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Implementation and Evaluation of Ensemble Learning Algorithm for Improved Drug Development

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Abstract:

Artificial intelligence (AI) & machine learning (ML) has emerged as the cutting-edge technologies most expected to revolutionize the pharmaceutical R&D industry during the previous decade (R&D). Part of the reason for this is that barriers that once prevented the collection and processing of massive amounts of data have been largely removed as a result of breakthrough developments in computer technology. Meanwhile, the expense of developing, testing, and delivering a new drug to market and eventually to patients has skyrocketed. The International Health Organization has advocated for pharma covigilance, the monitoring of adverse drug events, as a means of ensuring the security of medicines by facilitating the rapid and trustworthy transmission of information pertaining to drug safety issues. Our goal is to have a conversation about the use of machine learning techniques and causal reasoning paradigms in the field of pharma covigilance. Over the past two decades, ML methods have become increasingly integrated into the pharmaceutical industry's search for new therapeutics. Clinical study design, conduct, & analysis are the most recent areas of drug research to see beneficial disruption from AI/ML. We highlight three current paths or voids being explored to combine causal inference and machine learning in drug safety studies. Finally, our research found that using causal paradigms can help prevent common problems with ML models. Through a series of comparisons, we demonstrate that the proposed ensemble algorithms outperform state-of-the-art ML prediction algorithms over a wide range of metrics.

Keywords: pharma covigilance, Machine Learning, Artificial Intelligence, Drug Discovery & Management, Ensemble algorithms.

1. Introduction:

Especially in the realm of health and pharmaceuticals, it is one of humanity's primary goals to exert control over the inevitable and unavoidable flux that permeates every facet of life. The goal of these fields is to alleviate both physical and mental pain by developing and discovering new chemical compounds and mixes. Drug goods have been tested for many decades to verify quality of raw materials, in-process elements, finished product features, batch-based processes, and set process variables. [1].

Few other sectors have contributed as much to the advancement of fresh ideas or interpretations in basic chemical and mechatronics as the drug and biotech industries. There is a dire need for mechanical advancements in the pharmaceutical industry that would make it simpler to develop medicines for human consumption. Due to current constraints on technological resources [1], it has been difficult to develop and commercially produce complex process medications that really are safe for human use. The "one size fits all" approach used in conventional drug prescription is not optimal. New pharmacological advancement processes are needed, and novel approaches are needed in crucial areas of medicine. Recently developed analytical instruments and precise dosages have allowed for the development of novel pharmaceuticals and approaches thanks to advancements in genomics and diagnostics. The pharmaceutical industry as a whole would benefit from the development of such personalized medicines. Medical planning and manufacturing have progressed to a point where they can't yet address the problems with personalized medicine. The pharmaceutical industry needs innovative manufacturing assembly arrangements that enable the flexible assembly of individualized machinery and technology [1]. The increasing prevalence of AI has the potential to alter the nature of clinical evaluation and education. The promise of AI to considerably develop health care can be realized [2] if doctors are involved in developing the knowledge for application in medicinal & pharmaceutical businesses. There are now four major purposeS of AI in Pharmacy division. The first is in diagnosing illness and determining whether a given treatment will be effective before it's even given to a patient. Second, it is employed to either forestall or remedy treatment-related problems. Thirdly, it is used as a tool to help medical professionals perform their jobs while caring for patients. Last but not least, In order to improve patient safety and treatment efficacy, it is used to determine the rationale behind of choice of particular medicinal instruments or substances, and to develop or infer new applications for these tools & drugs.

The administration and analysis of massive data [3] is another area where AI plays a more broad role. The term "big data" refers to a relatively new paradigm that describes the accumulation of massive datasets and the use of advanced analytics to get new insights from these datasets [4,5]. Therefore, as the amount of data generated in the pharmaceutical industry continues to grow, conventional methods of storing this information are becoming inadequate. Pharmaceutical production could benefit from a three-stage process following acquiring, including the process listed: excavation & spread of big sections of dissolved & blueprint; data arrangement to guarantee standardized spelling & punctuation; and information processing by means of wide range of logical systems to generate a correct outcome, & interpretable results.

Because of these developments, expansion, and adaptations in the availability of excess quantities of information for producing useful insights, AI permitted knowledge is constantly used to undertake trivial yet significant concerned issues in the medication & improving industries. Because of this, the authors believe it is important to compile an in-depth article analyzing the role of artificial intelligence (AI) & machine learning (ML), in the Pharmacy sector, including the most recent developments in these areas, as well as the most novel studies conducted in this area and their implications for the future of the pharmaceutical industry.

1.1 Current context in drug development:

Creating a brand novel pharmaceutical is an expensive and lengthy endeavor. An intensely competitive and time-consuming process is required of all potential medications before they may be used in patients. There are four main "phases" in the drug development process. stage 0 includes fundamental study/drug development & preclinical examination to evaluate the drug candidate's efficacy and how the body processes it. Clinical trials are the final step, and they consist of three phases: Phase I, in which dose-toxicity, short-term adverse effects, and kinetics relationships are studied; Phase II, in which therapeutic performance is determined; and Phase III, in which the molecule is compared to the gold standard (Phase III). Phase IV research is not required but is recommended after a medicine has been commercialized to track any potential adverse effects or interactions with other treatments. The entire process of creating a new medicine is depicted in Fig. 1. It requires a minimum of 5 years [6] and maybe up to 15 years [7] to build this pipe. The minimum instance covers the preparation of clinical & preclinical testing (stage 0 to 3), including the moment to think about & jot behind the plan of the study, to recruit and choose participants, to evaluate the findings, and so on.

The duration of each subsequent phase of a drug's clinical development has grown longer. The average clinical development period for pharmaceuticals approved in 2015-2016 was 6.4 years, compared to 9.1 years for medication candidates in 2008-2012 [8]. This could be an indication of a problem with how drug benefits and risks are calculated. However, a major problem that has persisted for a long time [9] is the high rate of drug discovery pipeline failure, which typically occurs during the later stages of clinical testing. There was a 54 percent failure rate in Phase II and III clinical studies that took place between 1998 and 2008, according to reports in [10]. The absence of efficacy was the primary reason for failure (57% of the unsuccessful medication candidates) whereas safety concerns were the secondary reason for failure (17%). Increasing death risk or significant adverse effects were the primary causes for failing in Phases III and IV in 2012 [8] and 2019 [11]. Differences in predicted success rates across Phase II (first patient dosage) and Phase III (later stages of drug development) were especially large in 2012 for drug pipelines that had their genesis in 2007-2009. (first clinical trial-dose). Only 14% of medication candidates that made it to Step 2, which is associated to drug measuring performance, were subsequently launched, whereas 64% of drug pipelines made it to Phase III [11]. For drug pipelines, this trend persists as of 2015–2017 [12]. While 62% of drug pipelines make it to Phase III, just 25% of Phase II medication candidates are authorized.

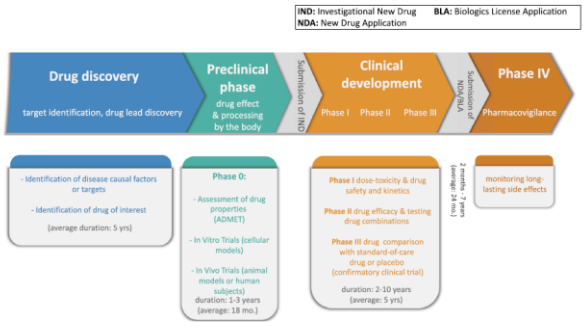

Figure 1: Various Phases of Drug Development [13]

2. Related Works:

Novel target identification, target-disease association understanding, drug election campaigns, protein predictions, molecular chemical optimization and design comprehension of pathogenic mechanisms, creation of novel predictive & prognostic biomarkers, biometric information study as of wearable's, and many other areas of R&D stand to benefit greatly from the application of AI/ML techniques, which could ultimately enhance the probability of achievement in drug improvement. Due to the rising trust on digital technologies for information collecting & monitoring, the COVID-19 pandemic may hasten the adoption of AI and ML in scientific study execution.

Identifying novel targets requires the use of both prescriptive analytics (used to predict protein complexes & facilitate single - molecule chemical design and optimization) and natural-language processing (used to fetch the tool to identify from science journals). Rapid developments in ML algorithms to deal with "Large p, Small n" dilemma, in which amount of changeables ("p") is larger than amount of examples ("n"), have been spurred by the growing volume of subject to excessive like genomics, photography, and the utilization of electronic wearable devices. After a drug has been on the market, researchers can use "big data" from real-time resources of data to do three things: I learn more about the drug's profit risk profile; (ii) learn more about how treatments are typically administered; and (iii) find patient subgroups who are more likely to experience positive outcomes from a particular treatment (precision medicine).

Although AI/ML have become increasingly prevalent in the last two decades in areas such as drug discovery, research programs, and the which was before phase, their adoption in clinical study processes and data analysis has been slower. In this context, "clinical trial operations" refers to the actions necessary for the planning, initiation, & completion of a clinical trial, for example finding a suitable trial location, finding and enrolling patients, monitoring the experiment, and analyzing the results. Clinical data analysis entails information management, data analysis, and statistical analysis of user medical studies. It has been difficult to recruit patients for clinical trials; 80% of trials fail to enroll participants by their target dates, and 30% of step iii trials are stopped early because of this issue [14]. Regulation requires a significant and costly quality control step: monitoring of trial sites (which requires actual travel to sites).

Clinical trial management has also become more time-consuming, expensive, and labor-intensive when multi-center, global trials are conducted. Furthermore, the time it takes to finish a study first from "last subjects last visit" endpoint of from the end of the last phase 3 study to when the data

package is submitted to the FDA for review is another region where AI/ML may have a big positive impact. For the better part of two decades, this time has stayed the same. If we can reduce this time significantly, we can get medicines to patients sooner at a lower cost. In between, you'll have to do things like clean and lock the trial database, run the final analysis for the phase 3 trial (which can involve hundreds of review tables, information classifieds, & records), write up the scientific study, finish incorporated outline of efficiency & security, and put together the application requires pack up. Because of the rising drive towards 99.56% or partly virtual (or "decentralized") trial as well as the increasing utilization of digital technologies in collecting patient information, COVID-19 may have an impact that further accelerates the drive to incorporate AI/ML in clinical examination operations. In addition to improving patient recruiting and project enrollment, AI/ML techniques can facilitate real-time, robotic, and "smart" checking of clinical value control & test site presentation. When it comes to trial data analysis, creating drug trial reports, and putting together data packages for regulatory submissions, we think AI/ML have the prospective to contain a game-changing impact on research trial action & analysis.

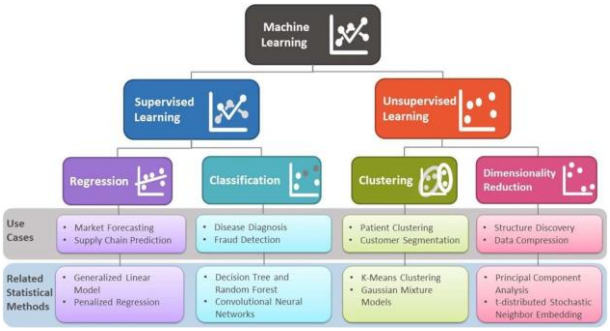

Fig. 2 Summary of Unsupervised and Supervised Learning[15]

Novel pharmacological success rate and experimental validation are time-consuming and expensive. When combined with cutting-edge innovations, high-throughput virtual screening (HTVS) has become an indispensable tool in the drug development process. Thus, AI/ML techniques are employed to comprehend the priority of promising therapeutic targets, which are taken forward for the succeeding tests [16]. [17] Valentini et al. created a method to rank the ordering of genes by combining functionally distinct gene network with kernel-based algorithms. Target-disease association data from public databases was used by Ferrero et al. [18] to anticipate new medication targets. To classify the human genes in light of this implication of aging, Arabfard et al. [19] used three positive unlabelled algorithms, including Nave Bayes, Spy, and Branched structure, to predict and rank around 3000 target associated with an aging gene. In drug research, the link between drugs' targets and illness is a hot topic [20]. Finding a small suitable chemical to disrupt the illness mechanism is the first step in the extensive process that follows.

In most cases, pharmaceutical companies are made aware of a promising drug candidate after the candidate has been designed and submitted to or placed in a large chemical library. The SVM technique was created by Vapnik et al. [21], while Burbidge et al. [22] combined the SVM model with chem. informatics. This separating hyper plane has crucial characteristic for classifying the need of initial environment [23], and the SVM classification is similar to other sample approaches as linear discrimination. While level is crucial, distance among the example & the flat surface is

increased, and the boundary is defined by a relatively small portion of the training example [24]. Some cases placed on the incorrect side of the hyper plane could be attributed to experimental mistake data or noisy data. In addition to the nonlinear and linear hyperplanes related with Mercer's theorem [25], the Knn algorithm is an innovative use of the SVM approach. Using this property, distances in strong nonlinear spaces can be computed without resorting to an explicit length transforma- tion [26]. SVMs use a wide range of decomposition algorithms for large-scale dataset analysis and regression (SVR). About 46,879 chemicals in the Nih (Cancer Institute Center) AIDS data set were tested using SVM approaches from Syngenta and Willett, and they were significantly less effective than using BKD with the UNITY fingerprint as a descriptor [27, 28].

Subsequently, 245,789 chemicals were tested for their pesticide efficacy, and it was shown that the polynomial kernel with degree five was superior than binary kernel differentiation (BKD). After using a collection of 120 samples containing Cox-2 antagonistic elements as a infirmation set, Franke et al. (2015) analyzed 3.2 million molecules from of the COBRA ligands database. Several compounds were investigated for this screening, however only three molecules showed significant activity. Particularly, one drug has demonstrated more potent inhibitory characteristics than both cele coxib & rofe coxib [29]. Lepp et al.[30] analyzed 21 MDDR depression-related data sets, classifying 30,000 ligands compounds per data set using SVM and atom-count descriptors. The positive recall in ML-based screening ranges from 44% to 89% [31], indicating that false negatives are accurately anticipated. Using the 50 known compounds for each pharmacological target as a training set, Jorissen and Gilson [32] reported the screening of 2058 elements from NCI data & 34,256 chemicals from the May bridge library [33] beside 4 compunds: 1AAR, CoX-2, PDE5, and CDK2. And over 10% of the screening database was obtained utilizing the DRAGON software's projected 2D descriptors using the SVM technique, making it superior to previous fusion meth- ods that rely on fingerprints [34]. Using support vector machine (SVM) techniques for G protein-coupled receptors (GPCRs), Saeh et al. (2005) identified 8975 elements as highest in a catalog of 129,994 compounds, with a success rate 69 times greater than randomized choice-based selections [35].

3. Methodology:

It is the three-dimensional (3D) structure of a protein that determines its biological mechanism, and this structure is encoded in the protein's one-dimensional (1D) strings of amino acid. Understanding the biological mechanisms of proteins requires an understanding of their structures, which in turn leads to the discovery of new medicines that can either block or stimulate the protein in question, which can then be used to treat certain diseases. Many illnesses, including type II diabetes and neurodegenerative disorders including Alzheimer's, Parkinson's, Huntington's, and amyotrophic lateral sclerosis, have been linked to protein misfolding [36, 37]. The ability to reliably predict protein 3d structures would greatly benefit the fields of drug development and protein-folding illness research, given the large gap in knowledge between a protein's 1D strand of amino acid sequences and its 3D structure. Deep Mind (GoogleAlpha)'s Fold [37, 38] is an artificial intelligence network that can predict the three-dimensional structure of a protein from its sequence of amino acids. The protein structure was predicted from its sequence using a DL method.

The heart of Alpha Fold is a convolution neural network that has been trained to make a probabilistic approximation of a 89 sections of proximity map, based on predictions of the lengths among each

pair of residues in a query protein. using information from the Protein Sequence alignment Bank. These sections are tiled together solely to obtain global distance predictions, and this is done so that the generated protein structure will be in agreement with the distance predictions. In 2020, AlphaFold [39] plans to reveal structural estimates of 5 SARS-CoV-2 target, such as the SARS-CoV-2 cell membranes, Nsp2, Nsp4, Nsp6, & Nuclease enzyme ase (C terminal domain domain).

3.1 Ensemble outperform single learning algorithm

Ensemble approaches have been shown to significantly increase performance in a number of studies. You can break this down into three main factors: This is due to statistics, which is the first explanation. Learning algorithms can be thought of as a search over a field H of hypotheses, with the goal of finding the most promising one. This statistical issue manifests when the quantity of training examples is insufficient in relation to the scope of the space of possible. A learning algorithm can identify several hypothesis in H yields the identical reliability on the preparation information if there isn't enough information to choose from. The method can lower the likelihood of making a poor classification decision by "averaging" the votes of multiple accurate classifiers that it has assembled into an ensemble.

A computational consideration is the second. Many learning algorithms rely on a sort of local search, which can get trapped at local optima. Even when there is an abundance of training data (and thus no statistical issue), the learning algorithm may have a hard time computationally determining which hypothesis is most plausible. The local search may be approximated more closely to the genuine undiscovered function using a group created by conducting the hunt from many starting points.

That's the third justification: it's symbolic. In most ML use cases, none of the hypotheses can accurately capture the underlying classification function. One alternative method for increasing the number of functions that can be represented is to create weighted sum of hypotheses derived from H. The current generation of learning algorithms largely suffers from these three primary flaws. These three major flaws of traditional learning algorithms [40] may be mitigated (or perhaps eliminated) with the help of ensemble approaches. To be more precise than the sum of its parts, an ensemble algorithm needs to have both accurate and diverse individual members [40-41]. Bagging and AdaBoost, as claimed by Dietterich (2000a) [40If your learning algorithm's output classifier fluctuates dramatically in response to even little varies in the training data, you may benefit from using a] which works well for unstable learning algorithms. Decision-tree and rule-based learning methods are both highly volatile. Most Naive Bayesian and Nearest Neighbor algorithms are quite stable [42]. The research backs up the assertion. However, when 1NN & NB are not employed as the basis novices, Bagging nor Ada Boost improved performance. This was the case when tree based C4.5 and 1R were utilized as the base learners.

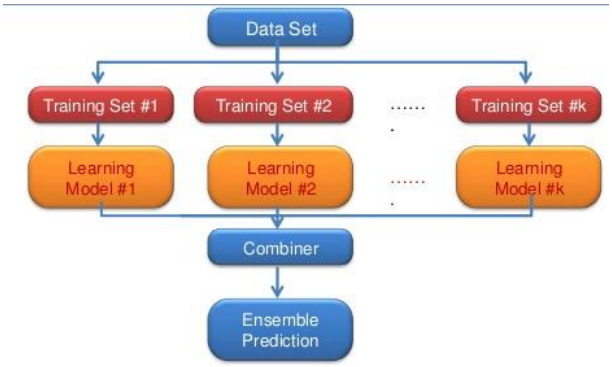

Figure 3.Ensemble algorithm working

4. Evaluation:

The Java AWT (Abstract Windows Toolkit) was utilized by the development team to create the program. There are 3,000 individual patient records and 30 health attributes included in the.arff file. The data is then used to generate a training dataset and a testing dataset. Explore the test findings and select a prediction algorithm from a pull-down menu, all within the user interface. Results are summarized and shown in further depth. The analysis is carried out by making predictions about the algorithms each time, while keeping in mind the quality parameters.

In this program, we use Machine Learning methods to create a user interface for determining the likelihood of coronary heart disease. The module is comprised of a computer and a user. It takes data and algorithm runs for the system to produce results for each model. Users, on the other hand, are restricted to viewing only their information and the model's predictions. However, they need to sign up and log in first. The user can access the models and the projected results once registration is complete.

1. Correctly classified instances: It will tell us how many of the test scenarios were successful.

2. Relative Absolute Error: One can use this method to calculate the magnitude of the gap between the observed value and the predicted one.

3.Root Relative Squared Error: If a straightforward forecast had been used instead, this would've been a step up. The relative mean square error is an estimate obtained from a simple predictor by halves the total squared error.

.Table 1.Analysis Results of Various Quality Parameters

Quality Parameters	**Performance of Various Prediction Algorithms**			
	Linear Regression	**Logistic Regression**	**Ada Boost**	**Ensemble Prediction**
Correctly Classified Instances	14.53	22.53	28.56	35.45
Relative Absolute Error	16.53	14.57	11.59	9.25
Root Relative Error	22.56	18.96	16.53	11.56
R-Squared	21.53	18.59	14.56	9.53

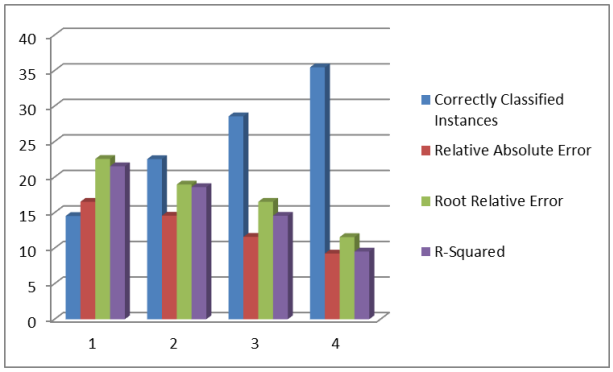

Figure 4. Evaluation Results of Various Parameters

The above graph shows the Comparison evaluation Results of Various Prediction algorithms. From the results of the graph it is evident that ensemble algorithm performs well when compared to remaining prediction algorithms.

5. Conclusion:

The pharmaceutical business is rapidly using machine learning. While group machine learning has long been a hot topic in the machine learning research field, it is just recently begun to be utilized by the drug discovery scientific community. Most studies involving machine learning and the development of new drugs still rely heavily on single-learning strategies. The classifiers in ensemble learning are thought to be well-suited for drug discovery and development application since they are encouraged from imperfect & noisy information. We verified here the value of using a variety of ensemble methods in the process of finding new medicines. When compared to other classifiers, the accuracy gained through the use of ensemble learning approaches is clear.

References:

[1] Rantanen J, Khinast J. The future of pharmaceutical manufacturing sciences. J Pharm Sci 2015;104(11):3612–38. doi:10.1002/jps.24594.
[2] Greenhill AT, Edmunds BR. A primer of artificial intelligence in medicine. Tech In- nov Gastrointest Endosc 2020;22(2):85–9. doi:10.1016/j.tgie.2019.150642
[3] Solanki P, Baldaniya D, Jogani D, et al. Artificial intelligence: new age of transformation in petroleum upstream. Pet Res 2021. doi:10.1016/j.ptlrs.2021.07.002.
[4] Kshirsagar A, Shah M. Anatomized study of security solutions for multimedia: deep learning-enabled authentication, cryptography and information hiding. Adv Secur Solut Multimed 2021. doi:10.1088/978-0-7503-3735-9CH7.
[5] Anthony CC. Big data in medicine: the upcoming artificial intelligence. Prog Pediatr Cardiol 2016;43:91–4. doi:10.1016/j.ppedcard.2016.08.021.
[6] Eliopoulos H, Giranda V, Carr R, Tiehen R, Leahy T, Gordon G. Phase 0 trials: an industry perspective. Clin Cancer Res 2008;14(12):3683–8.
[7] Xue H, Li J, Xie H, Wang Y. Review of drug repositioning approaches and resources. Int J Biol Sci 2018;14(10):1232.
[8] Schuhmacher A, Gassmann O, Hinder M. Changing R&D models in research- based pharmaceutical companies. J Transl Med 2016;14(1):105.
[9] Khanna I. Drug discovery in pharmaceutical industry: productivity challenges and trends. Drug Discovery Today 2012;17(19–20):1088–102.
[10] Hwang TJ, Carpenter D, Lauffenburger JC, Wang B, Franklin JM, Kesselheim AS. Failure of investigational drugs in late-stage clinical development and publication of trial results. JAMA Internal Med 2016;176(12):1826–33.
[11] Lowe D. The Latest on Drug Failure and Approval Rates.

[12] Available at: blogs.sciencemag.org/pipeline/archives/2019/05/09/the-latest-on-drug- failure-and-approval-rates. Accessed [September 16, 2019].
[13] Thomson Reuters (2014) CMR International Pharmaceutical R&D Executive Summary. Available at: citeseerx.ist.psu.edu/view doc/download? doi=10.1.1. 675.2511. Accessed [September 17, 2019].
[14] Clémence Réda, Emilie Kaufmann, Andrée Delahaye-Duriez, “Machine learning applications in drug development”, Computational and Structural Biotechnology Journal, Volume 18, 2020,Pages 241-252.
[15] Mitchell A, Sharma Y, Ramanathan S, Sethuraman V. Is data sci- ence the treatment for inefficiencies in clinical trial operations? White paper
[16] Kumar, M.S.,Harsha, B.K.,Jule, L.T.,"AI-driven cybersecurity modeling using quantum computing for mitigation of attacks in IOT-SDN network",Quantum-Safe Cryptography Algorithms and Approaches: Impacts of Quantum Computing on Cybersecur, 2023, pp. 37–47.
[17] Natarajan, V. Anantha, et al. "Segmentation of nuclei in histopathology images using fully convolutional deep neural architecture." 2020 International Conference on computing and information technology (ICCIT-1441). IEEE, 2020.
[18] Sreedhar, B., BE, M. S., & Kumar, M. S. (2020, October). A comparative study of melanoma skin cancer detection in traditional and current image processing techniques. In 2020 Fourth International Conference on I-SMAC (IoT in Social, Mobile, Analytics and Cloud)(I-SMAC) (pp. 654-658). IEEE.
[19] AnanthaNatarajan, V., Kumar, M. S., & Tamizhazhagan, V. (2020). Forecasting of Wind Power using LSTM Recurrent Neural Network. Journal of Green Engineering, 10.
[20] Arabfard M, Ohadi M, Rezaei Tabar V et al (2019) Genome- wide prediction and prioritization of human aging genes by data fusion: a machine learning approach. BMC Genom 20:832. https://doi.org/10.1186/s12864-019-6140-0
[21] Selvaraj C, Vierra M, Dinesh DC et al (2021) Structural insights of macromolecules involved in bacteria-induced apoptosis in the pathogenesis of human diseases. Adv Protein Chem Struct Biol 126:1–38. https://doi.org/10.1016/bs.apcsb.2021.02.001
[22] Davanam, G., Pavan Kumar, T., & Sunil Kumar, M. (2021). Novel Defense Framework for Cross-layer Attacks in Cognitive Radio Networks. In International Conference on Intelligent and Smart Computing in Data Analytics (pp. 23-33). Springer, Singapore.
[23] Ganesh, Davanam, Thummala Pavan Kumar, and Malchi Sunil Kumar. "Optimised Levenshtein centroid cross-layer defence for multi-hop cognitive radio networks." IET Communications 15.2 (2021): 245-256.
[24] Natarajan, V. Anantha, et al. "Segmentation of nuclei in histopathology images using fully convolutional deep neural architecture." 2020 International Conference on computing and information technology (ICCIT-1441). IEEE, 2020.
[25] Sreedhar, B., BE, M. S., & Kumar, M. S. (2020, October). A comparative study of melanoma skin cancer detection in traditional and current image processing techniques. In 2020 Fourth International Conference on I-SMAC (IoT in Social, Mobile, Analytics and Cloud)(I-SMAC) (pp. 654-658). IEEE.
[26] Ganesh, D., Kumar, T. P., & Kumar, M. S. (2021). Optimised Levenshtein centroid cross-layer defence for multi-hop cognitive radio networks. IET Communications, 15(2), 245-256.
[27] Balaji, K., P. Sai Kiran, and M. Sunil Kumar. "Resource aware virtual machine placement in IaaS cloud using bio-inspired firefly algorithm." Journal of Green Engineering 10 (2020): 9315-9327.
[28] Peneti, S., Sunil Kumar, M., Kallam, S., Patan, R., Bhaskar, V., & Ramachandran, M. (2021). BDN-GWMNN: internet of things (IoT) enabled secure smart city applications. Wireless Personal Communications, 119(3), 2469-2485.
[29] Balaji, K., P. Sai Kiran, and M. Sunil Kumar. "Power aware virtual machine placement in IaaS cloud using discrete firefly algorithm." Applied Nanoscience (2022): 1-9.
[30] Davanam, G., Kumar, T. P., & Kumar, M. S. (2021). Efficient energy management for reducing cross layer attacks in cognitive radio networks. Journal of Green Engineering, 11, 1412-1426.
[31] Kumar, M. Sunil, and K. Jyothi Prakash. "Internet of things: IETF protocols, algorithms and applications." Int. J. Innov. Technol. Explor. Eng 8.11 (2019): 2853-2857.
[32] AnanthaNatarajan, V., Kumar, M. S., & Tamizhazhagan, V. (2020). Forecasting of Wind Power using LSTM Recurrent Neural Network. Journal of Green Engineering, 10.
[33] Rupesh, B., & Kumar, M. S. (2015). Predicting the Hard Keyword Queries over Relational Databases. International Journal of Applied Engineering Research, 10(10), 26629-26640.

[34] Aversa A, Duca Y, Condorelli RA et al (2019) Androgen defi- ciency and phosphodiesterase type 5 expression changes in aging male: therapeutic implications. Front Endocrinol (Lausanne) 10:225. https://doi.org/10.3389/fendo.2019.00225

[35] Lo YC, Rensi SE, Torng W et al (2018) Machine learning in chemoinformatics and drug discovery. Drug Discov Today 23:1538–1546. https://doi.org/10.1016/j.drudis.2018.05.010

[36] Huang S, Cai N, Pacheco PP et al (2018) Applications of sup- port vector machine (SVM) learning in cancer genomics. Cancer Genom Proteom 15:41–51. https://doi.org/10.21873/cgp.20063

[37] Dill KA and MacCallum JL. The protein-folding problem, 50 years on. Science. 2012;338(6110):1042–6. https://doi.org/10. 1126/science.1219021.

[38] Senior A, Evans R, Jumper J, Kirkpatrick J, Sifre L, Green T, Qin C, Žídek A, Nelson AWR, Bridgland A, Penedones H, Petersen S, Simonyan K, Crossan S, Kohli P, Jones DT, Silver D, Kavukc- uoglu K, Hassabis D. Protein structure prediction using multiple deep neural networks in the 13th Critical Assessment of Protein Structure Prediction (CASP13). Proteins. 2019;87:1141–8. https:// doi.org/10.1002/prot.25834.

[39] Senior A, Evans R, Jumper J, Kirkpatrick J, Sifre L, Green T, Qin C, Žídek A, Nelson AWR, Bridgland A, Penedones H, Petersen S, Simonyan K, Crossan S, Kohli P, Jones D. T, Silver D, Kavukc- uoglu K, Hassabis. Improved protein structure prediction using potentials from deep learning. Nature. 2020;577. https://doi.org/ 10.1038/s41586-019-1923-7.

[40] John Jumper, Kathryn Tunyasuvunakool, Pushmeet Kohli, Demis Hassabis, and the AlphaFold Team, Computational predictions of protein structures associated with COVID-19, Version 3, Deep- Mind website, 4 August 2020, https://deepmind.com/research/ open-source/computational-predictions-of-protein-structures-associated-with-COVID-19.

[41] Woodcock J, LaVange L. Master protocols to study multiple thera- pies, multiple diseases, or both. N Engl J Med. 2017;377:62–70. https://doi.org/10.1056/NEJMra1510062.

[42] Sertkaya A, Wong H, Jessup A, Beleche T. Key cost drivers of pharmaceutical clinical trials in the United States. Clin Trials. 2016;13(2):117–26. https://doi.org/10.1177/1740774515625964.

[43] Hwang TJ, Carpenter D, Lauffenburger JC. Failure of investiga- tional drugs in late-stage clinical development and publication of trial results. JAMA Intern Med. 2016;176(12):1826–33. https:// doi.org/10.1001/jamainternmed.2016.6008