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Entrepreneurship Opportunities on Artificial Intelligence Applications to Nanoparticles Design for Neurological Diseases Treatment

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Abstract. Artificial Intelligent (AI) and Machine Learning (ML) are developing significant advances and gaining importance information processing in a huge number of fields such as chemical, pharmaceutical, biological etc. The Perturbation Theory (PT) is commonly combined with ML in order to generate PTML models and has been used in various disciplines to predict the biological activity of drugs and nanoparticles. In addition, this powerful tool has showed promising results in the field of nanoinformatics. As a consequence of evident achievements on a wide range of predictive tasks, ML

techniques are attracting significant interest across a variety of stakeholders. Therefore, In this review different type of application of machine learning in nanoparticles involve in neurological diseases will be discussed.

In addition, different startup, spin-off, Small and Medium Enterprises (SMEs), and also some BigPharman, Tech companies, Nanoform-Drug Particle Engineering, Precision Medicine, NanosticsNanotechnology-Baed Diagnostic etc. are developing AI-based nanomedicine, nanotechnology, brain diseases so on. This communication also lists some of these startup companies.

Artificial Intelligent (AI) and Machine Learning (ML) are developing significant advances and gaining importance information processing in a huge number of fields such as chemical, pharmaceutical, biological etc. [1] The Perturbation Theory (PT) is commonly combined with ML in order to generate PTML models and has been used in various disciplines to predict the biological activity of drugs and nanoparticles. In addition, this powerful tool has showed promising results in the field of nanoinformatics. As a consequence of evident achievements on a wide range of predictive tasks, ML techniques are attracting significant interest across a variety of stakeholders. [2] Therefore, In this review different type of application of machine learning in nanoparticles involve in neurological diseases will be discussed.

Firstly, Munteanu *et al.* created the PTML models to predict the probability of different pairs of drugs and nanoparticles creating drug-decorated nanoparticle (DDNP) complexes with anti-glioblastoma activity. The DDNP has become a very important task in medical applications. For this, the raw dataset by mixing the nanoparticle experimental data with drug assays from the ChEMBL database were recollected. Ten types of machine learning methods have been tested. Only 41 features have been selected for 855,129 drug-nanoparticle complexes. The best model was obtained with the Bagging classifier, an ensemble meta-estimator based on 20 decision trees, with an area under the receiver operating characteristic curve (AUROC) of 0.96, and an accuracy of 87% (test subset). This model could be useful for the virtual screening of nanoparticle-drug complexes in glioblastoma.[3]

Secondly, Santana *et al.* reviewed nanoparticles (NPs) decorated with coating agents (polymers, gels, proteins, etc.) form Nanoparticle Drug Delivery Systems (DDNS), which are of high interest in nanotechnology and biomaterials science. There have been increasing reports of experimental data sets of biological activity, toxicity, and delivery properties of DDNS. However, these data sets are still

[1] Simón-Vidal, L.; García-Calvo, O.; Oteo, U.; Arrasate, S.; Lete, E.; Sotomayor, N.; Gonzalez-Diaz, H. Perturbation-theory and machine learning (PTML) model for high-throughput screening of Parham reactions: experimental and theoretical studies. *Journal of Chemical Information and Modeling*, **2018**, *58*(7), 1384-1396.

[2] Mirzaei, M.; Furxhi, I.; Murphy, F.; Mullins, M. A Machine Learning Tool to Predict the Antibacterial Capacity of Nanoparticles. *Nanomaterials* **2021**, *11*, 1774.

[3] Munteanu, C. R.; Gutiérrez-Asorey, P.; Blanes-Rodríguez, M.; Hidalgo-Delgado, I.; Blanco Liverio, M. J.; Castiñeiras Galdo, B.; Porto-Pazos, A. B.; Gestal, M.; Arrasate, S.; González-Díaz, H. Prediction of Anti-Glioblastoma Drug-Decorated Nanoparticle Delivery Systems Using Molecular Descriptors and Machine Learning. *International journal of molecular sciences*, **2021**, *22*(21), 11519.

dispersed and not as large as the datasets of DDNS components (NP and drugs). This has prompted researchers to train ML algorithms that are able to design new DDNS based on the properties of their components. However, most ML models reported up to date predictions of the specific activities of NP or drugs over a determined target or cell line. In this work, they combine PT and ML (PTML algorithm) to train a model that is able to predict the best components (NP, coating agent, and drug) for DDNS design. In addition, this is the first multi-label PTML model that is useful for the selection of drugs, coating agents, and metal or metal-oxide nanoparticles to be assembled in order to design new DDNS with optimal activity/toxicity profiles.[4]

Lastly, Chen *et al.* used ML algorithms to process large datasets in order to understand and predict various material properties in nanomedicine synthesis, pharmacologic parameters, and efficacy. The reason that this authors worked with ML is because of nanomedicine design is often a trial-and-error process, and the optimization of formulations and *in vivo* properties requires tremendous benchwork. “Big data” approaches may enable even larger advances, especially if researcher capitalize on data curation methods. However, the concomitant use of data curation processes needed to facilitate the acquisition and standardization of large, heterogeneous data sets, to support advanced data analytics methods such as machine learning has yet to be leveraged. Currently, data curation and data analytics areas of nanotechnology-focused data science, or 'nanoinformatics', have been proceeding largely independently.[5]

In addition, different startup, spin-off, Small and Medium Enterprises (SMEs), and also some BigPharman, Nanoform-Drug Particle Engineering, Precision Medicine, NanosticsNanotechnology-Baed Diagnostics, Tech companies etc. are developing AI-based nanomedicine, nanotechnology, brain diseases etc. This communication also lists in the following Table 1 some selected startups in the area. There are a large number of interesting startups list, check it out by clicking on the reference below.

Table 1. AI-driven nanomedicine, nanotechnology, brain diseases startups[6]

Startup name	**Topic**	**Funding (M$)**	**Country**
Spring Health	AI to help patients with metal health problems better faster.	295.5	USA
Sophia Genetics	Bring data analytics solutions to the market for healthcare support.	250.2	Switzerland

[4] Santana, R.; Zuluaga, R., Gañán, P.; Arrasate, S.; Onieva, E.; González-Díaz, H. Predicting coated-nanoparticle drug release systems with perturbation-theory machine learning (PTML) models. *Nanoscale*, **2020**, *12*(25), 13471–13483.

[5] Chen, C.; Zvi, Y.; Apfelbaum, E.; Grodzinski, P; Shamay, Y.; Heller, D. A. Merging data curation and machine learning to improve nanomedicines. *Advanced Drug Delivery Reviews*, **2022**, 18(3), 114–172.

[6] Medical Startups 2022 Oct 23, https://www.medicalstartups.org/top/nano/

BioXcel Therapeutics	Clinical stage biopharmaceutical company that uses AI to identify the next wave of medicines across neuroscience and immune-oncology.	140	USA
Verge Genomics	Finding new cures for brain diseases 1000x by using network algorithms.	134.4	USA
Nanocarrier	Aevelopment of nano and bio technologies.	8.3B	Japan
iCeutica	Development of Encapsulated Organic Nanoparticles (EON^{TM})	5.1	Australia

To conclude, I think that in the future the applications of machine learning and artificial intelligence on nanotechnology and nanomedicine will be huge. In fact, it is really useful tool to predict interactions between drug-nanoparticles with promoting results as we saw previously. Certainly, these developments should be considered as a great opportunity for the creation of new startups.