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Application of Artificial Intelligence in the analysis of cardiovascular disease and its drug design

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I. INTRODUCTION

Technology is an inherent part of life – almost every phase of our lives are reliant on technology itself. Defined as the ”scientific knowledge” used for practical purposes that benefit our everyday lives, it has a wide range of applications as in education, healthcare, industries, banking etc. Current technological trends are Artificial intelligence, Deep Learning, Machine Learning, augmented reality, cyber security, virtual reality and many more. It all started from the invention of wheel and technology has advanced so much that it is now an integral part of each and every sector of present world. Technology has shown a huge advancement in HEALTHCARE that it has been able to cure diseases such as AIDS, cancer, Ebola, COVID-19 and a series of diseases. The methodology can be discussed later but the interesting thing is that Artificial Intelligence, Machine Learning and other computational methods can fasten the traditional methods of drug discovery and disease management, consequently reducing time and costs too. It has nothing to do with human intervention or needs minimal human intervention so that it provides appealing accuracy and precision. Be it renal diseases, cardiac diseases, orthopedic diseases or neurological diseases, artificial intelligence is being used in the drug discovery as well as management of all of these diseases. Artificial Intelligence, abbreviated as AI includes pattern recognition, probability theory, statistics, Machine Learning, neural networks etc. collectively known as Computational Intelligence.

Cardiovascular diseases are the major cause of deaths. The study of these diseases, known as Cardiology contains huge set of data and measurements for treatment, diagnosis and evaluation of disease. An important application of AI is Individualized decision making with the use of structured data and algorithms. Artificial Intelligence contains methods which suggest one of the best treatment for heart failure. The challenge resides in the discovery and design of drug or medicine for cardiovascular diseases.

The methodology of drug design includes target identification, hit discovery, lead creation followed by pre-clinical research. Traditional process of designing molecules, which have right properties to become safe and effective drug candidates - takes very long time and costs millions of dollars – the reason being the anti – correlation of important molecular properties such as potency, selectivity and solubility. Hence it is difficult to design for one drug property without negatively or adversely affecting other desirable properties.

This problem can be solved by using Artificial Intelligence and Physics – based methods which are complimentary to each other. Machine Learning systems are trained to dwell into large amounts of existing data which is called a Training Set, to detect patterns as well as predict outcomes and make decisions with minimal human intervention. But ML can only be effectively used to predict the properties of those molecules that are similar to the molecules present in the training set. To overcome this, physics – based methods are used. These methods can capture all rigorous physics i.e., binding of a molecule to a protein such that they help to predict the molecular properties without the need of existing data. These methods include free energy perturbations (FEPS) – methods to calculate relative free energy of binding of a ligand to a protein target, which in turn, gives binding affinity of the molecule – it is a measure of strength of the interlinkage between the ligand and the protein which relates to the potency of the ligand.

The paper includes – The basics of AI & its components, cardiovascular disease, application of AI in disease management and its drug design methodology (general discussion) followed by future possibilities and challenges.

1.1. ARTIFICIAL INTELLIGENCE & ITS COMPONENTS

Artificial Intelligence is a human made interface which can operate on its own using its knowledge. Being comparable to human intelligence, it can act and make decisions like humans. The basic components of AI include learning, reasoning, problem-solving, perception, knowledge representation and natural language processing.

1.1.1. LEARNING

Being an important component of AI, it enables AI to learn from existing data and improve its performance without being instructed by humans. AI systems learn by Data labeling, pattern discovery & reinforcement learning. An example can be voice recognition systems which are able to correct grammatical mistakes on their own.

1.1.2. REASONING AND DECISION MAKING

AI systems use probabilistic models, logical rules and algorithms, consequently draw inference and make decisions. For example, Grammarly, a writing assistant, knows when to apply punctuation marks or not.

1.1.3. PROBLEM SOLVING

AI systems take data, modify it and use it accordingly to solve a specific problem. Various digital games can be taken as example as they make best decisions based on the game's rules and also predict outcomes.

1.1.4. PERCEPTION

Perception means that the AI systems can take data and perceive suggested objects. They also determine its relationship with those objects. Examples being recognition of images, object detection, data analysis etc. For example, self-driving cars collect visual information to recognize lanes, roads, obstacles and then map these objects. Tesla's 3-D navigational map is also an example.

1.1.5. NATURAL LANGUAGE PROCESSING

NLP is an ability of AI which leads AI systems or machines to understand the language provided to them. Be it any language, AI systems convert it into feasible one and understand. Natural Language Processing has two stages: Natural Language Understanding and Natural Language Generation. These stages help the systems to understand as well as generate the text.

AI can be categorized in different forms such as Artificial Narrow Intelligence, Artificial General Intelligence and Artificial Super Intelligence. Each of these is an evolution of the former one.

1.2. ARTIFICIAL NARROW INTELLIGENCE

Being analogous to Machine Learning, Artificial Narrow Intelligence (ANI) systems focus on one particular area and problem at a time. This is the most familiar form of AI seen in present scenario. It focuses on completing tasks like prediction of weather forecast, recommendation of a product etc. These systems do not mimic human intelligence i.e., they don't have the ability of self- awareness, consciousness and genuine intelligence which other forms of AI definitely have. These can only solve those problems which lie within their range of intelligence. Google Assistant, Siri and other tools of Natural Language Processing are some illustrations of Artificial Narrow Intelligence.

1.3. ARTIFICIAL GENERAL INTELLIGENCE

This is the next level from Narrow AI and actually shows human intelligence. An AGI system needs to connect thousands of Narrow AI systems together to be able to mimic or exhibit human intelligence. Although it has not gained a globally accepted precise definition but can be explained by following properties:

1. Portrays same sort of general intelligence like humans;
2. Not limited to a highly specific or particular set of tasks;
3. Qualitative generalization of the concepts which it learns;
4. Interprets a broader view of the task which it is given (considering all possible parameters).

A clear definition of AGI is yet to be given but can be described as an improvised version of Artificial Intelligence.

1.4. ARTIFICIAL SUPER INTELLIGENCE

Systems which can transcend human intelligence lie in the category of Artificial Super Intelligence. These systems are creative, build relations, make rational decisions and can also differentiate between things i.e., can decide whether a task is for good or not. Science fiction can be thought of as a result of Artificial Super Intelligence. A super intelligent system would definitely be a revolution in the digital world and would save so much of human labor and workforce.

After dwelling into these above forms of AI, we should now understand the domains of AI which can be defined as: Machine Learning and Deep Learning. Both of these are mainly the applications that lie in the category of Artificial Narrow Intelligence. Before giving the explanation of AI being applied in treatment of diseases, which is a broader concept and is of much importance – basic concepts of the techniques like Machine Learning and Deep Learning should be clear.

II. MACHINE LEARNING

Machine learning is a process in which computer systems or machines gain intelligence through data. A certain range of machine learning algorithms are applied to the systems so that they can learn from the experiences of real or historical data. Algorithms are, basically, the programming codes used in building a website or to complete any digital task. Self-driving cars can be seen as an example of this learning. Tesla, a popular car manufacturing company uses unsupervised learning method by which car models can detect objects and people while driving.

Types of Machine Learning

1. Supervised Learning

This method uses existing data and teaches / trains the systems to develop a methodology to categorize a new piece of data. For example, data on the symptoms of diabetes is held by the system and when it gets blood test results, it is able to predict the diagnosis. Initially, a human trains the machine to classify symptoms as "diabetes" or "no diabetes" and with time, the machine having enough data, will create its different set of classification and make its own prediction for the classification under which the patient falls in.

2. Unsupervised Learning

Under unsupervised learning, machines try to categorize data without any previous knowledge. Algorithms, not having existing labels, determine on its own how to classify the data known as clustering. The algorithms try to find patterns themselves and group data accordingly. For example, if we go to a party and find a stranger, our mind classifies them according to their age, gender or clothing. Although we have no information about that particular person, still we can work on the classification. This is unsupervised learning.

3. Semi - supervised Learning

It is the intermediate of supervised and unsupervised learning. Suppose we have a large bunch of data, some of them are labeled and others are unlabeled. Then the machine will predict the existing classification based on the labeled data. It will further create boundaries of what it is looking for by training onto the unsupervised data and identify new classifications which the humans couldn't do while labeling. Hence this method enables the machine to classify unsupervised data using supervised one. For example, to detect fraud in banking, machine learning is being used. Initially, it could only classify the fraudulent activity which is known but a semi – supervised algorithm takes new data and informs the model each time to add to the classification methods. It has its limitations too as a computer assigned to perform this task will not be 100 percent accurate.

4. Reinforcement learning

Machines can learn to enhance behavior from experiencing previous results which could be positive or negative. Being a common method in robotics, reinforcement learning is an application about positive and negative outcomes for certain behaviors.

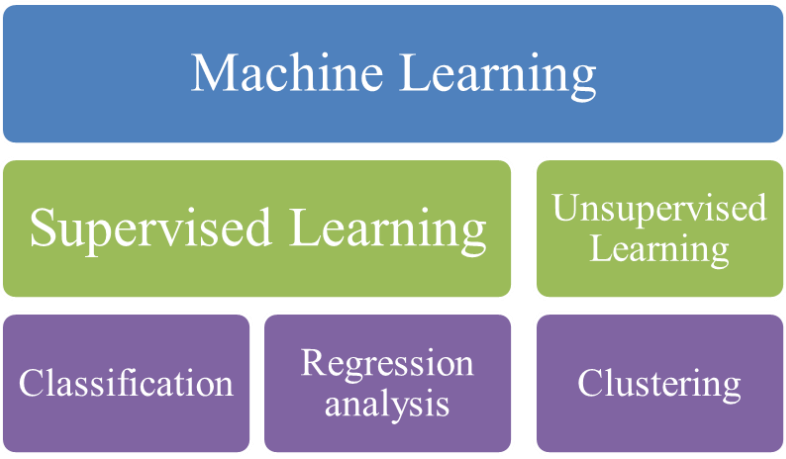

Figure 1. Machine Learning classification

Under reinforcement learning, machines learn with the help of trial and error processes or interactions with the dynamic environment. Apart from holding importance in the field of computer science, reinforcement learning can also be applied in disease management process as well as drug design.

Moreover, machine learning has a lot to do with the physics community as it involves the practice of sharing code and development of high – quality datasets. Machine learning also includes critical processes like clustering, classification and regression analysis which are of utmost importance while dealing with datasets. These processes will be discussed later in the article. Data mining is also an important term related with machine

learning. It is a basic requirement to indulge into the field of computational drug discovery. It refers to the process of picking useful information from a huge set of data and identification of patterns and trends.

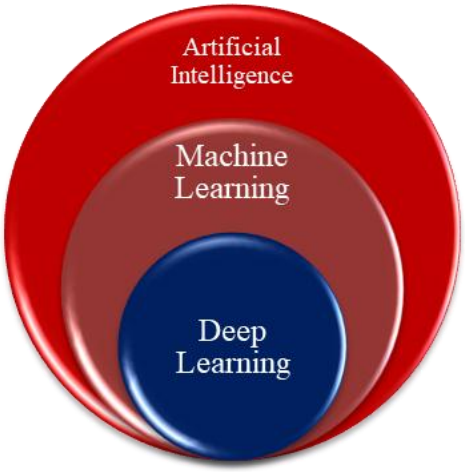

Figure 2. Comparison of Deep Learning with Machine Learning and Artificial Intelligence.

III. DEEP LEARNING

Being a subset of machine learning, it is often bemused with it. Deep learning algorithms have number of layers and each of these layers provide a different interpretation of data. This approach is called Artificial Neural Network. This term is attributed to deep learning as the function is designed to imitate human brain. The difference between machine learning and deep learning can be understood by the following example – let's suppose we want to differentiate between pictures of cats and dogs. So, in machine learning, the machine would be provided with labeled images of cats and dogs; the machine will analyze them and also predict the future pictures to be cat of cat or dog. In the contrary, deep learning would not need those labeled images; instead a new picture is provided through the different layers of neural network. The machine will then interpret different features of the pictures and will reach to a reasoned decision that whether the features lead the picture to be of a cat or dog. Hence it can be concluded that deep learning involves feature recognition and logical prediction, based on which our brain works too. Deep learning can be used when the ML algorithms have a lot of data to derive results from or have much complex problems. A technological application of deep learning would be autonomous vehicles. For the vehicles to think like a human, there should be a series of model networks – one of them will know the process of driving, another will perceive or predict the environment, some other will need to know about the road signs and similar patterns like these. If this advancement in deep learning would be possible in the near future, i.e. the machines will be able to do this much of multiple tasks at the same time and we will probably enter the generation of Artificial General Intelligence.

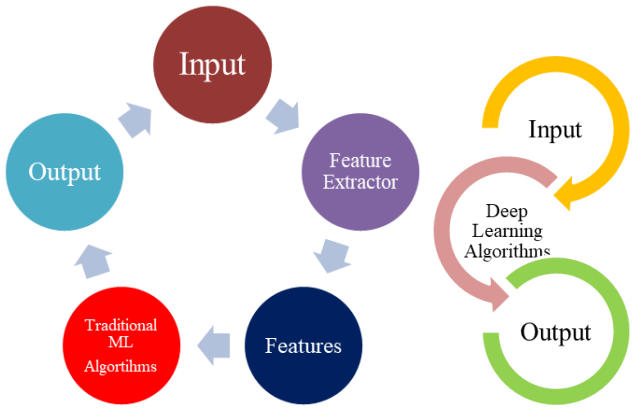

Figure 3. Comparison of machine learning with deep learning method.

The above diagram shows the difference between deep learning and machine learning methods showing that deep learning method does not need the features of the object initially but it predicts the features itself through a large pool of data.

Deep learning technology is originated from Artificial Neural Network. A neural network is composed of connected processors or processing elements called Neurons. The mathematical model of an artificial neuron consists of the following:

1. Processing element
2. Highlighting input (X_i)
3. Weight (w)
4. Bias (b)
5. Summation function ($\sum$)
6. Activation function (f)
7. Corresponding output signal (y)

Deep learning technology based on neural networks is widely being applied in sectors like natural language processing (NLP), business intelligence, cyber security, visual recognition, sentiment analysis, healthcare etc. The main focus of this paper will be healthcare – analysis of cardiovascular diseases and its drug design. It will include the generalized methodology of drug design for cardiovascular diseases, role of AI in it and involved physics in the drug designing (if applied).

Various deep learning techniques include Classic neural networks, Recurrent neural Networks, Convolutional neural networks, Generative adversarial Network, Boltzmann Machines, self-organizing maps and Autoencoders.

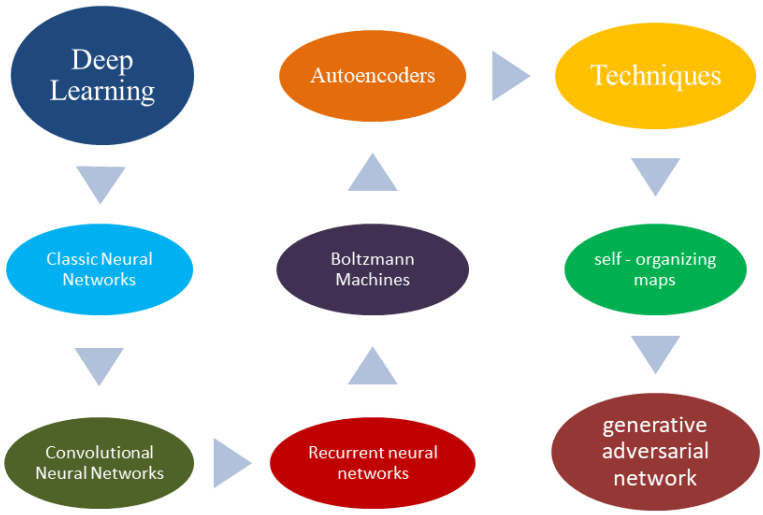

Figure 4: Deep Learning Techniques.

➢ **Classic Neural Networks -** Here, the algorithm is converted into data inputs of two digits. It is a kind of artificial neural network which is applicable for linear as well as non – linear functions. A multi – layered perceptron is employed to identify all connected neural networks.

➢ **Convolutional Neural Networks –** It is an advanced form of ANN (Artificial Neural Network) which has its application in pretreatment of data and its compilation. It is one of the most flexible methods of data processing due to its convertible algorithms. Recognition of images, analysis of visual data and natural language processing are some of the applications of CNNs.

➢ **Recurrent Neural Networks –** It helps in the prediction of sequences as well as produces short – term and long – term memory for the network. With the help of memory, it predicts data in time sequences. RNNs find their application in classification of images and videos, translation of languages etc.

➢ **Generative Adversarial Networks –** It uses a Generator and Discriminator approach of neural networks. The discriminator is able to differentiate real and fake information. The generator creates random data, whether real or fake, and then the discriminator plays its role. There is constant rift between these two components. This competition enhances the level of performance of the network. These networks are widely used in creation of texts and images, enhancement of images as well as discovery of new drugs.

Other classifications of deep learning techniques include Self – Organizing maps, Boltzmann machines and encoders. Self – organizing maps use unsupervised data to lessen the number of random variables. In this approach, the output dimension is represented as a 2D model. Boltzmann machines are unique in themselves as they have no set orientation. The network contains two layers – an input or visible layer and a hidden layer. These layers are composed of nodes (that are like neurons) to perform computations. It is the analogue of an unsupervised deep learning model. Moving further, encoders involve popular algorithms as they use an activation function to process the input and accurately predict the results.

Till now, we've encountered through concepts of AI such as machine learning, deep learning which are commonly based on data collection and extraction. Moving further in the survey, we will discuss how these domains of AI are applicable in the field of drug discovery and management of cardiovascular diseases.

4. Application of AI in the management of Cardiovascular Diseases

Artificial intelligence (AI) is a new area of computer science that uses machines to simulate human intellect. Cardiovascular disorders account for the second leading cause of death. The great majority of data and measures used in illness diagnosis, therapy, and assessment are found in cardiology. AI has an impact on cardiology in all its facets. One significant use of AI in cardiology is individualized decision-making through the use of automated algorithms and structured data that is readily available. AI increases the precision of the 12-lead ECG interpretation, enabling the early detection of cardiovascular events. Using certain methods, data from implanted loop recorders may be readily evaluated. The diagnosis of acute coronary syndrome from electrocardiographic alterations is another application of AI. AI-based models can potentially recommend the best course of action for heart failure patients. A few models have been proposed to assess the efficacy of cardiac resynchronization treatment in individuals suffering from severe left ventricular systolic dysfunction.

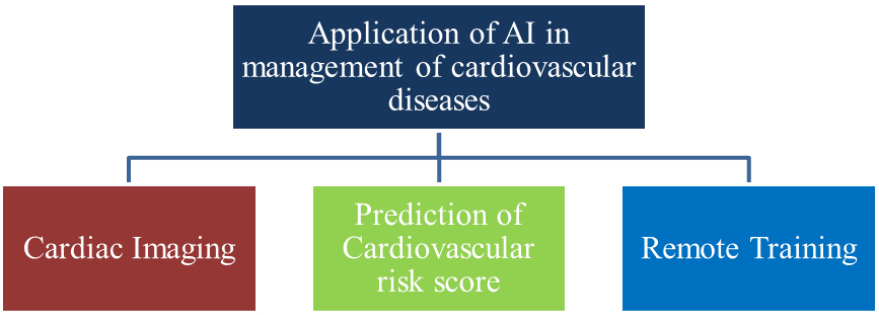

Figure 5: Application of AI in CVD management.

Heart imaging is the other area in which AI is used. As the most accessible imaging modality, echocardiography relies on the operator's ability. Artificial intelligence (AI) helps with probe positioning and noise reduction to mitigate this issue.

Cardiovascular risk score is also predicted by AI systems. By accurately identifying lesion severity, stent size and diameter, and even pre-procedural risk assessment such as FFR connected to coronary CT angiography, artificial intelligence assists interventional cardiologists. Artificial intelligence is also being used extensively in remote training. For example, even a novice echocardiogram operator may obtain clear, comprehensible images even in the absence of any prior instruction. Due to the feasibility of AI-based telemedicine, patients with chronic cardiovascular disease may readily get medical consultations. The phrase AI stresses the least amount of human involvement. As a result, there is less chance of inaccuracy. Machines do not weary as humans do. In cardiology, auscultation is the most crucial component of the physical examination; yet, the accuracy of this test differs across cardiologists and is contingent upon the circumstances. When it comes to deciphering heart sounds, AI is on par with doctors. The risk of stroke, cardiovascular mortality, and cardiovascular illness can be assessed by AI imaging of the retinal arteries. For those with a moderate to high risk of cardiovascular disease, this would be a very useful, non-invasive diagnostic. AI will also support routine checkups, blood pressure management, and medication compliance for patients. A subfield of computer science known as artificial intelligence (AI) allows machines to do activities that need human intellect, such as machine learning (ML), understanding and acquiring semantics, and creating analyses through the use of algorithms and cognitive computing. Deep Learning (DL) is a branch of machine learning which uses artificial neural networks (ANNs) and is composed up of layers of "neurons." Artificial intelligence (AI) has been gradually used to the field of cardiovascular medicine, revolutionizing drug development, clinical care, and diagnosis, therapy, and risk prediction. The following death rates are associated with heart failure (HF):22% at one year, 42.3% at five years, and 10.4% at 30 days. Heart failure is quite common, and treatment for HF patients includes surgical treatments and other medical care. Early identification of heart failure is crucial. According to reports, AI may successfully be employed as an "assisting resource" that physicians use in clinical practice, since it can remedy drug mistakes. Algorithms using machine learning can identify heart failure risk factors in the future. Patients with heart failures may not ordinarily be aware of some HF risk factors, but ML can find them. Predicting illness in patients who are not included in existing research might be another application of ML algorithms. A potential use of machine learning algorithms might be for illness prediction in patients not included in clinical trials or registries where conventional clinical prediction models were verified. In fact, research disparities and historical structural biases may be lessened by using a wide range of indeterminate factors rather than variables

created from homogenous study groups to predict disease. Globally, cardiovascular disease (CVD) accounts for roughly 17.3 million of all fatalities and 31.5% of all-cause mortality. It is the leading cause of death globally. With an estimated 5-6% hospital mortality rate in the US, shock-elevated myocardial infarction (STEMI) is the most severe and difficult CVD. It is possible to use techniques of machine learning to predict CVD in the study populations. The following findings were reached in a study in 2022 in England on the use of artificial intelligence to predict the risk of myocardial infarction through retinal vasculometry (RV): For MI and incident stroke, addition to RV, Framingham risk scores (FRS) were not able to improve model performance in both groups. Personalized medicine may be achieved by using machine learning (ML) to quickly assess various texts, vital signs, social media, electrocardiogram (EKG), echocardiogram, and data from wearable technologies. This allows ML to make intricate choices and predictive analytics. Early identification and preventative therapy of hypertension might be altered by the advancement of DL and pattern recognition, particularly in echocardiographic video and EKG. With their distinct properties, machine learning (ML) models may be trained for every pixel and feature in an image, enabling them to identify a wide range of anomalies and patterns. Accuracy would rise when doctors and AI diagnoses worked together. Additionally, ML models can operate at extremely high speeds without tiring themselves, making up for a personnel shortfall in clinics. AI may also be trained to recognize information that is hidden from the human sight. Wearable digital gadgets that can collect and store patterns and information to aid in more precise diagnosis and management are examples of the sophisticated AI-based technology that has arisen. According to a systematic review research, AI-based models for EKG analysis performed even better than traditional techniques. Furthermore, compared to the conventional method of measuring artery pressure waveform, digital technology may be less intrusive. This was all about the management of cardiovascular diseases using Artificial Intelligence. Moving forward, we should ponder about the drug design and development for these diseases. Rather than focusing on the drug design of the particular disease, we should first take a look at the basics of Computer – aided drug design (CADD) and then the application of Artificial Intelligence in CADD, improvement in the functioning of CADD with the use of machine learning and deep learning methods. Hence a general approach of drug design through AI will be presented through this literature survey, the inherent challenges in it and the way forward.

5.Computer – aided drug design

The process of employing computer algorithms to determine a drug's precise composition, develop it, and assess how well it works on a biological target is known as computer-aided drug discovery. These days, two different kinds of computer-aided drug discovery have been developed: structure-based drug designing and ligand-based drug designing. These methods both precisely identify the makeup and structure of a biological target, which helps to accelerate the drug development process. The speed at which medications are discovered is just as crucial as their discovery themselves. Finding the right dose, researching medications, and evaluating their effectiveness were all done by trial and error prior to the development of computers and algorithms. It goes without saying that this slowed down the process of finding new drugs and bringing them to market. But with the advent of the digital revolution, this process has accelerated thanks to computers and related algorithms. Computer-aided drug development offers a multidisciplinary method for determining a medicine's ideal composition, creating it, and assessing its performance.

Two types of computer – aided drug discovery can be given as: structure based and ligand based.

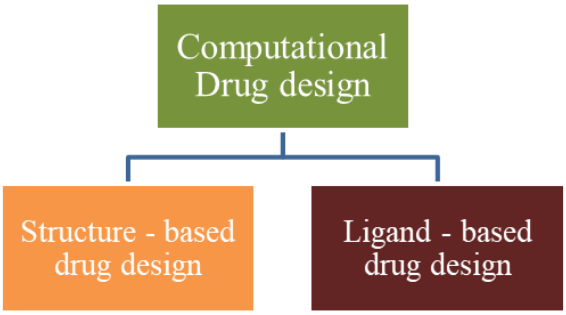

Figure 6: Types of computational drug design.

- **Structure – based Drug design**

Finding novel treatments and pharmaceuticals for a biological target can be considered as the main goal of structure-based drug designing, which uses an interdisciplinary method to determine the structural features of chemical compounds. Because it depends on the three-dimensional understanding of the biological target—a knowledge that may be attained by computational combinatorial chemistry, nuclear modeling approaches, and techniques like NMR spectroscopy, X-ray crystallography, etc.—structure – based designing is sometimes

referred to as direct drug design. The design of the drug candidate is chosen to optimize its efficacy based on the knowledge gathered about the biological target.

- **Ligand – based Drug design**

When finding new drugs for medical conditions, the biological target's structure is frequently unknown, with the exception of a few tiny molecules. In these situations, the data these tiny molecules give is utilized to build new drugs. The term "ligand-based drug-designing" refers to this process. Since ligand-based design of drug relies on the structure of other molecules rather than the biological target's structure directly, it is an indirect kind of computer-aided drug discovery. Several methods, including pharmacophore model mapping and machine learning, are used to extract information from these tiny compounds.

There are often four phases in the drug discovery process: i) Target validation entails identifying the precise disease and choosing a target linked to it. This calls for predictions made by bioinformatics, proteomic and genomic research, and genetic target evaluation. ii) To find lead compounds, molecules in molecular libraries are screened by throughput as well as virtual screening and combinatorial chemistry. To improve efficiency of drug candidate for cellular functional testing, an iterative cycle of QSAR/QSPR studies and in-silico work is carried out.

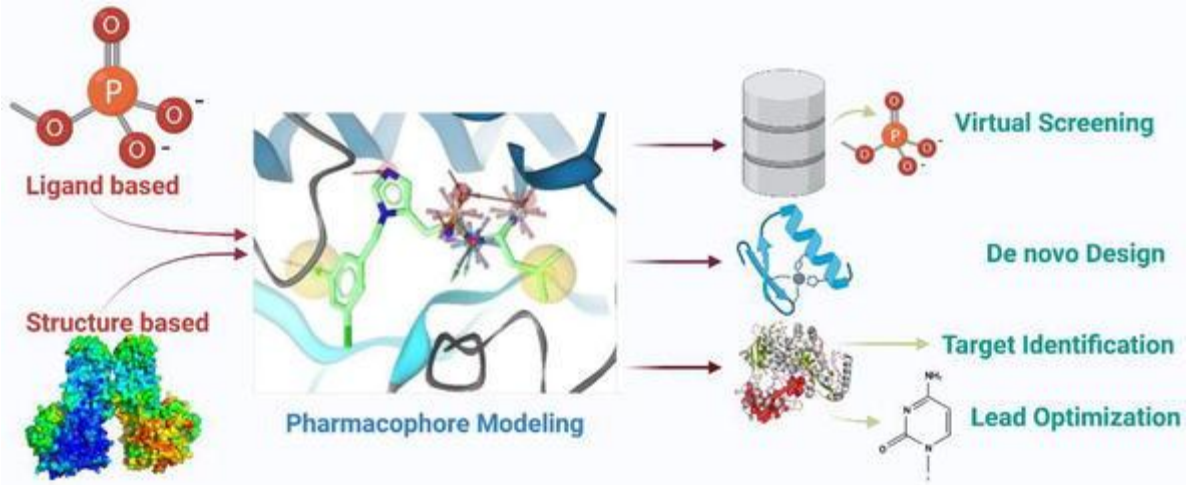

Figure 7: Processes involved in Ligand– based and Structure– based drug design.

CADD techniques play a very important role in identifying potential drug candidates, optimizing their structures, and predicting their interactions with specific targets relevant to cardiovascular conditions. An example of drug developed for these kind of diseases is Ivabradine (Corlanor). Ivabradine lowers heart rate in patients with certain heart conditions.

6.Use of CADD and Artificial Intelligence in the development of Ivabradine

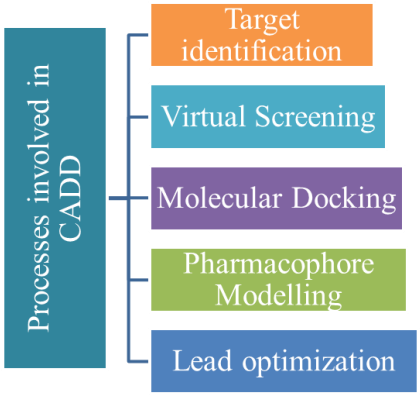

Figure 8: Processes involved in CADD.

1. **Target Identification** – Identify the molecular target associated with the therapeutic effect of the drug. Regarding Ivabradine, the target is the I_f (funny current) channel in the sinoatrial node of the heart.
2. **Virtual Screening** – Computational methods are used to screen databases of chemical compounds for potential candidates that may interact with the target.

3. **Molecular Docking** – Molecular Docking simulations are employed to predict how well these compounds bind to the target.
4. **Pharmacophore Modelling** – a pharmacophore model is developed based on the structural features necessary for the interaction between the drug and its target. This model is used to guide the design and optimization of lead molecules.
5. **Lead Optimization** : Lead compounds are identified from the virtual screening that show promising interactions with the target. The chemical structures of these lead molecules are optimized to improve binding affinity, selectivity and other pharmacokinetic properties. It involves QSAR (quantitative structure – activity relationship.
6. **Clinical Trials** – The optimized compounds are synthesized and processed for preclinical trials. If those are successful, the drug candidate proceeds for clinical trials involving human targets.

Scientists and researchers in the pharmaceutical sector are using AI more and more to solve these problems by streamlining operations, lowering total costs, and boosting productivity. Various steps of the process are utilizing AI-based approaches, such as predicting the three-dimensional structures of targeted proteins, in-silico chemical synthesis, complicated property calculations cell sorting based on real time images, quantum mechanisms, and assay creation. Deep learning, artificial intelligence, and machine learning may be used to standardize and improve these processes, which will significantly speed up the R&D drug development process. One of the earliest uses of AI techniques in the domains of molecular biology and chemistry was the estimate of protein secondary structure using sequential information. AI has long been used in medication development, especially when predicting the relationships between structure and activity. The concept of utilizing a descriptor set and experimental values can be traced back to the groundbreaking work of Hansch, the "father of QSAR," who used computers to identify and measure the physical and chemical characteristics of biological molecules, as well as to Hammett's groundbreaking approach to link equilibrium constants and reaction rates of derivatives of benzene. A variety of machine learning techniques, such as the random forest (RF) and support vector machines (SVM), were developed and used in drug discovery to close the difference between serendipity-based and rational drug development. The issue of "garbage in, garbage out" (GIGO) impacts all of these models. Determining which chemical qualities to combine in order to obtain the data that would yield the most accurate forecasts is the most enduring challenge. Since about 2010, deep learning has become a more well-defined concept, and in order to support this advancement, more efficient techniques have been looked for. Deep learning methods have the potential to produce more accurate results since they can analyze and predict complex relationships between chemical representations and observations (such as bioactivity and toxicity). Algorithms in machine learning (ML) are used to identify an interlinking relationship inside a classified data cluster. During the supervision of learning, regression and classification techniques are used to develop prediction models using information from input and output sources. The outcome of supervised machine learning (ML) comprises illness diagnosis under subgroup classification and ADMET prediction under subgroup regression. Unsupervised learning classifies and analyzes data based simply on input data, making use of feature-finding and clustering algorithms. Deep learning (DL), a subfield of machine learning, adapts to and makes sense of the massive volumes of experimental data by means of "perceptons," a collection of intricately linked computer components that mimic the dissemination of electrical impulses in the brain and resemble biological human neurons. Every node in an artificial neural network (ANN) takes a distinct answer and uses algorithms to transform it into useful output in order to solve problems as a group. Three types of artificial neural networks (ANNs) that may be either supervised or unsupervised include recurrent neural networks (RNNs), convolutional neural networks (CNNs), and multilayer perceptron (MLP) networks. Unsupervised machine learning can provide results like the recognition of disease targets and sickness subtypes by using feature-finding algorithms and grouping. While maintaining the necessary levels of safety and efficacy, predictive software model and machine learning approaches enable the identification of drug-particular targets and their relationship to the correspondence. Using modulator probes of small molecule or understanding their structural biology, a variety of in-silico profile selection techniques, such as virtual ligands or structure-based design methods, may be used. When choosing compounds, drug design approaches like Coulomb matrices and molecular fingerprinting also take into account the compounds' physical, chemical, and toxicological characteristics .The drug design logarithm also incorporates chemical descriptors like electron concentrations around molecules, potential energy scales, and three-dimensional atomic coordinates. Quantum mechanical approaches are considered to calculate the binding affinity of the drug onto the target. This shows that Artificial Intelligence along with physics is revolutionizing the field of drug design. It reduces costs and also saves a lot of time spent in the traditional drug discovery processes.

7. PHYSICS INVOLVED IN DRUG DISCOVERY

Drug design involves medicinal chemistry, biological phenomena as well as physics interfaces. The use of physics with computational methods has revolutionized drug discovery process. Interaction of drug candidate

with the target protein involves rigorous physical models such as binding affinity (measure of how the ligand is bonded with the protein), calculation of energy of the complex system (drug – target system) which includes the estimation of Gibbs' free energy of system. Reason behind concentrating on Gibbs' free energy is that most of the interactions take place at constant pressure. Another domain of physics used here is the quantum mechanical treatment of the complex system. Quantum models break the system into smaller units which are feasible to analyze which was near to impossible for the classical physics simulations as the system comprises of a large number of molecules which is difficult to study through classical mechanical approach (data – based). The Born–Oppenheimer approximation, which concludes that the high mass–to–electron ratio of atoms in a molecule (a factor of 1:1,836) enables for the separation of the nuclear motions and electronic motions and parameterization of the system's energy being a function of the nuclear coordinates, is the only reason why methods based on classical molecular mechanics are typically used to interpret the energy of a system in molecular modeling because the systems studied are too large for methods of quantum mechanics—even those which consider only valence electrons—to handle. Unquestionably, a deeper comprehension of the molecular aspects of drug binding is crucial for igniting the scientific curiosity of seasoned researchers and for promoting imagination, creativity, and invention as a fantastic opportunity for trainee scientists and students. This is an opportunity for creativity, and we think physics will keep becoming more and more significant in drug development in the future.

8. FUTURE PERSPECTIVE

A prospective chemical must satisfy a number of essential requirements in order to be approved as a powerful lead or medication. It also has to meet a number of pharmacological requirements. Merely 40% of medication or lead candidates, on average, successfully complete the various stages of clinical trials and receive approval for use in clinical settings. There are disadvantages to each of the computational techniques utilized in CADD, including as virtual screening, QSAR, pharmacophore modeling, molecular docking and molecular dynamics. Furthermore, there are several instances of these computational techniques being failed in the literature, and ADME and many toxicity measurement tools are not supported by trustworthy experimental data. It is imperative that tools and algorithms be updated on a regular basis in order to correct shortcomings and enhance the effectiveness of assessing powerful lead compounds. Enhancing database dependability is also essential for the development and upkeep of high-caliber experimental compounds. Many pharmacophores are unable to pass the biological activity test because there are insufficient high-quality datasets. Databases should provide comprehensive information on genomes and proteomics, high-quality sequencing data, and structural and physicochemical characteristics. Still, additional enhancements and optimization are required. Late-stage medication failures may be avoided by bringing together regulatory agencies, academic and industry scientists, and regulators to make judgments on standardizing, regulating, and validating the present platforms to guarantee precision, specificity, and repeatability. Additionally, by combining in silico and in vitro models of CVD based on personal genomes, environmental variables, and choices of lifestyle, it may be possible to provide in vivo predictions that are more accurate. This would benefit patients with CVD by giving them access to more effective and safer treatments. The current approach that uses animals as models in the preclinical stage may need to be changed in light of the new drug discovery paradigm.

9.CONCLUSION

In the modern era, CADD approaches like molecular docking, VS, homology modelling, QSAR modeling have offered an effective tool for novel drug discovery and formulation optimization development. The most promising medication candidate may be obtained by researchers in a highly economical manner thanks to the algorithms and computational tools, which also reduce time and lower the danger of discovering non-viable developing leads. Researchers and physicians continue to face significant challenges in the early detection of CVDs. CADD, however, can help scientists learn more about how medications and receptors interact. Current drug development is utilizing the pharmaco-informatics technique, which offers a wealth of fundamental knowledge on drug-receptor interactions. It offers useful details regarding lead compounds, target molecules, screening, and optimization. Not only Ivabradine, a number of drugs have been developed till now named as Atorvastatin, Clopidogrel (Plavix), Rivaroxaban (Xarelto), Iosartan etc. By employing computational methods, researchers can explore a vast chemical space, predict potential drug – target interactions, and optimize drug candidates. It will accelerate the drug discovery timeline and increase the possibility of identifying effective and safe cardiovascular medications.

REFERENCES

[1]. **https://extrapolations.com/the-role-of-ai-and-physics-in-the-future-of-drug-discovery/**
[2]. Askr, H., Elgeldawi, E., Aboul Ella, H., Elshaier, Y. A., Gomaa, M. M., & Hassanien, A. E. (2023). Deep learning in drug discovery: an integrative review and future challenges. Artificial Intelligence Review, 56(7), 5975-6037.
[3]. De Vivo, M., Masetti, M., Bottegoni, G., & Cavalli, A. (2016). Role of molecular dynamics and related methods in drug discovery. Journal of medicinal chemistry, 59(9), 4035-4061.
[4]. Blanco-Gonzalez, A., Cabezon, A., Seco-Gonzalez, A., Conde-Torres, D., Antelo-Riveiro, P., Pineiro, A., & Garcia-Fandino, R. (2023). The role of ai in drug discovery: challenges, opportunities, and strategies. Pharmaceuticals, 16(6), 891.
[5]. Yang, X., Wang, Y., Byrne, R., Schneider, G., & Yang, S. (2019). Concepts of artificial intelligence for computer-assisted drug discovery. Chemical reviews, 119(18), 10520-10594.
[6]. Singh, S., Gupta, H., Sharma, P., & Sahi, S. (2023). Advances in Artificial intelligence (AI)-assisted approaches in drug screening. Artificial Intelligence Chemistry, 100039.
[7]. Smith, J. S., Roitberg, A. E., & Isayev, O. (2018). Transforming computational drug discovery with machine learning and AI. ACS medicinal chemistry letters, 9(11), 1065-1069.
[8]. Sadybekov, A. V., & Katritch, V. (2023). Computational approaches streamlining drug discovery. Nature, 616(7958), 673-685.
[9]. Aminpour, M., Montemagno, C., & Tuszynski, J. A. (2019). An overview of molecular modeling for drug discovery with specific illustrative examples of applications. Molecules, 24(9), 1693.
[10]. Ferreira, L. G., Dos Santos, R. N., Oliva, G., & Andricopulo, A. D. (2015). Molecular docking and structure-based drug design strategies. Molecules, 20(7), 13384-13421.
[11]. Sharma, V. K., & Bharatam, P. V. (2022). Artificial Intelligence in Drug Discovery (AIDD). Current Research & Information on Pharmaceutical Sciences, 16(1), 3-7.
[12]. https://www.researchgate.net/publication/352308845_Artificial_Intelligence_in_Drug_Discovery_Applications_and_Techniques.
[13]. Sarma, H., Upadhyaya, M., Gogoi, B., Phukan, M., Kashyap, P., Das, B., ... & Sharma, H. K. (2021). Cardiovascular drugs: an insight of in silico drug design tools. Journal of Pharmaceutical Innovation, 1-26.
[14]. https://www.researchgate.net/publication/257804496_Physics_and_Its_Interfaces_with_Medicinal_Chemistry_and_Drug_Design.
[15]. https://www.researchdive.com/blog/computer-aided-drug-discovery-a-quick-look-at-its-types-and-examples.
[16]. Shameer, K., Glicksberg, B. S., Hodos, R., Johnson, K. W., Badgeley, M. A., Readhead, B., ... & Dudley, J. T. (2018). Systematic analyses of drugs and disease indications in RepurposeDB reveal pharmacological, biological and epidemiological factors influencing drug repositioning. Briefings in bioinformatics, 19(4), 656-678.
[17]. Shameer, K., Pugalenthi, G., Kumar Kandaswamy, K., & Sowdhamini, R. (2011). 3dswap-pred: prediction of 3D domain swapping from protein sequence using Random Forest approach. Protein and peptide letters, 18(10), 1010-1020.
[18]. Keiser, M. J., Setola, V., Irwin, J. J., Laggner, C., Abbas, A. I., Hufeisen, S. J., ... & Roth, B. L. (2009). Predicting new molecular targets for known drugs. Nature, 462(7270), 175-181.
[19]. Tripathi, N., Goshisht, M. K., Sahu, S. K., & Arora, C. (2021). Applications of artificial intelligence to drug design and discovery in the big data era: a comprehensive review. Molecular Diversity, 25(3), 1643-1664.
[20]. Chen, R., Liu, X., Jin, S., Lin, J., & Liu, J. (2018). Machine learning for drug-target interaction prediction. Molecules, 23(9), 2208.