

Evaluating big data using artificial neural networks for developing clinical decision support systems

Steven Walczak

Department of Health Informatics, University of South Florida, Tampa, USA

ABSTRACT

Medical data is growing by leaps and bounds resulting in very large data collections, referred to as "big data," for research and clinical systems development. Machine learning tools and artificial neural networks in particular are excellent methods to apply against decision problems that have the availability of big data sets. An examination of existing research that uses medical big data sets with greater than 10000 records is performed, with the two largest research data sets each having over one million records. A method for applying artificial neural networks to big data in medical settings is presented.

KEYWORDS

Artificial neural networks;
Big data; Clinical decision making; Decision support; Machine learning

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Introduction

Medical data is accumulating at an astronomical rate, resulting in what has come to be known as big data. The medical big data boom is facilitated by the ever-increasing number of electronic health/medical records (EHRs) [1], the growth of health information exchanges across medical systems, and the increase in personal medical devices (e.g., insulin pumps, mobile health apps, etc.) [2], which all lead to significant increases in electronic medical data records. A medical data record is defined as the values associated with a single diagnostic or treatment encounter with a patient. As an example, a single in-vitro fertilization treatment for a couple would constitute a record and subsequent treatments would create additional records. For personal medical devices such as pacemakers or insulin pumps, each record is associated with a single set of values from the device at a specific time, such as current insulin on board, time of day, and requested bolus amount for a new bolus using an insulin pump.

Medical big data is often collected in data warehouses, which are sometimes made available to researchers. There are numerous medical data warehouses around the globe with a few examples including the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP)¹, the Canadian Institute for Health Information², India Stat³, the National Trauma Databank⁴, among many others. As a specific example of the growth of medical big data, the ACS-NSQIP data availability, which reports all operations and associated information performed by affiliated hospitals annually, is shown in Table 1. Data is being added to the ACS-NSQIP database at a rate of approximately 1 million new operation records per year. Each surgical procedure record listed in Table 1 is for a single surgery performed on a single patient. If the same patient has multiple surgeries during the same reporting year, then a new record is generated for each procedure.

Medical big data plays an important role in medical research but presents problematic issues for storage, processing,

and utilization of the data in developing new research medical prediction models [3]. The storage of medical big data is most commonly satisfied using cloud storage technologies [4]. Individual researchers can then download whatever portions of the data are required for their next research project. The critical question is how can these very large amounts of data be analyzed to improve medical and clinical decision-making. Machine learning in general and artificial neural networks (ANNs) in particular are effective methods for analyzing medical big data to produce actionable results including disease or injury diagnosis, treatment recommendations, and outcomes predictions including morbidity, mortality length of stay, and patient satisfaction [5-8].

Table 1. Biomedical big data availability, example from ACS-NSQIP.

Year	Participating hospitals	Unique surgical procedure records
2022	702	1,011,899
2021	685	983,851
2020	706	902,968
2019	719	1,076,411
2018	722	1,020,511
2017	708	1,028,713
2016*	680	1,000,393

Background on ANNs

ANNs are a machine learning technique that is based on modelling the electrical neuronal activity in the human brain during problem-solving. Processing elements called neurodes are arranged in layers with weighted connections between

*Correspondence: Dr. Steven Walczak, Department of Health Informatics, University of South Florida, Tampa, USA. e-mail: swalczak@usf.edu

neurodes in one layer and subsequent layers and sometimes across all neurodes within a layer. The majority of ANN architectures are fully connected, meaning each node in a layer is connected to every node in a subsequent layer.

ANNs have several advantages over traditional statistical methods including linear and logarithmic regression. First, they are nonparametric which means that no prerequisite conditions on the data exist for the use of an ANN as a modeling tool. The nonparametric nature of ANNs means that variable interdependencies do not need to be prespecified. Next is that because ANNs employ a type of machine learning, they can learn extremely complex associations between independent and dependent variables, often much more complex than imaginable by humans.

They learn very fast, but this is dependent on computer memory size, processing speed, and the size of the training data set. A typical ANN of 2-50 independent variable values may be trained in under an hour. As indicated, training times increase as the size of the training set and the number of variables used increases. Finally, once trained, ANNs are resilient to noise [9]. A potential limitation in the use of ANNs in clinical decision support is the lack of an explanation facility to justify the ANN predictions. There are several methods in existence already that facilitate understanding of ANN outputs. A sum of the weights method uses the combined connection weights of an independent variable to determine that variable's contribution to the ANN's output [10]. The leave-one-out methodology iteratively drops out a single independent variable and re-trains an ANN from scratch and compares the resulting prediction accuracy against the original model to estimate the contribution of variables [11,12]. A novel explanation technique, Local Interpretable Model-Agnostic Explanations (LIME), has recently been introduced to take formatted data from a wide variety of classifiers including ANNs and produce explanations of independent variable importance [13]. As may be seen, all three approaches focus on identifying which variables in the set of independent input variables support the ANN's prediction and to what extent.

Two types of learning may occur in ANNs: supervised and unsupervised or a combination of both. Supervised learning is accomplished using data samples with known outcomes. The multilayer perceptron (MLP) as pictured in Figure 1(a), may utilize a variety of training methods to learn associations between data, with the backpropagation algorithm being the most used ANN training method in medical research [14,15]. The backpropagation algorithm works by determining the relative error in ANN predictions following a small number of training, called an epoch. The error is then propagated backwards through the ANN's connections and used to adjust the weights on each connection to bring the produced output closer to the correct output value. Various other training strategies exist but behave similarly. An important feature of MLP ANNs is the hidden layer, which permits nonlinear learning. ANNs may have more than the single hidden layer shown in Figure 1(a), with additional layers adding to the complexity of the nonlinear interactions that may be accurately modelled. Multiple hidden layers are known as deep learning architectures.

Unsupervised learning is used primarily for classifying image and/or audio data. Convolutional neural networks (CNNs) as pictured in Figure 1(b), are the current standard for unsupervised deep learning ANNs and have been shown to have superior performance over MLP-type ANNs when classifying image data [16]. The layers in a CNN are the convolution layer which aggregates pixels from the image input, followed by a pooling layer or ReLU (rectified linear activation unit) layer which serves to further condense the data from the convolution layer or serves as an activation function. These layers are repeated multiple times, hence why CNNs are deep learning technology, and the successive convolutional/pooling layers may end with a traditional supervised learning layer. The unsupervised nature of CNNs means that the learning occurs without guidance from a known outcome, meaning the CNN determines what parts of an image are meaningful by itself. Many current implementations turn CNNs into a hybrid ANN by including a supervised learning final layer in the CNN's architecture.

The type of data available from big data warehouses and the research question will determine whether to implement a supervised MLP or an unsupervised CNN. One other type of ANN merits mention and that is the recurrent neural network (RNN), which is a supervised ANN similar to MLP, but includes a feedback loop from hidden layers to the input layer to create a time delay in processing [17]. RNNs are used for classifying data that is time-dependent, such as EEG rhythmicity in seizure patients [18].

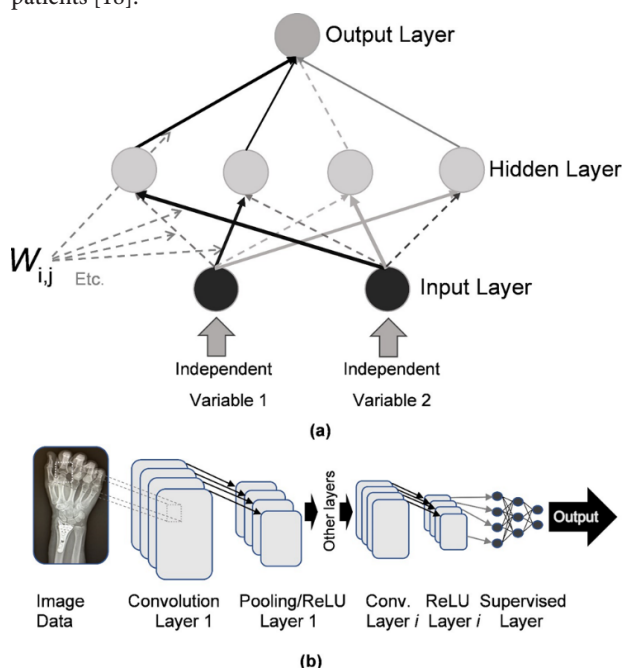


Figure 1. ANN architectures: (a) multi-layer perceptron, (b) convolutional neural network.

Mini-Review of Big Data ANN Applications

The search terms “ANN and (medicine or medical or clinical) and big data”, and the same search replacing ANN with MLP, then CNN, then RNN were conducted using Google Scholar. Our definition of big data is any collection of data that is too

large to comfortably handle with current technology standards for in-office computing equipment and that there is potential for continued growth of the data over time. For purposes of the mini-review, a minimum size n of 10,000 individual records with a maximum of 2,600 data points (p) per record, though p values in medical research are often much smaller, will be considered as big data and used to select the representative prior research literature examples. Data points provide the values for the variables of corresponding research models [19].

A sample of previous ANN research that utilizes big data is provided in Table 2. The examples in Table 2 are not meant to be exhaustive, but representative of the data sizes and types of research being done. The question of what represents big data should be addressed by any researcher. From Table 2, five of the represented research samples diagnose hypertension but utilize different data sources, periods, and independent variables [20-29,33,34]. Other medical prediction problems solved using big data include determining the level of cognitive impairment/Alzheimer’s disease [22], determination of skin cancer from images [30], prediction of morbidity and mortality

and re-admission following hernia repair [31], 30-day readmission rates for lumbar spinal fusion patients [28], 30-day readmission for diabetic patients [19], two studies predicted 30-day mortality following different hip surgeries [21,29], in-hospital mortality for congestive heart failure patients [27], general patient mortality (26), diagnosis of chronic diseases [25], prediction of surgical outcomes by discharge destination [32,35], prediction of patient transfusion needs during surgery [36], and a generalized tool for interpretation of various types of medical images [37]. These previous research studies are meant to show both the applicability of big data and the range of what may be considered big data in medical research, as well as the wide range of clinical decision problems supported by medical big data research.

An interesting observation about the prior medical research listed in Table 2 is that most of the ANN decision support models are focused on a single diagnosis or class of operation. This has been a common theme in medical ANN research both with and without big data utilization.

Table 2. Examples of ANN research using big data (where $n > 10,000$).

Sample size (n)	Type of ANN	Data set (if known)	Reference
10,766	CNN*	Health Facts database (Cerner Corporation)	(19)
		National Health and Nutrition Examination Survey (NHANES)	
19,799	MLP†		(20)
19,835	MLP	ACS-NSQIP	(21)
> 20,000	CNN	N/A	(22)
23,095	MLP	Henry Ford Affiliated Hospitals	(23)
24,434	MLP	NHANES	(24)
42,573 (31,919 unique patients)	Recurrent CNN	Single hospital database (Wuhan, China)	(25)
		Medical Information Mart for Intensive Care (MIMIC III)	
46,250	RNN‡		(26)
53,423	RNN	MIMIC III	(27)
63,533	MLP	ACS-NSQIP	(28)
77,145	MLP	ACS-NSQIP	(29)
129,450	CNN	N/A	(30)
148,214	MLP	ACS-NSQIP	(31)
159,069	MLP	ACS-NSQIP	(32)
		Centers for Disease Control-National Center for Health Statistics	
159,989	MLP, and fuzzy NN	(CDC-NCHS), epidemiological databases.	(33)
		Canadian Primary Care Sentinel Surveillance Network (CPCSSN) data set	
379,027	MLP		(34)
390,185	MLP	ACS-NSQIP	(35)
1,636,439	MLP	ACS-NSQIP	(36)
15,000,000	CNN	ADNI database	(37)

* CNN = Convolutional neural network, a type of deep learning neural network

† MLP = Multi-layer perceptron, a standard supervised learning architecture

‡ RNN = Recurrent neural network, a supervised learning ANN for time related data

Some more recent research has examined expanding clinical prediction models to encompass the complete range of medical cases or surgeries as a benefit of utilizing big data [26,36,37]. However, recent research has shown that keeping data separated by surgical discipline can improve outcome prediction performance over an aggregated data single ANN model [35]. Future research is needed to determine if big data will permit a more universal approach to specific types of ANN healthcare predictions and what aspects of medical data or types of medical prediction problems may lead to single composite ANN models versus the need for continuing the individual specialization type of ANN research models.

ANN Methodology for Designing Medical and Clinical Decision Support Using Big Data

Once a medical research question has been determined and a big data resource has been identified to help answer the research question, the desired ANN model and learning method need to be determined. A flow model showing the usage of ANNs and big data for developing clinical decision support systems is shown in Figure 2. The type of data available from the big data data warehouse for analysis will indicate a preference for MLP versus CNN versus RNN. All of these types of ANN require that data be divided into two sets, a training data set and a testing data set. While a pure unsupervised learning method does not require a validation data set, it is typically used anyway to demonstrate the ANN model's performance on out-of-sample data, mimicking the utilization of the ANN in the real world. The availability of big data sets facilitates interpretation of the generalizability of ANN models and limits site bias [38].

After data is acquired from a big data resource, the data will require cleaning and formatting. As an example, [24] stated that the big data set they used had over 20 million records, but their exclusion criteria for their research reduced this amount to 42573 records (as shown in Table 2).

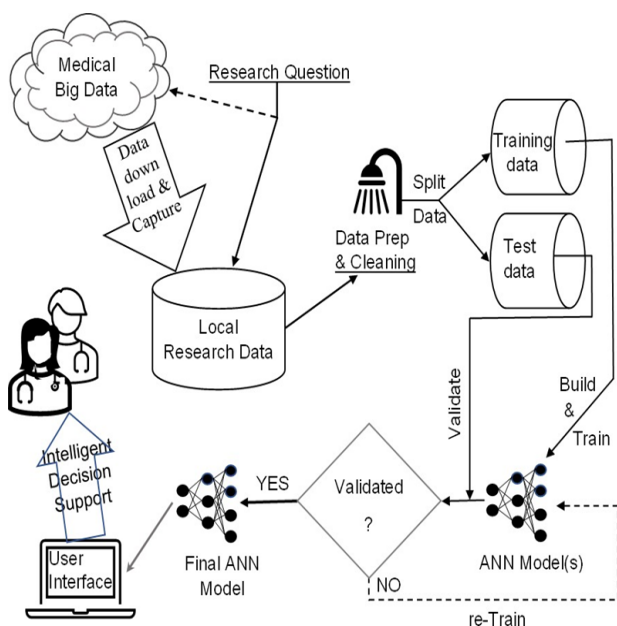


Figure 2. Workflow for developing intelligent decision support using ANNs and big data.

While ANNs can forecast using noisy data once trained, the training process requires data with minimal noise [39,40]. Data with missing values, which occurs frequently in medical data [41], will need to be eliminated or possibly using a zero value, if this does not interfere with the interpretation of the other values for the specific variable. Data elimination for purposes of noise reduction will necessarily reduce the size of the training data set. This also points out the critical need for higher quality data in medical data [42] and medical big data since researchers will most likely not have access to the original medical notes or patient records other than what is recorded in the big data set.

The ANN model selected for answering the medical research question is then developed and trained and finally evaluated on the out-of-sample test set of data once training is completed. A variety of guidelines for developing ANN research models have been published and the interested reader is directed to [43-45] for MLP, for RNN, and [46,47] for CNN. Due to the very large amount of test data available from medical big data resources, the need for cross-validation is eliminated since there is more than enough data to evaluate and validate ANN performance.

As mentioned, ANNs require further analysis for interpretation of the prediction results. Results from ANNs should be utilized by a user interface that can interpret the ANN output for the medical/clinical end-user. Prior research has shown how intelligent decision support models, including ANN-based decision support may be incorporated into EHR systems [48].

Conclusion

Big data is a tremendous resource for the development of medical clinical decision support models. The large quantity of data requires an efficient and effective method for analysis, which is provided by ANNs, a nonparametric machine learning method. Prior ANN research has demonstrated the utility of using big data in medical research with data sets numbering from tens of thousands to well over a million patient records. Big data further supports the generalization of ANN models and the end-user's perception of model validity. ANNs and other machine learning technologies research must continue as they provide information that may be otherwise difficult to discern and can lead to significant improvement in health outcomes. These technologies are efficacious in using big data, which in turn could improve ANN and other machine learning model performance.

Disclosure statement

No potential conflict of interest was reported by the authors.

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