

[Home](#)
[Call for Papers](#) [Journal Archives](#)
[Editorial Board](#)
[Contact Us](#)
www.computing-infosystemsjournal.info

Published Articles Vol 6, 2015 Series

A Study of Learning Stakeholders' Usage and Continuous Intention in Using e-Learning Innovations in Teaching-Learning Activities: A case study of Nigeria Universities

Osabor, V. O. & Chiemekwe, S. C.

A Contemporary Review of major developments of Social Issues in Management Thought and Theories

Ademola E.O. & Adeniji O.A

Sustainable Aircraft Maintenance Hangar: Imperative to the Nigerian Aviation Industry.

Olaniyi, T. K.

An Exploratory Research on the Regularity of Content Updates in Selected Nigeria websites

Salami, A.

Security Issues in the Internet of Things

Odulaja Godwin Oluseyi, Awodele Oludele, Kuyoro Shade & Omilabu A.A

Sustainable Development of Entrepreneurial Skills: Imperative for Aviation Training and Development in the Emerging Nigerian Economy

Olaniyi, T. K.

A Quantification of link Average Throughput Performance in HSDPA and HSUPA by Field Measurement

Joseph Isabona & Odion Ebhomien Andrew

Usability And Accessibility Enrichment E- Mail Application System for the Visually Impaired

Omowunmi.O Adeyemo, Samuel.T Oladosu & Babatunde Sanyerr

Students' Attitudes towards Wait Times in Students' Health Centers – The Case for Pseudo Aggravated Sicknesses

Ajibike O Iteboje PhD & Luria Young PhD & Olumide Longe PhD

Adapting High Probability Algorithms for Filtering Advance Fee Fraud E-Mails Using the Concept of Data Locality

Okesola, J.O., Ojo, F.O. & Longe, O.B.

Computer Based Testing (CBT): An Assessment of Student Perception of JAMB UTME in Nigeria

A. A. Sanni & M. F. Mohammad

A Trend Analysis of Boko Haram Insurgent and Computer Generated Intelligence in Counter-Insurgency in North East Nigeria

Ajike, C.A.

Improving The Security of Point of Sale Terminal Transactions Using Mobile Phone Embedded Authentication

Adedayo, O.S. & Bolaji, A.A.

A Rainfall Predictor Based on Fuzzy Inference Model

Ugwu, C., Ejiofor, C.I. & Nwosu. E.H

Development of an Electronic Diary Application for Windows Smartphones

Ibrahim A. Adeyanju, Oluwaseun O. Alo and Adedoyin O. Aderibigbe

Specific Absorption Rate and Temperature rise Computation in Human Tissues due to Electromagnetic Field emission from Mobile Phones at 900 MHz and 1800 MHz

K. Obahiagbon & J. Isabona

Software Visualization Approach for Monitoring Election Trends In Nigeria

Olagunju, M. Ph.D, Ayeshimi, Y.M PhD & Abdullahi A.B

Internet Security vs. Privacy: The Greater Monster

Osika, A. N. & Ekuobase, G.O.

Neuro-Fuzzy Framework for Finding Clinical Trials in the Drug Discovery Process

Oladele T. O., Williams F. E. & Sadiku J. S.

Automatic Phone Number Extraction System from Scanned Documents Using Finite State Automata

Ameen A. O., Ibiyemi T. S., Olubaji S. O, Awotunde J. B & Olagunju M

Design and Implementation of Ayo Olopon Game

Babatunde, A.N., Abikoye, O.C., Mabayoje, M.A., Akintola, G.A. & Oderemi, C.

The Society for Multidisciplinary & Advanced Research Techniques (SMART) and The African Society for Information and Communication Technology (ASICT) & Other Institutional Partners

The Society for Multidisciplinary & Advanced Research techniques (SMART), The African Society for ICTs (ASICT) and other collaborating institutional partners sets up the Computing, Information Systems & Development Informatics Journal as a medium for reporting research and collaborative efforts that globally address the multi-prong challenges of Africa and other parts of the world through ICT-based solutions which have contextual and cultural relevances. We seek to increase the influence of IT and Allied professionals among decision-makers in Africa by using collaboration and mentoring as viable tools for promoting informed policy on national and international ICT issues. Our membership cuts across academics, scientists, engineers, professionals, and businesses in the information technology and allied professions. Organizations and individuals who share a common interest in enabling Africa to participate as knowledge producers and not just knowledge consumers in today's information age are welcome to join the society.

Vision

The collaborations aims to provide a forum for interaction and knowledge sharing in the teaching, research and practice of ICT for Development in Africa.

Mission

To establish a global network of academics and practitioners who will participate as producers of knowledge on the teaching, research and practice of ICT for Development in Africa.

The Computing, Information Systems and Development Informatics Journal is indexed in the following academic and research publication databases

- * AIS Publication Index
- * Index Copernicus
- * Scribd
- * DocStoc list
- * GetCited

Indexing & Impact Factor



Adhoc Code Inspection Versus Checklist-Based Code Inspection: An Empirical Evaluation

Oladele, R. O., Adedayo, H. O. & Oladele, O. T.

An Enhanced Congestion Control System for Mobile Operation

Egwali, A. O. & Ukaoha, K. C.

Modeling Architecture for Multimedia Data Warehouse to Support Decision-Making Processes in Industries

Elusoji, A.A (PhD), Aiyegbusi A.E & Akeredolu, G.R

A Reputation Based fuzzy logic Framework for Virtual Enrolment in Grid Computing Environments

Olusanya, O.O., Olajoyetan M.C., Longe, O.B & Adeyemi, A.S.

Comparative Analysis of PHP and Java Programming Languages for a Semantic Filtering System

Adigun, A.A., Osofisan, A.O. & Longe, O, B

Towards A Mobile Drugs Authentication System For Nigerian Users

Ukaoha, K. C., Dim, C. N., & Daodu, S. S.

Optimal Design of Communication Networks with Memetic Algorithm

R. O. Oladele & H. A. Sanusi

A Review of Cryptography in Wireless Sensor Networks

Opara, C.

A Match-Making Agent Recommender Algorithm for Web based Human Resource Recruitment System

Akanbi C.O. & Akanbi B. E

The Detection of Phishing Adopting Modified Sift Algorithm

Babatunde, A.O. & Agboola, O.N.

Mathematical Models for Lassa Fever Transmission With Control Strategies

Omale D & Edibo Thomas E

AN Adaptive Neuro-Fuzzy Inference System (ANFIS) Model to Good Financial Saving Habit

Amadin, F. I & Obi, J.C.

An Improved Recommender Learning Styles for Distance Learners Based On Decision Tree Approach

Ugwu, Chidiebere & Ochiama, Grace

A Network Intrusion Detection System: Enhanced Classification via Clustering Model.

Balogun, A. O., Balogun, A. M., Adeyemo, V. E. & Sadiku, P. O.

Job Opportunity Factors Analysis Using Decision Tree Algorithms

Ganiyu, I.A & Awoyelu, I.O.

A Review of Soft Computing Techniques for analysis of Spatial, Temporal and Spatio-Temporal Databases

Adeyemo A.B. & Adegun A. A



Published by *The Creative Research Networks*
for the Systems, Multidisciplinary & Advanced
Research Techniques Interest Group .
Int Centre for Information Technology & Development
Southern University, Baton Rouge, LA, USA
www.icitd.com

Useful Links

[Research Resources](#)
[Grants & Funding](#)
[iSTEAMS](#)
[Conferences](#)
[Scholarships](#)
[Cousera](#)

Other Useful Links

[Plagiarism Checkers](#)

Follow the CISDI Journal



Contact the Computing, Information Systems & Development Informatics Journal

submissions@cisdijournal.org or cisdi@creativepublishers.org

A Neuro-Fuzzy Framework for Finding Clinical Trials in the Drug Discovery Process

¹Oladele T. O., ²Williams F. E. & ³Sadiku J. S.

^{1,3} Department of Computer Science, University of Ilorin, Ilorin, Nigeria.

²Department of Clinical Pharmacy and Pharmacy Practice, University of Ilorin, Ilorin, Nigeria.

¹oladele.to@unilorin.edu.ng +2348164916082, ²williams.fe@unilorin.edu.ng; +2348033354532,

¹Corresponding Author

ABSTRACT

The drug discovery process is complex, time consuming and very expensive. Typically, the time to develop a candidate drug is about 5 years, while the clinical phases leading, possibly, to the commercial availability of the drug are even longer (>7 years) for a total cost of more than 700 Million dollars. Declining pharmaceutical industry productivity is well recognized by drug developers, regulatory authorities and patient groups. A key part of the problem is that clinical studies are increasingly expensive, driven by the rising costs of conducting Phase II and III trials. It is therefore crucial to ensure that these phases of drug development are conducted more efficiently and cost-effectively, and that attrition rates are reduced. In this paper, a neuro-fuzzy framework is presented for finding clinical trials in the drug discovery process. The proposed framework was developed based on the combination of two artificial intelligence techniques known as artificial neural networks and fuzzy logic.

Keywords: Clinical Trial, Drug Discovery, Preclinical, Drug Target, Placebo.

1. INTRODUCTION

Pharmaceutical innovation is increasingly risky, costly and at times inefficient, which has led to decreased industry productivity (Booth et al, 2004; Gilbert et al, 2003; Kola et al, 2004). Estimates for the average cost of bringing a new drug to market range between \$800 million and \$2 billion, in which late-stage failures and the rising costs of Phase II and III trials represent key components (Budget US Gov., 1993-2003; Adams et al, 2009). Conducting these phases of development more effectively and reducing attrition rates are therefore major goals. The traditional approach to drug development separates clinical development into sequential, distinct phases, in which progress is measured at discrete milestones, separated by 'white space'. It is argued that the effectiveness of the clinical development can be improved by adopting a more integrated model that increases flexibility and maximizes the use of accumulated knowledge. In this model, broader, more flexible phases leading to submission for approval are designated 'exploratory' and 'confirmatory'. This model is adaptive, parallel and data-led, and allows all available knowledge to be appropriately shared across the breadth of development studies to improve the quality, timeliness and efficiency of the process (Orlof, 2009).

In recent years, there have been important advances to help ensure that therapies for serious conditions are approved and available to patients as soon as there are sufficient data to show that the therapies' benefits outweigh their risks. Despite this progress, there is much more work to be done. Many scientific discoveries still need to be translated into treatments for patients in need of new lifesaving therapies (Woodcock, 2014). Modeling and simulation approaches can be used to represent dose-response and time-response behaviour of safety and efficacy endpoints. Furthermore, these approaches can be combined with Bayesian methods to provide a continuous flow of information across different phases of development. For example, preclinical data can be used to construct models and to provide prior information on model parameters. Likewise, the results from a proof-of-concept (PoC) study can be used to form prior distributions for a similar model to be used in a subsequent dose-finding study (Sheiner et al, 2000; Lalonde et al, 2007). An additional benefit of modeling in early development is that it allows the use of external information (for example, baseline values for safety endpoints) to estimate characteristics of interest about the population. Given the vast quantity of data from other development programmes that are available in most pharmaceutical companies, as well as current discussions within the industry about sharing placebo data across companies, this has huge potential for improving the efficiency of investigation in early development (Orlof, 2009).

The rate of late stage clinical trial failures is the single biggest determinant of returns on pharmaceutical Research and Development. The lion's share of discovery and development costs come at the end of the process, and if those trials fail (whether for safety or lack of efficacy), all the capital invested up to that point is lost (Grainger, 2015). Clinical trials constitute only a small part of the research that is involved in developing a new treatment. Potential drugs, first have to be discovered, purified, characterized, and tested in labs (in cell and animal studies) before ever undergoing clinical trials. In all, about 1,000 potential drugs are tested before just one reaches the point of being tested in a clinical trial.

In this paper, the proposed framework for finding clinical trials in the drug discovery process was developed using both neural networks and fuzzy logic which are artificial intelligence techniques.

2. RELATED WORKS

2.1 Bayesian Modelling Combined With Use Of External Baseline Data To Improve Efficacy and Safety Signal Detection In Early Development

Early development studies for establishing PoC often use small patient cohorts (10–20 subjects). These patients are typically observed for a relatively short period of time (several weeks) to evaluate early efficacy and safety signals, which are frequently measured on a continuous scale and observed several times over the duration of the study. However, the endpoints for the decision to proceed with development or not are typically based on a single time point (for example, change from baseline at the end of the study) and use dichotomized versions of the original variables to characterize responder and non-responder behaviour.

An example of the latter is the transformation of continuous liver function test measurements (for example, alanine aminotransferase (ALT) and aspartate aminotransferase (AST)) into binary indicators (for instance, exceeding three times the upper limit of normal (ULN)). There are, therefore, two types of information loss that often occur in PoC studies: the dichotomization of continuous endpoints and a failure to use all of the available longitudinal measurements collected in the study (Berry, 2006).

2.2 Adaptive Trial Designs In Early Development

The core concept of adaptive trial design (also known as flexible design) is that it uses accumulating data to decide on how to modify aspects of the study mid-trial, in a pre-planned manner, without undermining the validity or integrity of the study (Berry, 2007; Gallo et al, 2006). Possible adaptations include adjustments to sample size, allocation of treatments, the addition or deletion of treatment arms, inclusion and exclusion criteria for the study population, adjusting statistical hypotheses (such as non-inferiority or superiority), and combining trials or treatment phases. Adaptive trials have the potential to translate into more ethical treatment of patients within trials, more efficient drug development and better use of available resources.

2.3 The Coactive Neuro-Fuzzy Expert System (Canfes) Model

The motivation for approximating fuzzy systems by neural networks is based upon the inherent capability of neural networks to perform massive parallel processing of information. This is important in the fuzzy controllers or more generally fuzzy expert systems that are required to process large numbers of fuzzy inference rules in real time. When the neural network representing a given fuzzy expert system is implemented all relevant fuzzy inference rules are processed in parallel. This results in high computational efficiency, which is crucial in many applications such as diagnosis, prediction and so on.

Moreover, the neural network representation is eminently fitted for introducing suitable adaptive capabilities into the system. This is due to the inherent learning capabilities of neural networks which can be used for modifying fuzzy inference rules of the system on the basis of experience. Learning ability is another strength of neural networks. Among the three classes of learning schemes as reported in Hinton (1989), the unsupervised procedures which construct internal models that capture regularities in their input vectors without receiving any additional information (Kosko, 1991), are suitable to find clusters of data indicating the presence of fuzzy rules. The supervised procedures which require a teacher to specify the desired output vector, and the reinforcement procedures which only require a single scalar evaluation of the output are good to adapt the ruling of membership functions for the desired output in fuzzy logic systems.

Hence, a hybrid learning algorithm is being used for the CANFES model. The learning algorithm for this model combines unsupervised learning and supervised learning procedures to build the rule nodes and train the membership functions. The hybrid learning algorithm performs superiorly to the purely supervised learning algorithm such as, back propagation or learning algorithm (Rumelhart et al, 1986), due to the prior classification of training data through an overlapping receptive field before the supervised learning. The learning rate of the original back propagation learning algorithm is limited by the fact that all layers of weights in the network are determined by the minimization of an error signal which is specified only as a function of the output, and a substantial fraction of the learning time is spent in the discovery of internal representation.

This observation was also reported in the two papers (Moody et al, 1989; and Huang et al, 1988). The hybrid learning rule being used for the CANFES model combines both the back propagation (BP) and Kohonen Self Organizing Features Map (KSOFM). While BP is a supervised learning algorithm, KSOFM is an unsupervised learning algorithm. The CANFES model also maintains the concept of human thinking and reasoning as in fuzzy inference systems. So, experts' knowledge can easily be incorporated into the structure. The CANFES structure also saves the rule-matching time of the inference engine in the traditional fuzzy inference system (Oladele et al, 2014, Oladele et al, 2015).

3. METHODOLOGY

The term Neuro-Fuzzy modeling refers to the way of applying various learning techniques developed in the Neural Network literature to fuzzy inference systems. The essential part of Neuro-Fuzzy synergisms comes from a common framework called adaptive networks, which unifies both neural networks and fuzzy models (Jang et al, 1995). An adaptive network is a network structure consisting of a number of nodes connected through directional links. All or part of the nodes is adaptive, which means the outputs of these nodes depend on modifiable parameters pertaining to these nodes. Hence, an adaptive network is used for system identification.

A class of adaptive networks that are functionally equivalent to Fuzzy Inference Systems are known as Adaptive Network Fuzzy Inference System (ANFIS) or Adaptive Neuro-Fuzzy Inference System. ANFIS possesses certain advantages over neural networks (Sugeno et al, 1988; Tagaki et al, 1985). The ANFIS architecture represents both the Sugeno and Tsukamoto fuzzy models. It is basically used in control systems. It has been applied to a wide range of areas such as: nonlinear or function modeling (Jang, 1991; Jang, 1993 (b)), time series prediction (Jang, 1993), online parameter identification of control systems (Jang, 1993) and fuzzy controller design (Jang, 1991; Jang, 1992).

A generalized ANFIS, which extends the characteristics of a more fused neuro-fuzzy system that enjoys many of the advantages claimed for neural networks and the linguistic interpretability of FIS, is called CANFIS (Takagi et al, 1985). CANFIS stands for Co-active Neuro-Fuzzy Inference System, where in both NN and FIS play active roles in an effort to reach a specific goal (Jang, 1991). CANFIS has extended the notion of a single-output system as found in ANFIS, to produce multiple outputs.

In this paper, a hybrid learning algorithm comprising of both supervised learning (such as back propagation network) and unsupervised learning (such as Kohonen self organizing feature map) were employed in order to enhance the adaptive capability of the expert system and make it handle fresh cases that have not been predefined in the knowledge base.

The Coactive Neuro-Fuzzy Expert System (CANFES) model is being used in the proposed framework (Oladele et al, 2014). The model was adopted from the Coactive neuro-fuzzy inference system (CANFIS) which is basically used for the development and simulation of controllers. The Coactive neuro-fuzzy expert system aims at capturing both the linguistic and numeric parameters in order to be able to adequately represent the human expert's reasoning and decision making capability in the process of finding clinical trials in the drug discovery process. The CANFES model is shown in Figure 1 (a) and architecture of the Back Propagation Network is shown in Figure 1 (b).

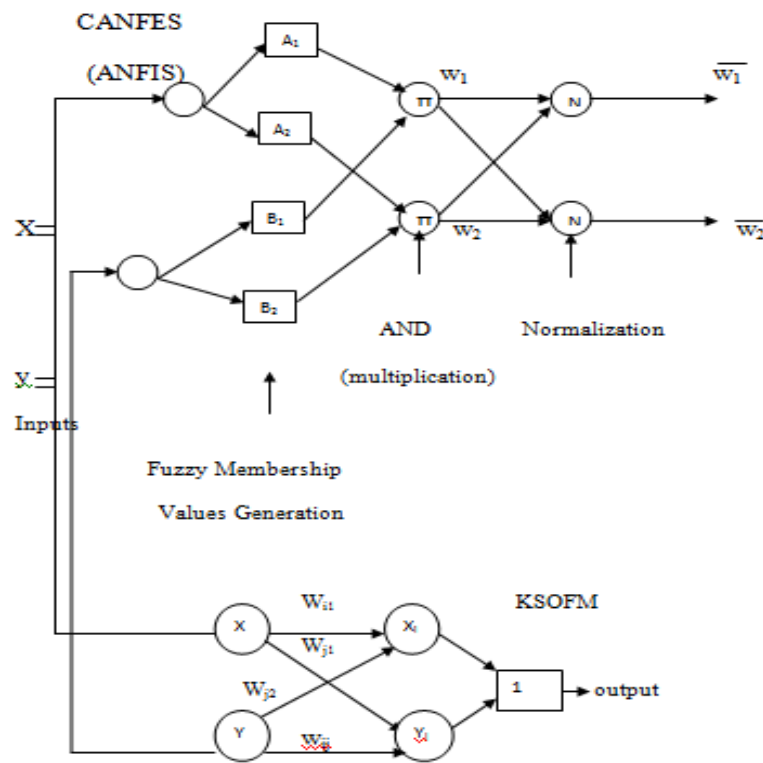


Figure 1 (a): The CANFES Model

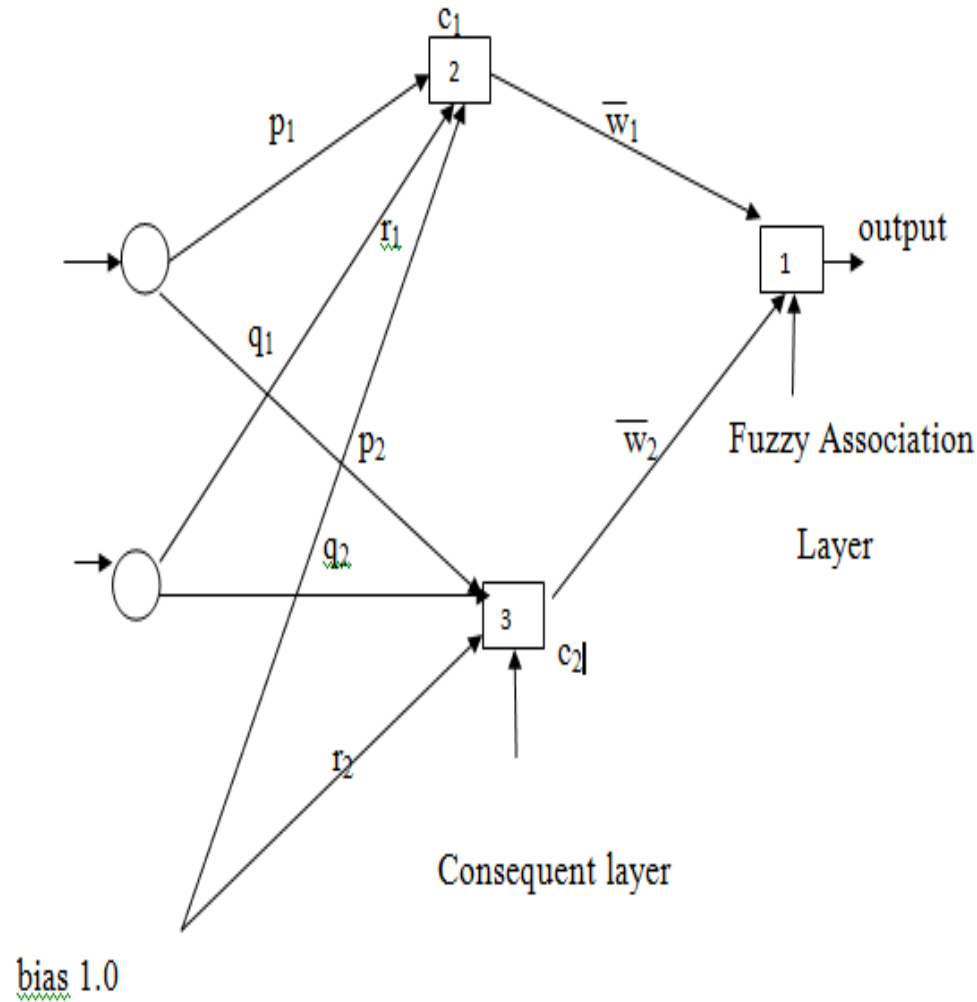


Figure 1 (b): Architecture of the Back Propagation Network.

Normally, clinical data on the relationship between activity of the therapeutic targets, markers of inflammation and remission of symptoms are captured using mathematical models which are continuously adjusted to fit emerging data. Simulation is then used to propose a suitable dose and dosing regimen to achieve the desired response for the majority of patients. In this instance, an 80% probability that 90% of patients would remain flare-free for 2 months. The data derived from this modeling exercise normally allows for selection of a dosing regimen being investigated and confirmed in a Phase III trial.

4. CLINICAL TRIALS

Experimental studies carried out on human subjects with the aim of evaluating an intervention are often referred to as clinical trials. These are research studies that involve testing drugs on patients. Biotechnology companies use clinical trials to assess the efficacy and safety of new therapies and to answer specific health-related questions. Typically, there are three phases during a clinical trial.

These are:

1. Phase I – designed to evaluate the safety of the product in humans.
2. Phase II – analyses the effects of dose escalation
3. Phase III – evaluates the clinical efficacy of the product.

Clinical trials that involve new drugs are commonly classified into four phases. The drug development process will normally proceed through all the four phases over many years. If the drug successfully passes through phases I, II and III, it will usually be approved by the national regulatory authority for use in the general population.

The four phases of clinical trial are as follows and also depicted in table 1:

1. Phase I trial: clinical pharmacology and toxicity. It is designed to evaluate the safety rather than the effectiveness of the drug.
2. Phase II trial: initial clinical investigation for treatment effect. This is to establish the preliminary information or effectiveness or potential promise of the drug for more intensive testing. It also aims to assess the side effects of the drug.
3. Phase III trial: full-scale evaluation of treatment. This is to compare a new drug to an available treatment regimen.
4. Phase IV trial: post-marketing surveillance. The main purpose of phase IV trial is to investigate the long term effects of a drug. After the drug has been approved for marketing, research needs to be undertaken for monitoring for adverse effects on the human populace.

Table 1: Phases of a Clinical Trial (Antonisamy et al., 2010).

	Phase I	Phase II	Phase III	Phase IV
Purpose	To determine safety and dosage	To evaluate the effectiveness	To evaluate clinical efficacy	To evaluate the long-term effects of the drug
Test Population	10 – 30 subjects	20 – 50 subjects	100 – 1000 subjects	>1000 subjects

4.1 Study Design

It is very important that clinical trial be designed so that its result are unbiased and valid conclusions are drawn. Clinical trials to introduce a new drug or other therapy are based on the concept of the randomized, placebo-controlled clinical trial which is also called the gold standard of research studies. The study sample which represents the population is divided at random, into two groups, which are equal in every way. One which is the experimental group is given the drug and the other which is the control group is given either a placebo or an existing treatment (comparator).

4.2 Control Group

In most clinical trials, subjects are grouped into one group which receives the drug under investigation and a second group which receives either standard treatment for the illness or a placebo. The latter set is the control group which provides the researcher with a base from which results can be compared and the effects of the test drug can be interpreted. The control group explains the nature of what would have happened to patients if they had not received the test treatment or if they had received a different treatment known to be effective. Hence, a control is the standard by which experimental observations are evaluated. A Schematic Presentation of a Clinical Trial is shown in Figure 2.

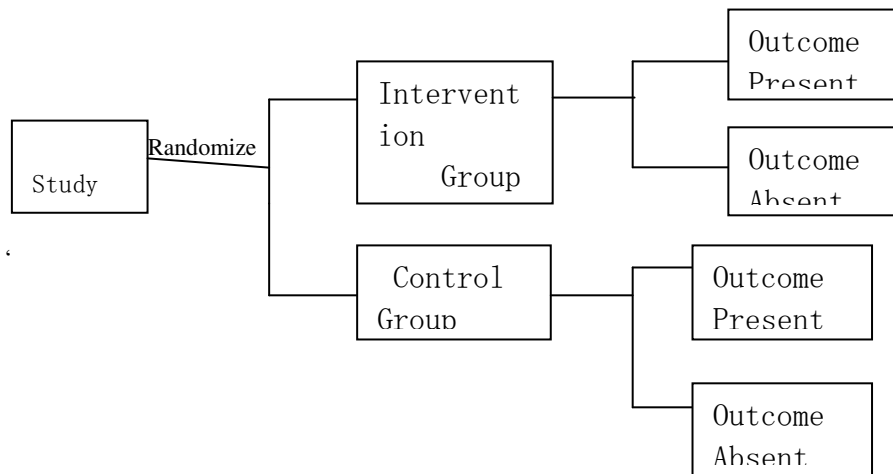


Figure 2: Schematic Presentation of a Clinical Trial (Antonisamy et al., 2010).

4.3 Randomization

Randomization is a term that refers to the process or mechanism that allocates the study subjects to different treatment groups by chance (Altman D. G. 1991). Random allocation means that each and every person has a known chance or probability, generally an equal chance of being given each treatment (i.e. either intervention or control). Randomization introduces an element of chance into the assignment of treatment to subjects in a clinical trial. The simplest version is tossing a coin to decide the allocation of a subject to a study group. The primary aim of randomization is to remove the potential of bias in assignment to one intervention over another.

4.4 Drug Discovery Process

The drug discovery process is a critical issue in the pharmaceutical industry since it is a very cost-effective and time consuming process to produce new drugs. Drug target identification which is the first phase in drug discovery is becoming an extremely time consuming process (Rao and Srinivas, 2011). An important goal of a drug development programme is the selection of a dose and dosing regimen that achieves the target clinical benefit while minimizing undesirable adverse effects. Biological and pharmacological modeling can be very useful in this context. Simulation can be used to propose a suitable dose and dosing regimen to achieve the desired response for the majority of patients.

4.4.1 Algorithm

1. Start
2. Identify the drug
3. Evaluate the population
4. Random selection of participants into two groups (Treatment Group and Placebo Group)
5. Selection of appropriate dose to be administered over a period of time to test for treatment effect
6. Participants in each group are evaluated for outcome of treatment by using statistical methods
7. Evaluate the long-term effect of the drug on the participants
8. Stop

4.4.2 Flowchart

The proposed framework for finding clinical trials in the drug discovery process is depicted in Figure 3. The stages of the drug discovery process which include identification of target, validation of target, hit and lead identification and pre-clinical are shown sequentially. The four phases of clinical trial and approval by Regulatory Agency are also depicted in the framework.

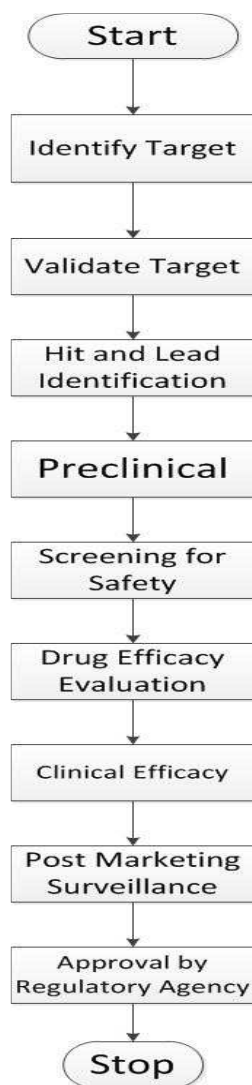


Figure 3: Schematic Flowchart

5. CONCLUSION

A key challenge for the implementation of tools and techniques which advance the quality, timeliness and efficiency of drug development is the ability to work across disciplines and amongst stakeholders to understand how and when to apply these solutions. To address this challenge, we make the following recommendations. First, a common vocabulary and a common understanding of the value of modern trial designs to all stakeholders needs to be defined and disseminated. Second, at the same time, guidelines and case studies for assessing situations in which tools should be applied, as well as for those scenarios when they should not be utilized, should be developed and disseminated. Third, there is a need to create a methodology for dialogue with regulatory authorities to facilitate discussion of clinical strategies which utilize these tools and address potential constraints and issues. Finally, it will be crucial to identify specific solutions to address all mindset obstacles and factual objections that inhibit the adoption of modern tools and adaptive study designs.

REFERENCES

- Adams, C. and Brantner, V. V. (2006). Estimating the cost of new drug development: is it really \$802 million? *Health Aff.* 2, 420–428.
- Adams, C. P. and Brantner, V. V. (2009). Spending on new drug development. *Health Econ.* 26 Feb 2009 (doi: 10.1002/hec.1454).
- Alman D. G. (1991), Randomization. *B.M.G.* 302, 1481–1482.
- Antonisamy B., Christopher S., and Samuel P. P. (2010), *Biostatistics Computing*. PHI Learning Private Limited, New Delhi.
- Bernard, J. A. (1988). Use of rule-based system for process control. *IEEE Control Systems Magazine*, 8(5) 3–13.
- Berry, D. A. (2005). Introduction to Bayesian methods III: use and interpretation of Bayesian tools in design and analysis. *Clin. Trials* 2, 295–300.
- Berry, D. A. (2006). Bayesian clinical trials. *Nature Rev. Drug Discov.* 5, 27–36.
- Berry, D. A. (2006). Bayesian statistics. *Med. Decis. Making* 26, 429–430.
- Berry, D. A. (2007). Adaptive trial design. *Clin. Adv. Hematol. Oncol.* 5, 522–524.
- Booth, B and Zimmel, R. (2004). Prospects for productivity. *Nature Rev. Drug Discov.* 3, 451–456.
- Breimer, D. D. and Danhof, M. (1997). Relevance of the application of pharmacokinetic–pharmacodynamic modeling concepts in drug development. The “Wooden Shoe” paradigm. *Clin. Pharmacokinet.* 32, 259–267.
- Bretz, F., Schmidli, H., König, F., Racine, A. and Maurer, W. (2007). Confirmatory seamless Phase II/III clinical trials with hypotheses selection at interim: general concepts. *Biom. J.* 48, 623–634.
- Danhof, M., Alvan, G., Dahl, S. G., Kuhlmann, J. and Painteaud, G. (2005). Mechanism-based pharmacokinetic/pharmacodynamic modeling — a new classification of biomarkers. *Pharm. Res.* 22, 1432–1437.
- Demuth, H. Beale, M. and Hagan, M. (1992). *Neural Network Toolbox™ User’s Guide*. MATLAB. The Mathworks Inc.
- DiMasi, J. A., Hansen, R. W. and Grabowski, H. G. (2003). The price of innovation: new estimates of drug development costs. *J. Health Econ.* 22, 151–185.
- Gallo, P. *et al.* (2006). Adaptive designs in clinical drug development - an executive summary of the PhRMA Working Group. *J. Biopharm. Stat.* 16, 275–283.
- Gilbert, J., Henske, P. and Singh, A. (2003). Rebuilding big pharma’s business model. *In Vivo* 21, 1–4.
- Goggin, T. *et al.* (2002). Modeling and simulation of clinical trials: an industrial perspective. In *Simulation for Designing of Clinical Trials* (eds Kimko, H. C. & Duffull, S. B.) 227–224 (Marcel Dekker, New York, USA.).
- Golub, H. L. (2006). The need for more efficient clinical trials. *Stat. Med.* 25, 3231–3235.
- Grainger D. (2015). Why Too Many Clinical Trials Fail - And A Simple Solution That Could Increase Returns On Pharma R&D. www.forbes.com.
- Hinton, G. E. (1989). Connectionist Learning Procedures. *Artificial Intelligence*, 40(1), 143–150.
- Holford, N. H. G., Kimko, H. C., Monteleone, J. P. R. and Peck, C. C. (2000). Simulation of clinical trials. *Annu. Rev. Pharmacol. Toxicol.* 40, 209–234.
- Hopgood, A. A. (1993). *Knowledge-Based Systems for Engineers and Scientists*. CRC Press. ISBN 0-8493-8616-0.
- Huang, W. Y. and Lippmann R. P. (1988). *Neural Net and Traditional Classifiers in Neural Information Processing Systems*. New York: American Institute of Physics, 387–396.
- Hubbard R.E. (2006), *Structure-based Drug Discovery. An overview*. Royal Society of Chemistry, Cambridge, UK.
- Jang, J-S. R. (1991), Fuzzy modeling using generalized neural networks and Kalman filter algorithm. In *Proceedings National Conference on Artificial Intelligence (AAAI-91)*, pp.762–767.
- Jang, J-S. R. (1991)b. A self-learning fuzzy controller with application to automobile tracking problem. In *Proceedings IEEE Roundtable Discussion on fuzzy and neural systems, and vehicle application*. Tokyo, Japan, Institute of Industrial Science, University of Tokyo. Paper no. 10.
- Jang, J-S. R (1991)c. Self-learning fuzzy controller based on temporal back-propagation. *IEEE Transaction on neural network*, 3, 714–723.
- Jang, J-S. R. (1993). ANFIS: Adaptive network based fuzzy inference systems. *IEEE Transaction on Systems, Man, and Cybernetics*, 23, 665–685.
- Jang, J-S. R, (1993)b. Predicting chaotic time series with fuzzy if then rules. In *Proceedings of IEEE International Conference on Fuzzy System*. San Francisco.
- Jang, J-S. R., and Gulley N. (1995). *MATLAB Fuzzy Logic Toolbox User’s Guide*. Version 1. The Mathworks, Incorporated.
- Jang, J-S. R., Sun, C.T. and Mizutani, E. (1997). *Neuro-fuzzy and Soft Computing (A Computational Approach To Learning And Machine Intelligence)*, Prentice Hall, Inc. pp1–90.
- Kola, I. & Landis, J. (2004). Can the pharmaceutical industry reduce attrition rates? *Nature Rev. Drug Discov.* 3, 711–716.
- Kosko, B. (1991). *Neural networks and fuzzy systems: a dynamical systems approach*. Prentice Hall. Upper Saddle River, NJ.
- Kumar, Y. and Jain Y. (2012). Research aspects of expert system. *International Journal of Computing & Business Research*. ISSN (online); 2229-6166. *Proceedings of I-society 2012 at GKU, Talwandi Sabo Krams, M. et al.* (2007).

- Adaptive designs in clinical drug development: opportunities, challenges, and scope reflections following PhRMA's November 2006 workshop. *J. Biopharm. Stat.* 17, 957–964.
36. KMR General Metrics Study (KMR Group, Chicago, USA, 2007).
 37. Kulikowski, C. A. and Weiss, S. M. (1982). Representation of Expert Knowledge for Consultation: The CASNET and EXPERT Projects. in Szolovits, P. (Ed.) *Artificial Intelligence in Medicine*. Westview Press, Boulder, Colorado.
 38. Lachmann, H. J. *et al.* (2009). Use of canakinumab in the cryopyrin-associated periodic syndrome. *N. Engl. J. Med.* 360, 2416–2425.
 39. Lalonde, R. L. *et al.* (2007). Model-based drug development. *Clin. Pharmacol. Ther.* 82, 21–32.
 40. Mamdani, E. H. & Assilian, S. (1975). An experiment in linguistic synthesis with a fuzzy logic controller. *International Journal of Man-Machine Studies*. 7(1), 1–13.
 41. Mehdi, N. and Mehdi Y. (2009). Designing a Fuzzy Expert System of Diagnosing the Hepatitis-B Intensity Rate and Comparing it with Adaptive Neural Network fuzzy system. *Proceedings of the World Congress on Engineering and Computer Science*, Vol. II WCECS 2009, San Francisco, USA.
 42. Mehta, C. R. and Patel, N. R. (2006). Adaptive, group sequential and decision theoretic approaches to sample size determination. *Stat. Med.* 25, 3250–3269.
 43. Miller, R. *et al.* (2005). How modeling and simulation have enhanced decision making in new drug development. *J. Pharmacokinet. Pharmacodyn.* 32, 185–197.
 44. Müller, P., Berry, D. A., Grieve, A. P., Smith, M. and Krams, M. (2007). Simulation-based sequential Bayesian design. *J. Stat. Plan. Inference* 137, 3140–3150.
 45. Miller III, W. T., Sutton, R. S. and Werbos, P. J. eds. (1990). *Neural Networks For Control*. MIT Press.
 46. Mizutani, E. and Jang, J-S. R. (1995). Coactive neural fuzzy modeling. *IEEE International conference on Neural Network (ICNN'95)*.
 47. Mizutani, E. Jang, J-S, R. and Nishio, K. (1995). Coactive Neuro-fuzzy modeling for color recipe prediction.
 48. Moody, J. and Darken C. J. (1989). Fast Learning in Networks of Locally-tuned Processing units. *Neural Computation*, 1, 281–294.
 49. Niwa, K., Sasaki, K. and Ihara, H. (1998). An Experimental Comparison of Knowledge Representation Schemes, in *Principles of Expert Systems* (Eds. A. Gupta and E.B., Prasad), IEEE press, New York. pp.133–140.
 50. *International Journal of Engineering and Informatics*, 1(1), 7–17.
 51. Oladele T. O., Sadiku J. S. and Oladele R. O. (2014), Coactive Neuro-Fuzzy Expert System: A Framework for Diagnosis of Malaria. *African Journal of Computing & ICTs*. A Publication of the Computer Chapter of the Institute of Electrical & Electronics Engineers (IEEE) Nigeria Section. . 7 No. 2. ISSN 2006-0781. www.ajocict.net.
 52. Oladele T. O., and Sanni Y. (2015), Coactive Neuro-fuzzy Dental Expert System. *International Journal of Applied Information Systems (IIAIS)*. Published by Foundation of Computer Science (FCS), New York, U. S. A. www.ijais.org.
 53. Orloff J. *et al.* (2009). *The future of drug development: advancing clinical trial design*. *Nature Reviews Drug Discovery* 8, 949–957 | doi:10.1038/nrd3025.
 54. Passino, K. M. and Yurkovich, S. (1988). *Fuzzy control*. Addison Wesley Longman Inc., California.
 55. Perros, H. (2009). *Computer Simulation Techniques: The definitive Introduction*. Computer Science Department, NC State University, Raleigh. NC.
 56. Pomerleau, D. A. (1991). Efficient training of artificial neural networks for autonomous navigation. *Neural Computation*, 3, 88–97.
 57. Pomerleau, D. A. (1992). *Neural network perception for mobile robot guidance*. PhD. Thesis, Department of Computer Science, Carnegie Mellon University.
 58. Poole, D., Mackworth, A. and Goebel, R. (1996). *Computational Intelligence: A Logical Approach*, Oxford University Press. ISBN 0–19–510270–3.
 59. Psaltis, D., Sideris, A. and Yamamura, A. (1988). A multilayered neural Network controller. *IEEE Control Systems Magazine*. 8(4), 17–21.
 60. Rao S. V. and Srinivas K. (2011), Modern drug discovery process: An insilico approach. *Journal of Bioinformatics and Sequence Analysis*. Vol. 2(5), pp. 89–94. http://www.academicjournals.org/JB_SA . ISSN 2141-2464 © 2011 Academic Journals.
 61. Reigner, B. G. *et al.* (1997). An evaluation of the integration of pharmacokinetic and pharmacodynamic principles in clinical drug development. Experience within Hoffman La Roche. *Clin. Pharmacokinet.* 33, 142–152.
 62. Rosenblatt, F. (1962), *Principles of Neurodynamics: Perceptrons and the theory of brain mechanisms*. Sparten, New York.
 63. Rumelhart, D. E., Hinton, G. E. and Williams, R. J. (1986). Learning internal representations by error propagation. In D.E., Rumelhart and James L. McClelland, editors, *parallel distributed processing: explorations in the microstructure of cognition*, volumes 1, chapter 8, pages 318–362. MIT Press, Cambridge, MA.
 64. Sheiner, L. B. and Steimer, J.-L. (2000). Pharmacokinetic/pharmacodynamic modeling in drug development. *Ann. Rev. Pharmacol. Toxicol.* 40, 67–95.
 65. Sivanandam, S. N. and Deepa, S. N. (2007). *Principles of Soft Computing*, Wiley India (P) Ltd.
 66. Sivanandam, S. N., Sumathi, S. and Deepa, S. N. (2007). *Introduction to Fuzzy logic using MATLAB*. Springer.
 67. Sugeno, M., editor (1985). *Industrial applications of fuzzy control*. Elsevier Science.
 68. Sugeno, M. and Kang, E. T. (1988). Structure Identification of Fuzzy model. *Fuzzy Sets and Systems*. 28, 15–33.

69. Takagi T. and Sugeno M. (1985). Fuzzy Identification of Systems and its Application in Modeling and Control. *IEEE Transactions on Systems, Man and Cybernetics*, 15, 116-132.
70. Tek, F. B., Dempster, A. G. and Kale, I. (2009). Computer Vision for Microscopy Diagnosis of Malaria. *Malaria Journal*, 8,153.
71. The World Health Report 2006: Working together for health available at <http://www.who.int/whr/2006/en/> last accessed 30 March, 2009.
72. Tsoukalas, L.H. and Uhrig, R.E. (1993). Fuzzy and Neural approaches to Engineering. John Wiley & Son, Inc.
73. Werbos, P.J. (1991). An overview of neural network for control. *IEEE Control Systems Magazine*, 11(1), 40-41.
74. Woodcock J. (2014). 21st-Century Cures: Modernizing Clinical Trials and Incorporating the Patient Perspective. <http://www.fda.gov/NewsEvents/Testimony/ucm404647.htm>
75. Zadeh, L. A. (1965). Fuzzy Sets. *Information and Control*, 8, 338 – 35.
76. Zadeh, L. A. (1973). Outline of a New Approach to the Analysis of Complex Systems and Decision Processes. *IEEE Transaction Systems, Man and Cybernetics*. 3(1), 28-44.
77. Zilouchian, A and Jamshidi, M,. (2001). Intelligent Control Systems using Soft Computing Methodologies. CRC Press. ISBN 0-8493-1875-0.

WEB REFERENCES

<http://www.aptronix.com/fuzzynet/app/note/reactor.htm>.
<http://www.controleng.com/>, Temperature Control: PID Vs fuzzy logic.
<http://www.fuzzy-logic.com> fuzzy logic tutorial.

Authors' Biography



Dr. (Mrs.) Oladele, Tinuke Omolewa is a lecturer in the Department of Computer Science, Faculty of Communication and Information Sciences, University of Ilorin, Ilorin, Nigeria. She obtained her BSc. in Computer Science from the University of Benin, Benin City, Edo State. She bagged her MSc. in Mathematics (Computer Science Option) from the University of Ilorin and a Ph.D. in Computer Science also from the University of Ilorin. She is known across the board for her innovative research work in Bioinformatics and Computational Biology. Her research interests include Artificial Intelligence, Data Mining, and Software Development.



Pharm (Mrs.) Williams E. Felicia is a lecturer in the Department of Clinical Pharmacy and Pharmacy Practice, University of Ilorin, Nigeria. She obtained her Bachelor of Pharmacy from University of Benin, Benin City. Masters in Business Administration, Masters in Community Health and Postgraduate Diploma in Education were obtained from University of Ilorin, Ilorin. She is a fellow of the Institute of Corporate Administrators, Honourary Fellow of the Chemical Society of Nigeria (Kwara Chapter) and a Merit Award Winner of Pharmaceutical Society of Nigeria, Kwara State Branch. Her research interests include Drug Development, Drug Utilization Studies, Pharmacoepidemiology, Pharmacogenomics, Pharmaceutical Care, Pharmacovigilance, Pharmacokinetics, Drug Quality and Bioinformatics. She can be contacted through: +2348033354532 and Williams.fe@unilorin.edu.ng.



Professor Joseph Shuaibu Sadiku had his B.Sc, M.Sc, and Ph.d degrees from the University of Ibadan. He joined Kwara State College of Technology (now Kwara State Polytechnic) in 1973. He Headed the Department of Mathematics from 1980 to 1982, also headed and started the Centre for Mathematical Analysis and Computation (Computer Science Department and Computer Services) from 1982 to 1990. He was the Chairman Computer Acquisition Committee and Chairman Research and Publications Committee. He later joined the University of Ilorin in 1993. There, he taught Mathematics and Computer Science courses to Undergraduate and Postgraduate students. He headed the Computer Science Department for eight years (2004 – 2008, 2009 - 2013). He also supervises M.Sc & Ph.d students in Mathematics and Computer Science. He is a member of Computer Association of Nigeria (COAN), Computer Professionals of Nigeria (CPN), Mathematical Association of Nigeria (MAN) and Nigeria Mathematical Society (NMS). He is a fellow of the following Associations: Nigeria Computer Society (2006) and Mathematical Association of Nigeria (2004).