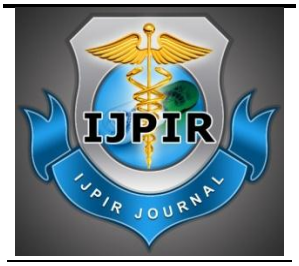
Research Article



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STIMULUS OF ARTIFICIAL NEURAL NETWORK IN DRUG DISCOVERY, DEVELOPMENT AND RESEARCH

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ABSTRACT

Artificial neural networks (ANNs) methods are representation of pattern gratitude proficiencies of the neural networks of the human brain. Also, to a single neuron in the brain, artificial neuron unit receives signals from many external sources, processes them, and makes pronouncements. Fascinatingly, ANN simulates the biological nervous system and draws on analogues of adaptive biological neurons. Experimental designs for the ANNs methods are laid-back and can map functions using historical or incomplete data, which makes them a powerful key for simulation of several non-linear systems. ANNs in particular, have involved enormous attention due to the variety of advantages they offer over the conventional methods. Among these advantages the ability to adapt, fast speed, massive parallelism, and robustness are the most profound. Since of their capacity for making predictions, pattern recognition, and modelling, ANNs have been very useful in many aspects of pharmaceutical research including modelling of the brain neural network, analytical data analysis, drug modelling, protein structure and function, dosage optimization and manufacturing, pharmacokinetics and pharmacodynamics modelling, and in vitro in vivo correlations.

INTRODUCTION

The pharmaceutical industry now-a-day conversant with the merits of espousing the quality -by-design principle together with process analytical technology in drug development and manufacturing [1]. Spreads in computational competences have given a noteworthy enhancement in the area of drug designing and delivery, which includes the applications of understanding molecules characteristics and chemical bonding, towards analysing the pharmacological and toxicological features of drugs and designing effective and innovative drug delivery systems. This research work presents some advanced computational intelligence tools

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beneficial for modelling the situations that inhibit in the process of designing drugs. By designing a drug indicates the selection some variables of drug formulation, for finding optimal physiognomies of drug. In this methodology, when applied alone or in concurrence, can provide a diversity of data in drug designing and development processes, includes:

- Synthesis and screening of a molecule
- Structural and physicochemical features associated with the biological profile
- Mechanism of action, chemical reactivity, and selectivity of a drug and the macromolecule
- Specific biological activity and toxicity
- Ligand-based drug designing
- Biological screening;
- Toxicity screening
- Optimization of the drug designing and development process.

METHODOLOGY

Artificial Neural Networks

Artificial neural networks (ANNs) are computational methods instigated by software programs that analyse data similar to human brain roles such as learning, generalising and finding solutions to the problems based [1] on knowledge that contains a collection of neuron units interactive with each other via axon connections. Alike to the brain structure, the network encompasses of numerous processing elements or nodes which are competent to extract nonlinear relationships from the data and use this information to interrupt the results from required situation. Neuron system contains the units such as input, weights associate with each input, transfer function and output. The Back-Propagation (BP) algorithm is perchance the most widely used supervised training algorithm in multivariate calibration. The network constructed input, hidden and output nodes in three layers. A foremost assistance of ANNs is that they do not need rule-based, well-structured experimental designs and can map functions using past or partial data. ANNs are capable of distinguishing linear and nonlinear designs by means of inexact input data. Hence, ANN is now and then denoted to as knowledge-based multidimensional modelling. The transfer functions usually have a sigmoid function, but they may also take the form of other nonlinear functions, piecewise linear functions, or step functions. They are also often monotonically collective, continuous, differentiable and bounded.

Data processing

The term general error is frequently used in neural network which is calculated by means of cross-validation. In this method the calibration set is randomly divided into two subsets, one used for training (including 70% of the calibration samples), and the other for [2] testing (the remaining samples). The test set is held out during training, which avoids the overlay among training data and test data, yielding a more precise estimation for overview presentation of the method. With the purpose of performing a supervised training and prediction we need a way of evaluating the ANN output. The most generally used stopping criterion in neural network training is the Sum-Square-Error,

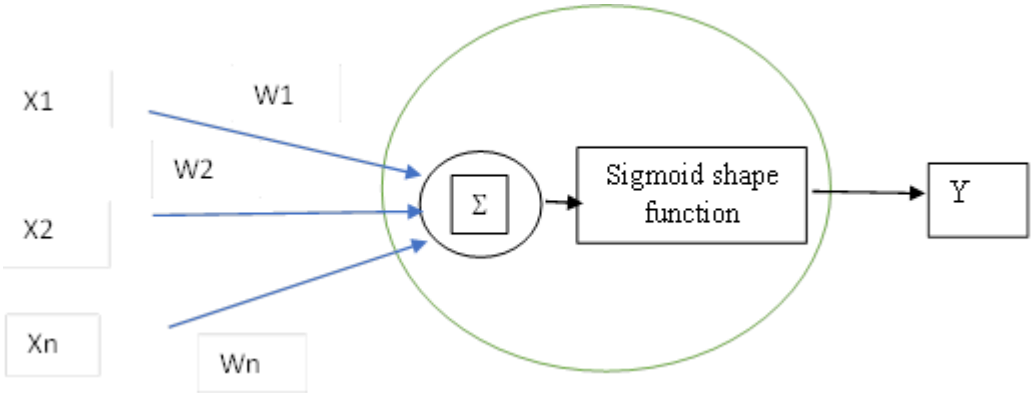

Figure 1 An Artificial Neuron

Training

One of the furthermost momentous attributes of an ANN is its aptitude to learn or train by interrelating with its environment or with an information source. Learning in an ANN is usually proficient through an adaptive technique, recognized as learning rule or algorithm, whereby the weights of the network are incrementally [2, 3] attuned so as to progress a predefined presentation measure over a time. Training can be of two kinds: supervised and unsupervised. In supervised a global error signal rules the edition of weights of the network, classically using an error correction or gradient descent method. In unsupervised training the network creates internal representations of the impinging vector stream using information that is locally available to a connection.

Back propagation algorithm

The gradient descent algorithm for multi-layered feed forward neural networks where neurons have sigmoid signal functions is called the back propagation learning algorithm [4]. It trains a neural network using a gradient descent algorithm in which the mean square error between the network's output and the desired output is diminished. This generates a global cost function which is minimized iteratively by back propagating the error from the output nodes to the input nodes. Once the network's error has reduced to less than or equal to the specified value, the network has converged and is painstaking to be trained.

ANNs classification

General sorting of ANNs is graphically presented in Fig 2. Literature review showed in the field of EPI proposes that [4] Hopfield networks and feed forward networks using back propagation algorithm are more common.

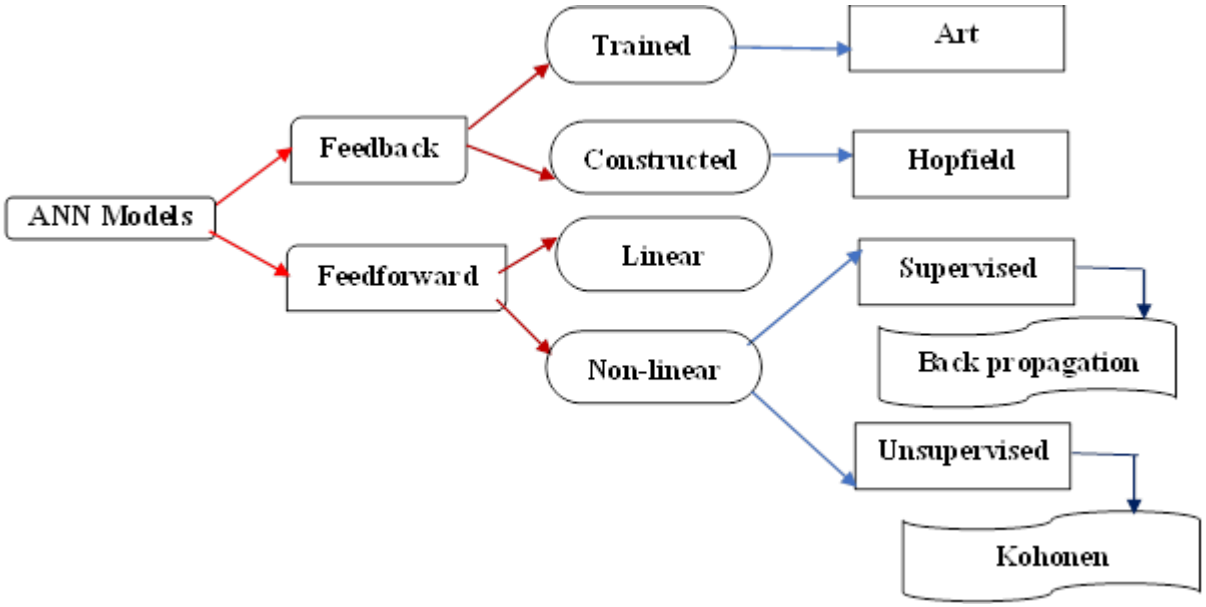

Figure 2 General sorting of ANN

TARGET CORROBORATION IN DRUG DISCOVERY AND DEVELOPMENT

The word "target" is discussed to molecules and sites that contribute in the instigation and evolution of diseases. Their inhibition or down-regulation decreases the pathological function of diseases and helps in restoring the normal [5] state of cells/tissues/organ. Animal models, such as transgenic and knockout models, are used widely for the identification and validation of the target during initial studies.

Nevertheless, the eventual endorsement of the validation process is through the formation of therapeutic potential via studies in humans where the therapeutic potential is well-known by the decrease in disease burden and the improvement of patient existence time. Target validation includes the identification of a viable target, its role in the pathological pathway, and the assessment of chemically hindering it with drug.

A robust target validation process likewise encompasses the determination of anti-targets and counter-targets [6]. Anti-targets are molecules that play important role in the normal functioning of cells and tissues, and their down-regulation can result in side effects or virus progression. Counter-targets are proteins that have no momentous role in the disease; though, when they are curbed by a drug, they can have momentous undesirable side effects. Genomic and proteomic studies can help in the identification and correlation of specific genes and proteins as tumour drug targets in cancer therapy.

These goals should have a clear role in the establishment and evolution of cancer cells, and care must be taken to evaluate for the down-regulation of target by other pathways or mediators or a modification in the expression level due to a pathological condition and bio variability among individuals. The validation process of these tumour targets should involve inclusive testing on prevailing drugs that can alter their function, confirmation of the overexpression of proteins resultant in disease progression, strong evidence of the target role in disease pathogenesis, or endorsement.

VALIDATION IN DRUG DISCOVERY AND DEVELOPMENT

ANNs and other machine learning algorithms have been implemented in the field of drug design and delivery. For example, Wale [1] conferred the increasing role of machine learning in drug discovery and highlighted several aspects and glitches within drug discovery that are utilizing machine learning technology (MLT) to improve and speed up the drug discovery process [1].

IMPLENTATION OF ANN IN TARGET VALIDATION

Target validation, and drug design all together, can present formidable tasks for users of ANNs. The number of advantages can be very great, often tens of thousands [4], thereby invoking the curse of dimensionality; that is, given that each feature contains a assortment of values, a congruently large amount of training data must be obtained to successfully span the input space [1, 5], exclusively given that the distribution of such data may be unknown. Moreover, the choice of ANN type can have a thoughtful effect on both the training time and organization accurateness; even with the same training and testing data, two different algorithms can produce intensely different results.

Target Discovery

The first two stages of target validation involve, in succession, the discovery of biomolecules of interest and the evaluation of such biomolecules for their potential as drug targets, a process we shall collectively refer to as target discovery [8]. Given the large number of types of molecules that can be targets (e.g., receptors, proteins, genes, enzymes, etc.), a correspondingly large number of methodologies (e.g., in vitro investigation, data mining of existing data, phenotype screening, etc.) are used in target discovery; in many cases, however, ANNs can increase both the speed and effectiveness of these procedures. ANNs can serve as a great tool in optimization stage of the method development to help save time and cost during this stage of research. Further, ANNs may help to detect dealings in analysis of inspiring sets of data such as characterization of mixtures.

Target Screening

Once potential drug targets are known, a bioassay must be designed to identify the activity from chemical interactions with such targets, a high throughput screening (HTS) process must be developed to test thousands (if not millions) of candidates, the screening performed, and any observed interactions (i.e., “hits”) verified. Given the interconnections between these steps, we shall

refer to the entire process as target screening [8, 9]. As ANNs are commonly used tools in QSAR modelling, they find use at multiple places in the target discovery process.

For instance, it has been defined how machine vision can replace human eyes in HTS, thereby increasing throughput. In such situations, ANNs can be used to both identify whether targets are present in known locations and identify previously unknown target locations as well as to predict other properties of the agents being investigated once the data are acquired. Moreover, ANNs also have been successfully used in design of stable formulations for multiple active components, such as rifampicin and isoniazid microemulsions. ANNs are certainly very useful in the reformulation design and would help reduce the cost and length of reformulation learning.

Hit Evaluation

Hit evaluation includes the evaluation of the pharmacological and toxicological properties of hits and as such has considerable overlap with Absorption, Distribution, Metabolism, Excretion, and Toxicity (ADMET) and drug delivery; accordingly, in the interest of simplicity, applications of ANNs to these topics will be covered in the next section. With respect to the pharmacology of confirmed hits, ANNs see extensive use in the prediction of side effects; notable examples include [10], which use decision trees (DTs) and inductive-logic programming and kernel regression methods, respectively.

CONCLUSIONS AND FUTURE PERSPECTIVES

The contribution of ANN in decision making in the medical field has been enormously effective specifically as it is implemented to disease diagnosis, classification and modelling. The ANNs are technologically advanced new approaches as an alternate to classical modelling methods. Applications of ANNs in the pharmaceutical area have been of improved interest due to their ability to model process that cannot be effectively characterized using classical statistical methods. The ANNs do not need special computer as neural nets are described using mathematical models and executed using ordinary computer software. Training time for networks is long but noticeably beneficial. ANNs are an enhancement over comeback surface methodology since they permit integration of literature and experimental data to solve common problems in pharmaceutical industry. It is capable of solving problems involving complex pattern recognition, which is advantageous in pharmaceutical product development. The use of artificial neural network in pharmaceutical research drug discovery is growing at a fast rate with very promising prospects.

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