   371 non-null    int64  
 10  Cell Morphology                     371 non-null    int64  
 11  Cell Source                         371 non-null    int64  
 12  Exposure Time (h)                   371 non-null    int64  
 13  Test                                371 non-null    int64  
 14  Test Indicator                      371 non-null    int64  
 15  Biochemical Metric                  371 non-null    int64  
 16  % Cell Viability                    371 non-null    float64
dtypes: float64(4), int64(13)
memory usage: 49.4 KB
None
```

Fig.5: - Dataset detailed overview

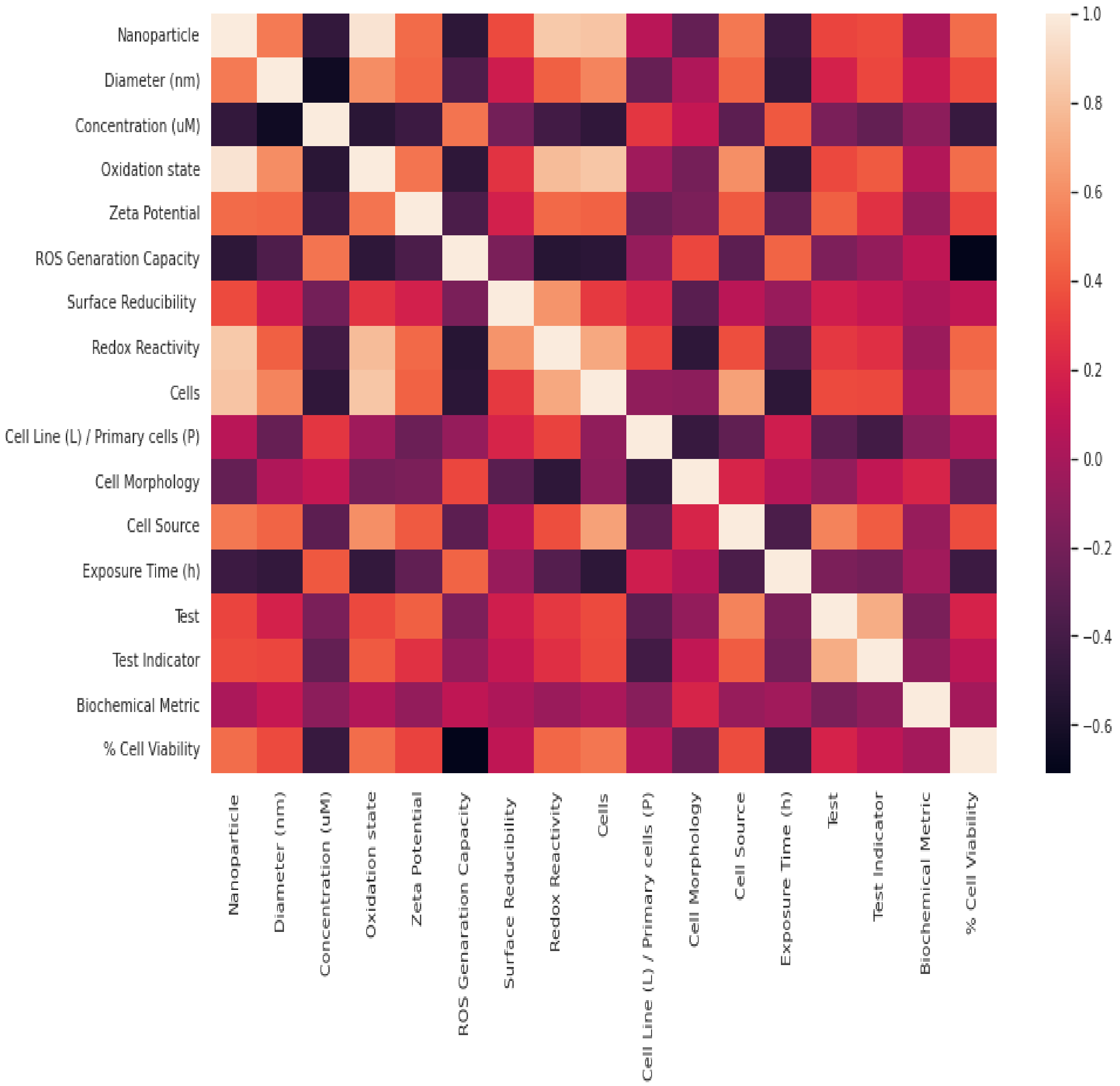
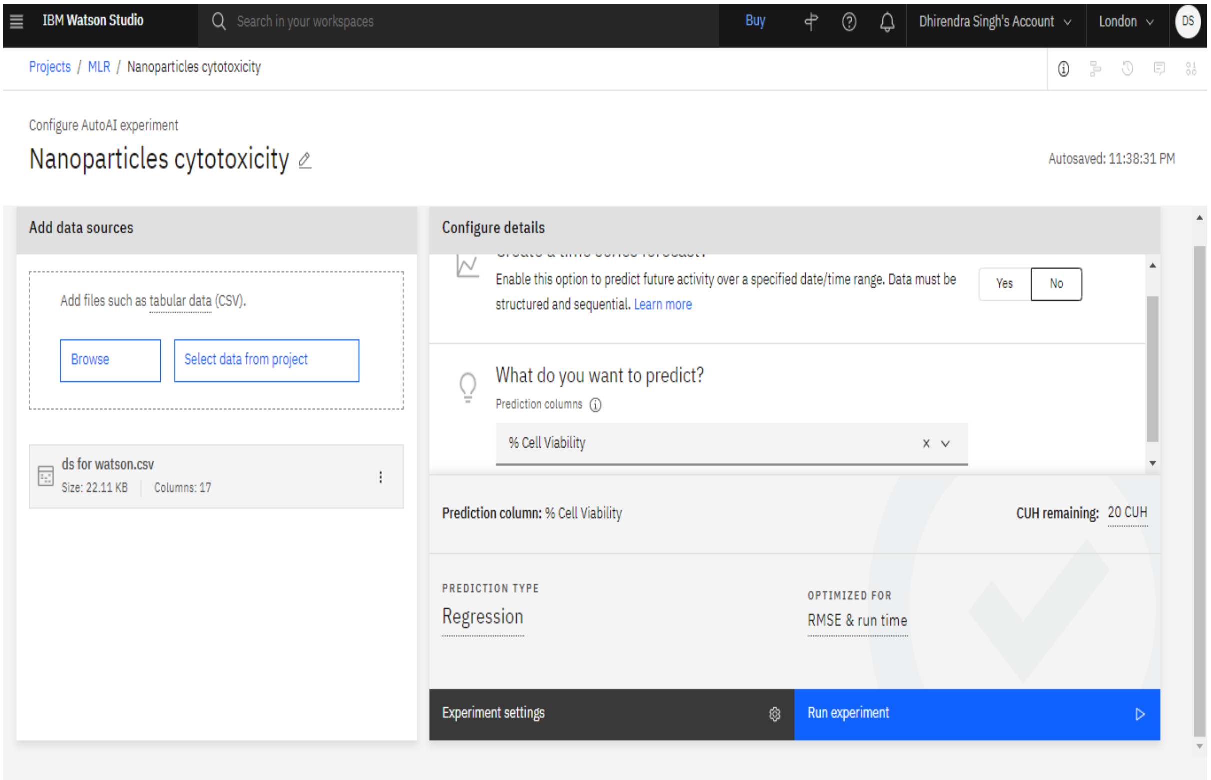


Fig.6: - Heatmap for nonlinear relationship

ML algorithm prediction using IBM Watson Studio

After curation of dataset, it was analyzed by this web server for finding the best fitted machine learning model for it. As this studio is very safe in terms of data privacy, it does not make copies of the dataset which is uploaded to the server. Hence the dataset was uploaded to IBM Watson studio.



Nanoparticles cytotoxicity

Add files such as tabular data (CSV).

ds for watson.csv
Size: 22.11 KB | Columns: 17

Enable this option to predict future activity over a specified date/time range. Data must be structured and sequential. Learn more

What do you want to predict?
Prediction columns
% Cell Viability

Prediction column: % Cell Viability
CUH remaining: 20 CUH

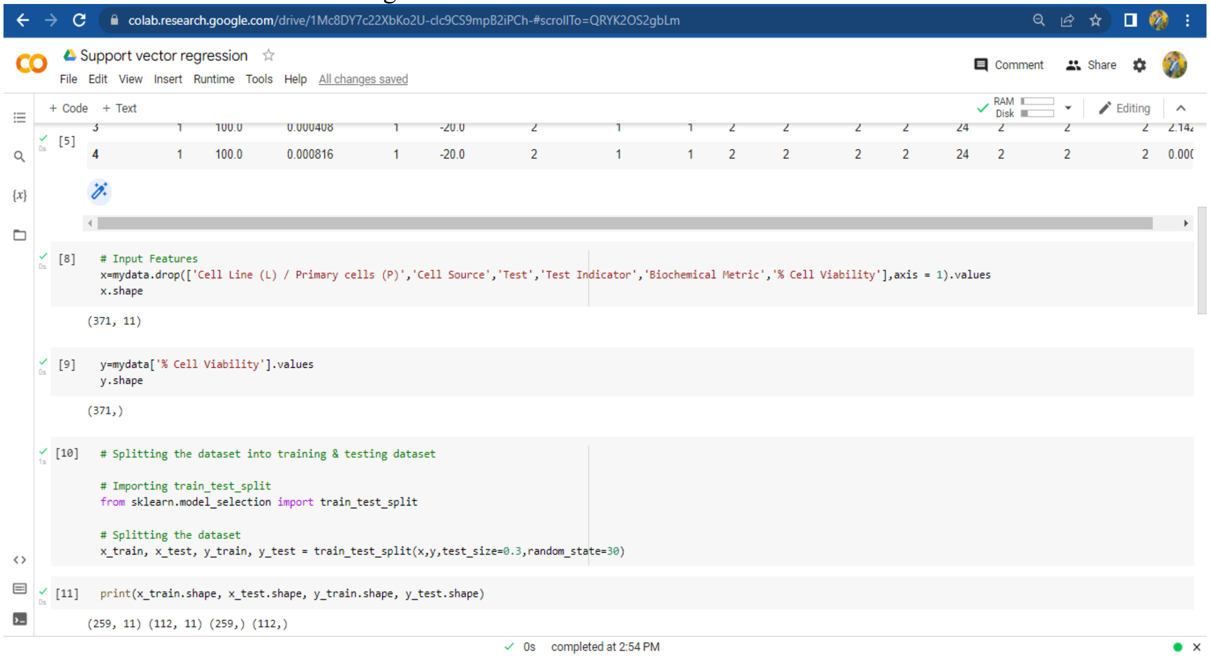
PREDICTION TYPE
Regression

OPTIMIZED FOR
RMSE & run time

Fig.7: - Output of IBM Watson studio

Output of SVR Algorithm

Fig.8: - X and Y selection for SVR model



```
[5]
3    1   100.0   0.000408   1   -20.0   2   1   1   2   2   2   2   24   2   2   2   2.14
4    1   100.0   0.000816   1   -20.0   2   1   1   2   2   2   2   24   2   2   2   0.00
```

```
[8]  # Input Features
     x=mydata.drop(['Cell Line (L) / Primary cells (P)','Cell Source','Test','Test Indicator','Biochemical Metric','% Cell Viability'],axis = 1).values
     x.shape

    (371, 11)

[9]  y=mydata['% Cell Viability'].values
     y.shape

    (371,)

[10] # Splitting the dataset into training & testing dataset

     # Importing train_test_split
     from sklearn.model_selection import train_test_split

     # Splitting the dataset
     x_train, x_test, y_train, y_test = train_test_split(x,y,test_size=0.3,random_state=30)

[11] print(x_train.shape, x_test.shape, y_train.shape, y_test.shape)

    (259, 11) (112, 11) (259,) (112,)
```

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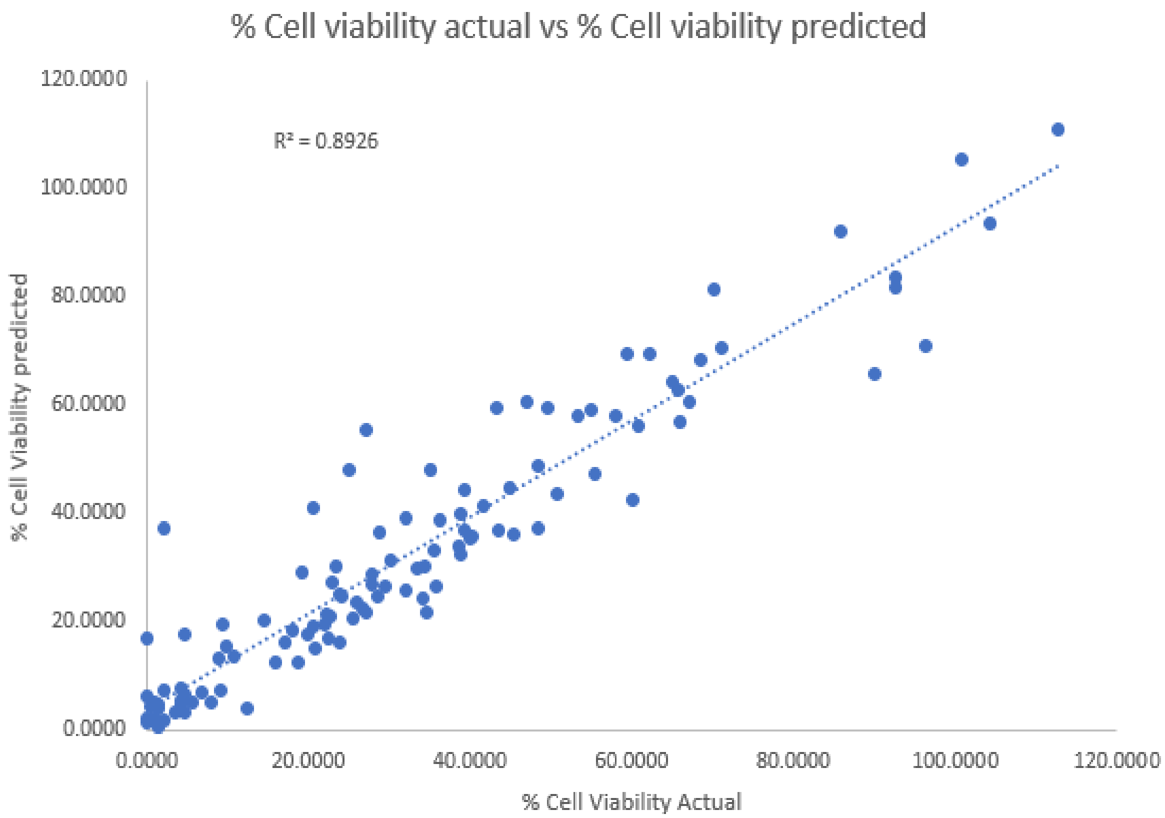

Fig.9: - Scatter plot between % Cell viability actual vs % Cell viability predicted

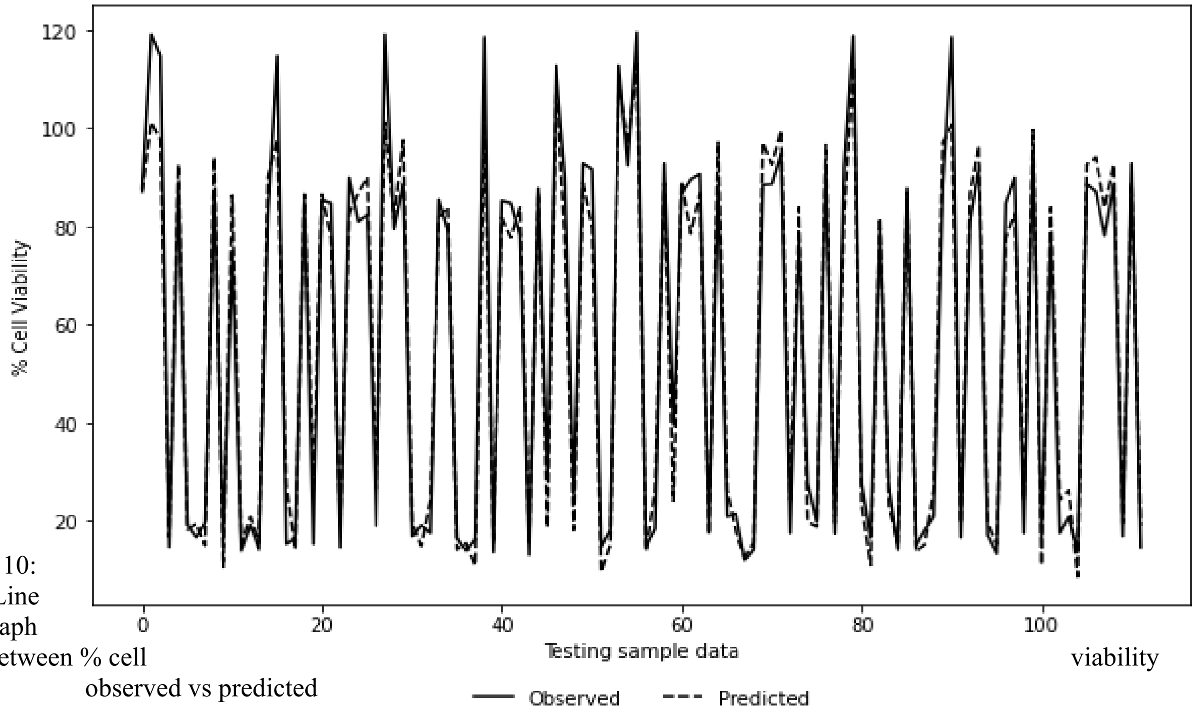

Fig 10: - Line graph between % cell viability observed vs predicted

The SVR model was implemented on dataset. The dataset was divided into x and y where; X is assigned with independent variables while y for dependent variable i.e., % Cell Viability. Total 11 variables were given to x and 1 variable given to y axis.

The model was build using sklearn library of python. The dataset was bifurcated into two parts; training one and testing dataset. The dataset used for training was 70 % of total dataset while the 30% was testing dataset. A random state for selection of the dataset was also incorporated to avoid any type of biasness in the model.

As SVR model is sensitive to the biasness, hence data needs to be transformed using scaler function. Training dataset of X was transformed using scaler method. Similarly, the testing dataset of X was also transformed in same way. While the training and testing dataset for Y remained same.

Then the model was trained using training dataset and prediction was done using the testing dataset. After this, the line graph plotted between observed cell viability and predicted. After it, performance measures were calculated.

The model had R squared value over 0.87 and RMSE value was below 0.5. Hence model was acceptable (Reuther et al., 2019).

Validation of models using k – fold cross validation method

In k – fold cross validation method, k represents the number of iterations. In this method, whole dataset is broken into 2 parts; training one and testing dataset. For each cycle the datasets change, hence biasness of the model can't be possible. Hence this method is used to check the validity the model. As the result showed, The SVR model had the validation score for training and testing dataset is 0.9031 and 0.8853 respectively, which tells that model performed well in each cycle of validation.

Hence the model is acceptable for further use (Xiong et al., 2019).

Case No	Training Dataset	Testing Dataset
1.	0.9616	0.9594
2.	0.9347	0.9187
3.	0.9541	0.8988
4.	0.9658	0.8956
5.	0.9023	0.8408
6.	0.8403	0.9515
7.	0.8175	0.8191
8.	0.8972	0.8256
9.	0.8256	0.8465
10.	0.9324	0.8975

Table 1: Cross validation score for SVR

Conclusion

The increment in production and consumption of metallic nanoparticles, including silver (Ag) NPs, zinc oxide (ZnO) NPs, Titanium Dioxide (TiO_2) NPs, copper (Cu) NPs, and gold (Au) NPs, have raised major concerns regarding their environmental persistence and potential impacts on human health. Owing to their widespread applications in biomedical, industrial, agricultural, and consumer products, these nanomaterials are continuously introduced into environmental compartments through wastewater discharge, industrial effluents, agricultural runoff, and improper disposal practices. Their small size, high reactivity through surface, and enhanced mobility facilitate interactions with biological systems, thereby increasing the likelihood of adverse ecological and toxicological consequences.

This study highlights that metallic nanoparticles can induce cytotoxicity through multiple interconnected mechanisms, including reactive oxygen species (ROS) generation, oxidative stress, mitochondrial dysfunction, membrane damage, inflammation, and DNA impairment. Such cellular disturbances may ultimately lead to apoptosis, necrosis, and organ-specific toxicity affecting the liver, kidneys, lungs, brain, and cardiovascular system. The severity of these effects is strongly influenced by nanoparticle physicochemical properties such as particle size, morphology, surface charge, concentration, exposure duration, and dissolution behavior.

To address the challenges associated with conventional toxicity assessment, this study proposes the integration of machine learning techniques, particularly Support Vector Regression (SVR), for predicting nanoparticle-induced cytotoxicity. By utilizing physicochemical descriptors as predictive variables, SVR provides a robust framework for modeling complex nonlinear relationships between nanoparticle characteristics and biological responses. The computational *in silico* approach offers a cost-effective and time-efficient alternative to extensive experimental testing while supporting rapid toxicity screening and environmental risk assessment.

The findings emphasize the importance of combining mechanistic toxicology with artificial intelligence-driven predictive modeling to advance the field of nanotoxicology. Such integration can facilitate the development of safer-by-design nanomaterials, improve regulatory decision-making, and enhance environmental monitoring strategies. Future studies should focus on incorporating larger multi-omics datasets, environmental exposure scenarios, and advanced machine learning algorithms to improve prediction accuracy and strengthen the understanding of nanoparticle behavior in complex biological and ecological systems. Ultimately, the convergence of nanotechnology, toxicology, and machine learning holds significant promise for promoting sustainable innovation while minimizing risks to environmental and public health.

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