Preliminary Steps towards Efficient Classification in Large Medical Datasets: Structure Optimization for Deep Learning Networks through Parallelized Differential Evolution

Ivanoe De Falco¹, Giuseppe De Pietro¹, Antonio Della Cioppa², Giovanna Sannino¹, Umberto Scafuri¹ and Ernesto Tarantino¹

¹ICAR, National Research Council of Italy (CNR), Via P. Castellino 111, Naples, Italy ²NCLab, DIEM, University of Salerno, Via Giovanni Paolo II 132, Salerno, Italy

Keywords: Medical Databases, Deep Learning, Optimization, Deep Neural Network Structure, Differential Evolution.

Abstract: Deep Neural Networks are being more and more widely used to perform several tasks over highly-sized datasets, one of them being classification. Finding good configurations for Deep Neural Network structures is a very important problem in general, and particularly in the medical domain. Currently, either trial-and-error methodologies or sampling-based ones are considered. This paper describes some preliminary steps towards effectively facing this task. The first step consists in the use of Differential Evolution, a kind of an Evolution-ary Algorithm. The second lies in using a parallelized version in order to reduce the turnaround time. The preliminary results obtained here show that this approach can be useful in easily obtaining structures that allow increases in the network accuracy with respect to those provided by humans.

1 INTRODUCTION

Nowadays, thanks to the ever-increasing use of sensors in the medical field, a huge amount of datasets are being created starting from the continuous monitoring of bio-signals. In many cases, these datasets consist of a very high amount of data, even tens of millions of items or more, where each item, on its turn, could be composed by dozens of parameters.

One of the main and most frequent tasks that should be carried out on such datasets makes reference to the classification of all the items making up the dataset, especially in a supervised way. This latter involves the division of the available items into a training set and a test one.

Already several years ago, as long as the amount of sensors that were applied to a subject showed an increasing trend, and the duration of their use increased as well, it became evident that the classical tools that were applied at that time to perform classification tasks could be no longer suitable for these new, very large datasets. For example, among Artificial Neural Networks (Hertz et al., 1991), the classically used Multi Layer Perceptron (MLP) models (Rumelhart et al., 1985), showing good performance over the small-sized datasets typically gathered in the nineties, could no longer effectively face this burden of data. Consequently, new structures, as auto-encoders and Restricted Boltzmann Machines, were put forward. Later on, it was noted that those structures can be stacked so as to obtain networks with a high number of internal layers, referred to as *Deep* Neural Networks (DNNs) (LeCun et al., 2015). The good news was that these latter can be trained one layer at a time, which helps strongly reducing the problems of vanishing gradient and over-fitting. Structures as stacked auto-encoders, deep belief networks, and convolutional networks have become very popular in these last years.

As a consequence, classification over largelysized datasets can be effectively performed by taking advantage of the DNNs, that are nowadays the standard *de facto* in many fields and for many application problems (Najafabadi et al., 2015), with excellent results being obtained in, e.g., computer vision, speech recognition, and machine translation, apart from, of course, classification. *TensorFlow* (Abadi et al., 2016) is probably the most widely used opensource software library for machine learning, and it is extremely popular to experiment with DNNs.

Yet, these powerful methods suffer from one important drawback. Namely, given a dataset onto

De Falco I., De Pietro G., Della Cioppa A., Sannino G., Scafuri U. and Tarantino E.

In Proceedings of the 11th International Joint Conference on Biomedical Engineering Systems and Technologies (HEALTHINF 2018), pages 633-640 ISBN: 978-989-758-281-3

Copyright © 2018 by SCITEPRESS - Science and Technology Publications, Lda. All rights reserved

Preliminary Steps towards Efficient Classification in Large Medical Datasets: Structure Optimization for Deep Learning Networks through Parallelized Differential Evolution. DOI: 10.5220/0006730006330640

which classify, the user has to manually configure the DNN. This means to perform the choice of a set of parameters, as the number of hidden layers, the configuration of each layer, and the setting of some more parameters related to the learning. Finding good ways to effectively face this multivariable optimization problem is a far-from-trivial task, and may highly impact the results that can be obtained in the analysis of Big Data. As concerns possible ways to effectively make this set of choices, the state of the art is quite simple, as it relies on approaches based either on user ability with a trial-and-error approach, or on just slightly more sophisticated algorithm-driven approaches as the so-called grid search and random search. In the former, for each configuration parameter a suitable range is chosen, so that a uniform grid is obtained in the search space of the possible configurations, and uniform sampling takes place in the grid. In the latter, instead, the search is not uniform, rather some parameters are considered as more important and the search samples more thoroughly the configuration space along these parameters. The activity involved in all of the three above methods is very laborious for the user, and there is no guarantee that the obtained structure is satisfactory.

In this paper we move some preliminary steps to help users overcome this tricky step. Namely, we propose the use of an Evolutionary Algorithm (EA) (Bäck et al., 1997) to find a good parameter setting for the DNN. EAs are stochastic heuristic optimization algorithms based on mimicking in a computer the behavior of a population subject to the pressure of the environment. Although EAs do not provide any formal proof for convergence, they have frequently proved their ability to find good sub-optimal solutions to multivariable optimization problems in many different areas. Actually, many EAs exist. Here we consider Differential Evolution (Price et al., 2006), one of the most recent and successful EAs.

One well-known drawback of EAs is that they need time to evolve a good solution, because many iterations should be performed, in each of which new solutions must be obtained from the currently available ones, and each of them should be evaluated in terms of its quality in solving the given problem. This drawback becomes of much higher relevance whenever the time needed to evaluate the quality of a solution is high, as it is the case of classification over big datasets. In fact, for such a problem, the evaluation of a possible configuration requires for the related DNN a learning phase over an extremely large training set, and this task can require minutes, and even hours. Consequently, the whole evolution requires an amount of time ranging from hours to days, up to weeks. This is not a problem for the classification task itself, because, once a good model is found, its use to classify a new, previously unseen, item requires just an extremely small amount of time, so it is a real-time activity, yet the turnaround time to obtain the model can be excessive.

To relieve the search from this drawback, the design of parallel models for EAs and their implementation and utilization on parallel machines is of great help. As here the main problem is related to the computation of the quality of each proposed DNN model, the idea is to run a parallelized master-slave model (Tomassini, 2006) in which the DE population evolves on a master node of the parallel architecture, while at each iteration the evaluation of the quality of each individual is delegated to one of the available slave nodes. In this way, if there are N slave nodes, the search can show a speed up of a factor up to about N, being the time for all the evolutionary operations in the order of, say, a few seconds, thus negligible with respect to the evaluation activities.

This paper gives in Section 2 a description of the state of the art in the use of EAs to optimize ANN and DNN structures. Section 3 details the methodology followed, in terms of the software architecture of our algorithm. The specific medical case study on which our approach has been tested, i.e. Obstructive Sleep Apnoea, is described in Section 4, together with the dataset we have worked on. Section 5 reports on the experiments performed and on the results obtained. Finally, Section 6 contains our conclusions and the related future work.

2 STATE OF THE ART: EAS FOR NNS

From a historical point of view, the attempt at finding good configurations for ANNs by means of EAs dates back to the nineties of last century. In those times there was a line of research called *neuro-evolution*. Basically, two different goals can be seen in this research line. In the first, the aim is to find a satisfactory structure for an ANN in terms of number of hidden layers and other learning parameters, whereas in the second the target is to optimize the connection weights in an ANN. Sometimes these goals have been faced at the same time.

The first neuro-evolution paper was probably (Ronald and Schoenauer, 1994), in which the authors used a Genetic Algorithm to update the weights of a network in the simulation of the control of soft landing for a toy lunar module.

In the same year two more papers, i.e. (Gruau

et al., 1994; Angeline et al., 1994) described the use of two different EAs, respectively Genetic Programming and Evolutionary Programming, to tackle the evolution of both network structure and learning parameters.

Since then, lots of papers were written within this line of research, too numerous to be mentioned here, as, e.g., (Yao and Liu, 1997; De Falco et al., 1998; Stanley and Miikkulainen, 2002; Sher, 2012; Kassahun and Sommer, 2005; Siebel and Sommer, 2007; Edlund et al., 2011).

It is worth mentioning here that in these last months high interest in neuroevolution is growing from the major companies and universities dealing with Big Data, as for example Google, Sentient Technologies, MIT Media Lab, Johns Hopkins, Carnegie Mellon, and their number continues to increase, and so are the related efforts.

As an example, in 2017 a group of Google researchers (Real et al., 2017) used a tailored EA to find the best possible configuration for a convolutional network. They faced both CIFAR-10 and CIFAR 100 datasets, and obtained very good results, showing that neuro-evolution can be useful.

As a further example, in 2017 as well, researchers from Sentient Technologies (Miikkulainen et al., 2017) put forward an evolutionary-based methodology for the optimization of DNN structures called CoDeepNeat, and successfully applied it to the task of captioning images on a magazine website in an automatic way.

Apart from applications, also research on neuroevolution is being carried out. As an example, in the same year Vasconcellos and Murata (Vargas and Murata, 2017) suggested a unified representation for most of the ANN features, and a new method useful to preserve diversity, called spectrum diversity. The positive impact of their proposal was shown by the results obtained on five representative problems, among which one related to the simulation of the motion of a car on a hilly path.

3 METHODOLOGY

The software architecture of our approach is sketched in Algorithm 1, that provides the pseudocode for both the *master* module and a generic *slave* one. The master makes here reference to a maximization problem.

The master module performs the evolution relying on a DE algorithm. Basically, an initial set, called *population*, composed by *NP* candidate solutions, called *individuals*, is randomly generated. Each individual *x* contains the values of the parameters reAlgorithm 1

```
Master Process
Begin
   best_ind(0) = -1;
    f(best_ind(0)) = VALMIN //very negative value
   //initial generation
    for ( i = 1; i <= NP; i++)
        randomly initialize individual x[i](0)
    for ( i= 1; i <=NP ; i++)
        send solution x[i](0) to a slave
    for ( i =1; i <= NP; i++)
        receive from the slave the fitness
            of x[i](0), f(x[i](0))
        if
          (f(x[i](0)) > f(best_ind(0))
            best_ind(0) = x[i](0)
            f(best_ind(0) = f(x[i](0))
    //perform the cycle of generations
    for ( t = 1; t <= Max_Gen; t++)</pre>
        for ( i = 1; i <= NP; i++)
            apply DE operators and create a
                trial solution ts[i](t)
        for ( i = 1; i <= NP; i++)
            send trial solution ts[i](t)
              to a slave
        //create the next population
        for ( i =1; i <= NP; i++)
            receive the fitness of ts[i](t)
              f(ts[i](t)))
            i f
                 (f(ts[i](t) \ge f(x[i](t)))
                    x[i](t+1) = ts[i](t)
                else
                    x[i](t+1) = x[i](t)
            i f
                (f(ts[i](t) > f(best_ind(t)))
                    best_ind(t) = ts[i](t)
                    f(nest_ind(t) = f(ts[i](t))
    output the best structure found
      best_ind(Max_Gen)
End
Slave process:
```

```
Begin
for (i = 0; i <= NP; i++)
begin
receive from the master the DNN
structure to evaluate
//Perform the tensorFlow actions:
train the DNN
test the DNN
send to the master the accuracy of
the DNN over the test set
end
end
Fnd</pre>
```

End

presenting a structure for a DNN. The quality of each individual is evaluated by means of an invocation to the *fitness* function f (this computation will be exe-

cuted by a slave module). Then, starting from the individuals currently available, a new population is created thanks to operators specific to the DE as mutation, recombination, and selection. Namely, in correspondence to the generic i-th individual in the current population, by application of those operators a new solution, referred to as trial, is created, and its quality is evaluated by means of the fitness function. The individual with the higher fitness between the current i-th and the trial is inserted in the i-th position of the population being created. The creation of a new population from the current one is repeated for a number of iterations, called generations, equal to Max_Gen. At the end of the evolution, the best found solution in terms of higher fitness value is proposed to the user. For more details on DE, interested readers can make reference to (Price et al., 2006).

The slave module, instead, is invoked by the master each time the fitness of a newly created individual has to be evaluated. It receives the values of the configuration parameters encoding for a specific DNN, prepares a proper file in python language and invokes the execution of this latter file in the *TensorFlow* library (Abadi et al., 2016). TensorFlow executes the learning phase for the proposed DNN over the training set, and then yields the accuracy of the trained network over the test set. The slave sends this value back to the master and becomes waiting for the next structure to train and test.

For this classification problem, we consider as the fitness of a DNN structure the accuracy it achieves over the test set, i.e. the ratio between the number of the test set items correctly classified and the total number of items in the test set. With this choice, the optimization problem becomes a maximization problem, aiming at finding structures with as-high-aspossible accuracy values in the range [0.0 - 100.0].

3.1 The Implementation Choices

To encode a DNN structure into a DE individual, firstly a number of DNN parameters has to be suitably chosen. In this preliminary work we have decided to consider the following parameters:

- the number of hidden layers NHL
- for each of the hidden layers, the number of neurons making up the layer (for the i-layer, it is *NNL_i*)
- the activation function *AF*
- the number of learning steps *LS*

For each of these parameters, an admissible range has been set, as reported in Table 1.

It should be noted that all the parameters can take on integer values, but AF, which can take values from a set of three possible values: rectified linear unit (*relu*), hyperbolic tangent (*tanh*), and *sigmoid*.

Another important choice is that related to the encoding for the parameter values. Actually, DE is well suited to deal with real-valued problems, whereas the parameters accounted here can take on integer values. To make all things consistent, each parameter has been encoded as a real value in the range [0.0 - 1.0], and the integer value *I* represented by a real value *R* is given by: $I = R \cdot (MAX - MIN) + MIN$, where *MIN* and *MAX* represent the minimum and the maximum admissible values for that parameter, respectively.

4 THE MEDICAL CASE STUDY

4.1 Obstructive Sleep Apnoea

Obstructive sleep apnea (OSA) (McNicholas and Levy, 2000) is a breathing disorder that takes place in the course of the sleep and is produced by a complete or a partial obstruction of the upper airway that manifests itself as frequent breathing stops and starts during the sleep. In the medical practise, it is defined as a cessation of airflow for at least 10 seconds, and people with OSA disorder stop typically hundreds times per night, during the sleeping, and each stop lasts about 10–30 seconds.

Statistics report that about 4% of the general population suffer from this condition to some extent, and it is estimated that fewer than 25% of OSA sufferers are actually aware that they have this problem (Alqassim et al., 2012). These undiagnosed patients cause, in the USA for example, a loss of 70 billion dollars, 11.1 billion in damages, and 980 deaths each year (Almazaydeh et al., 2012).

Monitoring OSA, by detecting and classifying the apnoea episodes, becomes crucial for people suffering from this condition, especially in case of the followup evaluation of some given medical therapies or certain drugs, in which it is required to check side effects, such as sleep or breathing disturbances, like OSA episodes. In general, the task of aiming at the evaluation of the quality of sleep for a subject and at investigating the presence of OSA episodes during the nights is highly important in order to ameliorate health con-

Table 1: The ranges for all the considered parameters.

	NHL	NNL_i	AF	LS
minimum	1	1	1	500
maximum	10	30	3	10,000

ditions for citizens suffering from OSA, and, at the same time, to reduce both mortality and healthcarerelated costs. In fact, it should be remarked here that this disease results in problems as asphyxia, hypoxemia, and awakenings, and often has consequences as increased heart rate or high blood pressure, and, on the other hand, may yield long-term symptoms that negatively influence life quality.

With respect to the literature, there are numerous proposed systems to monitor and classify OSA episodes in a less invasive and more accurate way (Shokoueinejad et al., 2017). Among them, some approaches just use data gathered by a single-channel ElectroCardioGram (ECG), as for example (Sannino et al., 2014; De Falco et al., 2015) or (Al-Abed et al., 2007) in which a three-layer Multi-Layer Perceptron (MLP) classifier was used, or (Acharya et al., 2011) in which a four-layered feed-forward neural network with two hidden layers and 11 neurons was employed to process five non-linear parameters. However, in all these works the structures of the networks are manually configured.

4.2 The Original Database

To perform experiments on the use of an EA to find a good parameter setting for a DNN able to classify OSA episodes by using data gathered by a ECG signal, we have created a new dataset starting from the apnea-ECG database (Penzel et al., 2000), freely downloadable from www.physionet.org. The apnea-ECG database consists of 70 recordings, one for each patient. Only thirty-five of them contain annotations about OSA episodes, each of them are related to 1minute segment of the record. So, we took into consideration these 35 recordings only.

Among the 35 recordings, 20 (labelled as a01 - a20) are related to people definitely suffering from OSA, five (b01 - b05) are borderline, and ten (c01 - c10) are people with no OSA at all or with a very low level of the disease.

Starting from these recordings, we have created a new dataset and have let it undergo the classification task by the DNN. Namely, we have taken each recording, and for each 1-minute segment we have computed the values of a set of twelve typical Heart Rate Variability (HRV) parameters, related to the frequency domain, the time domain, and the non-linear domain, as better described in the next subsection.

4.3 The Obtained Dataset

Firstly, each ECG record was cleaned from power line interference, and muscle and movement artefacts,

by using an innovative recurvise denoising scheme (Cuomo et al., 2016). Then, the filtered signals were processed by using Kubios (Niskanen et al., 2004), a Matlab based software package for event-related biosignal analysis able to extract and analyze HRV features. Standard linear HRV analysis was performed according to the guidelines of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (of the European Society of Cardiology et al., 1996). Additionally, non-linear features were computed according to the literature (Sannino et al., 2014). The computed measurements are:

• Frequency Domain:

- the power in the Ultra-low frequency band: ULF
- the power in the Very low frequency band: VLF
- the power in the Low frequency band: LF
- the power in the High frequency band: HF
- the total Power of the signal (i.e. the sum of the four above powers): P
- the low frequency/high frequency ratio: LF/HF
- Time Domain:
 - the average value of NN intervals: ANN
 - the standard deviation of the average NN intervals: SDANN
 - the proportion of NN50 divided by the total number of NNs, where NN50 is the number of pairs of successive NNs that differ by more than 50 ms: pNN50
 - the square root of the mean squared difference of successive NNs: rMSSD
- Non-linear Domain:
 - the approximate entropy: AE
 - the fractal dimension: FD

Each database item is constituted by those 12 values, together with the class of the instance as known from the annotations related to that recording. These latter will be represented by a 1 for a non-apnoea minute and by a 2 for an apnoea minute. The resulting dataset is composed by a total of 11,752 items, that are then divided into a training set and a testing set consisting of 7,051 and 4,701 items, respectively. Table 2 shows the details of the data used for this study.

5 THE EXPERIMENTS

Both the master and the slave processes have been implemented in C language. The hardware available for our experiments is an iMac Pro platform endowed with processing nodes constituted by cores running at 3,0 GHz. Ten of them have been used by us to run the slave processes, and one to execute the master one. Depending on the value chosen for the population size *NP*, each of the cores reserved for the slaves will execute several such processes at each generation. For example, should *NP* be equal to 30, each slave would be called upon three times at each generation.

To evaluate the fitness of each proposed DNN configuration, we have made use of a TensorFlow program based on the DNNClassifier function. Python version is the 3.6.3, whereas for TensorFlow the 1.3.0 version has been employed. The evaluation of the quality of each DNN requires an amount of time indicatively ranging within about one and three minutes, depending on the structure and on the number of steps proposed by the DE for the specific network.

The experiments have been divided into two phases, as described in the following.

5.1 Manual Configuration

A first phase of the experiments has consisted in letting a user find manually the best configuration for the DNN by performing a wide set of trials. For each manually-configured network the parameters values used are within the limits shown in Table 1.

The first remark related to this phase of manual settings is that the vast majority of the manually-tested DNN configurations yields as accuracy 52.99%, which tells us that the problem is far from easy. In all these situations, all the test set items are assigned to the majority class (non-OSA), which implies no understanding at all of the problem. As an example of this situation, Table 3 shows the confusion matrix for the DNN constituted by 5 hidden layers with 10, 20, 20, 20, 10 neurons respectively, rectified linear unit as the activation function, and a number of steps equal to 3000.

As a result of this laborious manual phase, the best configuration tailored by hand has resulted to be the following: 3 hidden layers with 15, 15, 15 neurons respectively, rectified linear unit as the activation function, and a number of steps equal to 3000. This configuration yields a percentage of accuracy over the test set equal to 57.69%.

Table 2: The details of the data used for this work.

	class 1 OSA episodes	class 2 no-OSA episodes	Total
Training Set	3,707	3,344	7,051
Testing Set	2,491	2,210	4,701
Total	6,198	5,554	11,752

Table 4 reports the confusion matrix obtained by using this configuration.

As it can be seen, this DNN attempts to predict by assigning the majority of the items related to class 1 events to the class 2. This means that actually the problem is not well understood by the network under account, and results in a large number of false positives (top right), so that the specificity is very low. From a medical viewpoint, a large number of non-OSA segments is incorrectly considered as OSA events. As a general comment, this DNN structure is quite unsatisfactory.

5.2 DE-driven Configuration

The next phase has resided in using the parallelized version of the DE in order to improve the above result. Before carrying out the experiments, several decisions should be taken about DE. Firstly, DE can use many different search strategies. Within this paper we have set it as a DE/best/1/bin, the actions of which can be found in (Price et al., 2006). Basically, to create each new trial individual, a difference vector between two individuals randomly chosen in the current population is added to the current best individual. As for the DE search parameters, we have set them as follows: *NP* = 50, *Max_Gen* = 30, *F* = 0.2, *CR* = 0.2. All these choices have been made without any preliminary tuning phase for the values, and are based on our experience on the use of DE to face other problems. The value chosen for NP implies that each slave core will be called upon five times at each generation.

The best configuration obtained at the end of the run is a DNN composed by three hidden layers with respectively 4, 16, and 15 units, with relu as activation function and a number of steps equal to 5012. Its accuracy over the test set is equal to 68.35%. The time needed to find it has been of about five hours and 10 minutes.

The most important result is that a noticeable improvement has been obtained in terms of accuracy over the manual configuration.

Figure 1 shows the best fitness value obtained at each generation as a function of the generations. Also the average of the fitness values of the individuals at each generation is reported.

As it can be seen, already in the first generations

Table 3: The confusion matrix for the majority of handmade configurations.

		assigned to class 1	assigned to class 2
ľ	real class 1	2491	0
	real class 2	2210	0

Table 4: The confusion matrix for the best hand-made configuration found.

	assigned to	assigned to
	class 1	class 2
real class 1	1018	1473
real class 2	516	1694

Table 5: The confusion matrix for the best solution provided by DE.

	assigned to	assigned to
	class 1	class 2
real class 1	1671	820
real class 2	668	1542

the DE allows finding improving solutions. Moreover, as the number of generations increases, so do both the best fitness value (sometimes) and the average fitness value (very frequently). These two trends show that the evolution is effective in finding better and better configurations.

Moreover, Table 5 shows the confusion matrix for the best solution evolved by DE.

In this case the results show that evolution has provided a DNN structure that does not attempt to assign the items by relying on the majority class, so understanding of the problem has been obtained. The number of false positives shown in the top right corner of the table is much lower than that for the hand-tailored solution, about half, which is a much better situation from the medical viewpoint.



Figure 1: The evolution of the DE run.

6 CONCLUSIONS AND FUTURE WORK

This paper has described some preliminary steps towards finding good configurations for Deep Neural Network structures, which is a very important problem in general, and particularly in the medical domain, especially when highly-sized data sets are to be faced. The first such step consists in the use of Differential Evolution, and the second lies in using a parallelized version based on a master-slave model in order to reduce the turnaround time.

The preliminary results obtained here show that this approach can be useful in easily obtaining structures allowing increases in the accuracy with respect to those provided by humans.

There are many issues that have not been considered here, yet they are of high importance to further improve the validity of the approach. Among them the most important is that this approach should be tested on more datasets, and special attention should be paid to those with higher sizes, so as to investigate its usefulness when Big Data are to be faced. In this latter case it is very likely that the times needed to find good Deep Neural Network structures will highly increase, resulting in days of turnaround time. This problem could require the use of larger, more powerful parallel machines, consisting of a larger number of computing nodes so as to test many more possible configurations at the same time.

Moreover, experiments should be conducted on the use of distributed models for EAs (Tomassini, 2006) to find good DNN configurations. In fact, these models have been successfully employed in recent years for many multivariable problems, resulting in many cases in both improvement in solution quality and reduction in the time needed to find a good solution. Some examples of this can be found in (De Falco et al., 2014; De Falco et al., 2017) with reference to the design and the implementation of distributed DE models.

REFERENCES

- Abadi, M., Agarwal, A., Barham, P., Brevdo, E., Chen, Z., Citro, C., Corrado, G. S., Davis, A., Dean, J., Devin, M., et al. (2016). Tensorflow: Large-scale machine learning on heterogeneous distributed systems. arXiv.
- Acharya, U. R., Chua, E. C.-P., Faust, O., Lim, T.-C., and Lim, L. F. B. (2011). Automated detection of sleep apnea from electrocardiogram signals using nonlinear parameters. *Physiological measurement*, 32(3):287.
- Al-Abed, M., Manry, M., Burk, J. R., Lucas, E. A., and Behbehani, K. (2007). A method to detect obstructive sleep apnea using neural network classification of time-frequency plots of the heart rate variability. In *IEEE Int. Conf. of Engineering in Medicine and Biology Society*, pages 6101–6104.
- Almazaydeh, L., Elleithy, K., and Faezipour, M. (2012). Detection of obstructive sleep apnea through ecg sig-

nal features. In *IEEE Int. Conf.on Electro/Information Technology (EIT)*, pages 1–6.

- Alqassim, S., Ganesh, M., Khoja, S., Zaidi, M., Aloul, F., and Sagahyroon, A. (2012). Sleep apnea monitoring using mobile phones. In *IEEE 14th Int. Conf.* on e-Health Networking, Applications and Services (Healthcom), pages 443–446.
- Angeline, P. J., Saunders, G. M., and Pollack, J. B. (1994). An evolutionary algorithm that constructs recurrent neural networks. *IEEE transactions on Neural Networks*, 5(1):54–65.
- Bäck, T., Fogel, D., and Michalewicz, Z. (1997). Handbook of evolutionary computation. *Release*, 97(1):B1.
- Cuomo, S., De Pietro, G., Farina, R., Galletti, A., and Sannino, G. (2016). A revised scheme for real time ecg signal denoising based on recursive filtering. *Biomedical Signal Processing and Control*, 27:134–144.
- De Falco, I., De Pietro, G., and Sannino, G. (2015). On finding explicit rules for personalized forecasting of obstructive sleep apnea episodes. In *IEEE Int. Conf. on Information Reuse and Integration (IRI)*, pages 326– 333.
- De Falco, I., Della Cioppa, A., Maisto, D., Scafuri, U., and Tarantino, E. (2014). An adaptive invasion-based model for distributed differential evolution. *Information Sciences*, 278:653–672.
- De Falco, I., Della Cioppa, A., Scafuri, U., and Tarantino, E. (2017). Exploiting diversity in an asynchronous migration model for distributed differential evolution. In *Genetic and Evolutionary Computation Conf. Companion (GECCO)*, pages 1880–1887.
- De Falco, I., Iazzetta, A., Natale, P., and Tarantino, E. (1998). Evolutionary neural networks for nonlinear dynamics modeling. In *Parallel Problem Solving from Nature (PPSN)*, pages 593–602.
- Edlund, J. A., Chaumont, N., Hintze, A., Koch, C., Tononi, G., and Adami, C. (2011). Integrated information increases with fitness in the evolution of animats. *PLoS computational biology*, 7(10):e1002236.
- Gruau, F. et al. (1994). Neural network synthesis using cellular encoding and the genetic algorithm.
- Hertz, J. A., Krogh, A. S., and Palmer, R. G. (1991). Introduction to the theory of neural computation, volume 1.
- Kassahun, Y. and Sommer, G. (2005). Efficient reinforcement learning through evolutionary acquisition of neural topologies. In *ESANN*, pages 259–266.
- LeCun, Y., Bengio, Y., and Hinton, G. (2015). Deep learning. *Nature*, 521(7553):436–444.
- McNicholas, W. and Levy, P. (2000). Sleep-related breathing disorders: definitions and measurements.
- Miikkulainen, R., Liang, J., Meyerson, E., Rawal, A., Fink, D., Francon, O., Raju, B., Navruzyan, A., Duffy, N., and Hodjat, B. (2017). Evolving deep neural networks. arXiv.
- Najafabadi, M. M., Villanustre, F., Khoshgoftaar, T. M., Seliya, N., Wald, R., and Muharemagic, E. (2015). Deep learning applications and challenges in big data analytics. *Journal of Big Data*, 2(1):1.
- Niskanen, J.-P., Tarvainen, M. P., Ranta-Aho, P. O., and Karjalainen, P. A. (2004). Software for advanced

hrv analysis. *Computer methods and programs in biomedicine*, 76(1):73–81.

- of the European Society of Cardiology, T. F. et al. (1996). Heart rate variability: standards of measurement, physiological interpretation, and clinical use. *Circulation*, 93:1043–1065.
- Penzel, T., Moody, G. B., Mark, R. G., Goldberger, A. L., and Peter, J. H. (2000). The apnea-ecg database. In *Computers in cardiology 2000*, pages 255–258.
- Price, K., Storn, R. M., and Lampinen, J. A. (2006). *Differential evolution: a practical approach to global optimization.*
- Real, E., Moore, S., Selle, A., Saxena, S., Suematsu, Y. L., Le, Q., and Kurakin, A. (2017). Large-scale evolution of image classifiers. *arXiv*.
- Ronald, E. and Schoenauer, M. (1994). Genetic lander: An experiment in accurate neuro-genetic control. In *Int. Conf. on Parallel Problem Solving from Nature*, pages 452–461.
- Rumelhart, D. E., Hinton, G. E., and Williams, R. J. (1985). Learning internal representations by error propagation. Technical report, California Univ San Diego La Jolla Inst for Cognitive Science.
- Sannino, G., De Falco, I., and De Pietro, G. (2014). An automatic rules extraction approach to support osa events detection in an mhealth system. *IEEE journal of biomedical and health informatics*, 18(5):1518–1524.
- Sher, G. I. (2012). Handbook of neuroevolution through Erlang.
- Shokoueinejad, M., Fernandez, C., Carroll, E., Wang, F., Levin, J., Rusk, S., Glattard, N., Mulchrone, A., Zhang, X., Xie, A., et al. (2017). Sleep apnea: a review of diagnostic sensors, algorithms, and therapies. *Physiological measurement*, 38(9):R204.
- Siebel, N. T. and Sommer, G. (2007). Evolutionary reinforcement learning of artificial neural networks. *International Journal of Hybrid Intelligent Systems*, 4(3):171–183.
- Stanley, K. O. and Miikkulainen, R. (2002). Evolving neural networks through augmenting topologies. *Evolutionary computation*, 10(2):99–127.
- Tomassini, M. (2006). Spatially structured evolutionary algorithms: artificial evolution in space and time.
- Vargas, D. V. and Murata, J. (2017). Spectrum-diverse neuroevolution with unified neural models. *IEEE* transactions on neural networks and learning systems, 28(8):1759–1773.
- Yao, X. and Liu, Y. (1997). A new evolutionary system for evolving artificial neural networks. *IEEE trans. on neural networks*, 8(3):694–713.