

PERSPECTIVES

Technical and practical aspects of artificial intelligence in cardiology

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ABSTRACT

Artificial intelligence (AI) is here to stay. It is not a future anymore, and there are many particular problems in cardiology that are already being solved via machine learning (ML), and many more are to come. AI cannot solve complex tasks yet, and probably this will not change in the upcoming years. Therefore, cardiologists do not have to be afraid that computers will replace them. However, cardiologists who will not be able to use ML algorithms in their clinical practice will be replaced by those who will. (*Fig. 2, Ref. 50*). Text in PDF www.elis.sk

KEY WORDS: artificial intelligence, cardiology, potential machine learning, survival models, classification algorithms, computer vision, automated analysis of various imaging examinations, ECG interpretation, phenotype clustering, pathophysiological mechanisms.

Introduction

Artificial intelligence (AI), a popular but unprofessional phrase that usually refers to machine learning (ML) algorithms, is one of the most discussed topics of current science. ML is expected to significantly influence almost all scientific fields, including medicine and health care. The stakes are high: it is expected that ML could offer substantial improvement for patient and clinical team outcomes, reducing costs, and improving population health (1, 2).

ML algorithms' usefulness becomes evident with the ever-growing datasets. Physicians are flooded with data while being expected to work more efficiently. Moreover, following the introduction of efficient techniques, e.g., genome-sequencing or biometric data from telemedical devices, medical staff will soon be required to interpret and theoretically act on information coming from many distinct fields of biomedicine (3).

Potential implementation of ML in cardiology is broad and ranges from predicting the patient-specific treatment outcomes (survival models, classification algorithms) (4) through computer vision (an automated analysis of various imaging examinations, ECG interpretation) (5, 6) to phenotype clustering and discovery of pathophysiological mechanisms (3, 7).

In this paper, we would like to explain the basics of ML algorithms concisely and outline their use in cardiology.

What is machine learning

Encyclopedically, ML is a scientific field that studies computer algorithms that improve automatically through experience (8). Generally, an ML algorithm is capable of building a model based on sample data given by the researcher in order to make predictions or decisions without being explicitly programmed to do so (9).

Approaches within machine learning are typically divided into three broad categories, depending on the nature of the signal and feedback available to the learning algorithm. The most classical and used is supervised learning, where the learning system is given example inputs and desired outputs by the "teacher", and the goal is to find the most appropriate mapping from input space to the outputs. Secondly, for unsupervised learning, the system is not given any outputs nor labels, and the goal is to uncover structure within the data. Finally, reinforcement learning is when the program interacts with its dynamical environment where it must perform towards a particular goal that is achieved via feedback in the form of rewards, which it tries to maximize (10).

This paper focuses mainly on supervised learning as it is the most widely used type of ML within medicine. We will also provide some details of unsupervised learning systems but omit the possibilities of reinforcement learning in medicine and cardiology, albeit recently, some interest arose around reinforcement learning (11, 12).

Supervised machine learning

Supervised learning is the most ubiquitous type of ML currently used. It is about finding an appropriate mapping from an in-

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Acknowledgement: This work was supported by the independent research grant of the Ministry of Education, Science, Research and Sport of the Slovak Republic VEGA [grant number 1/0563/21].

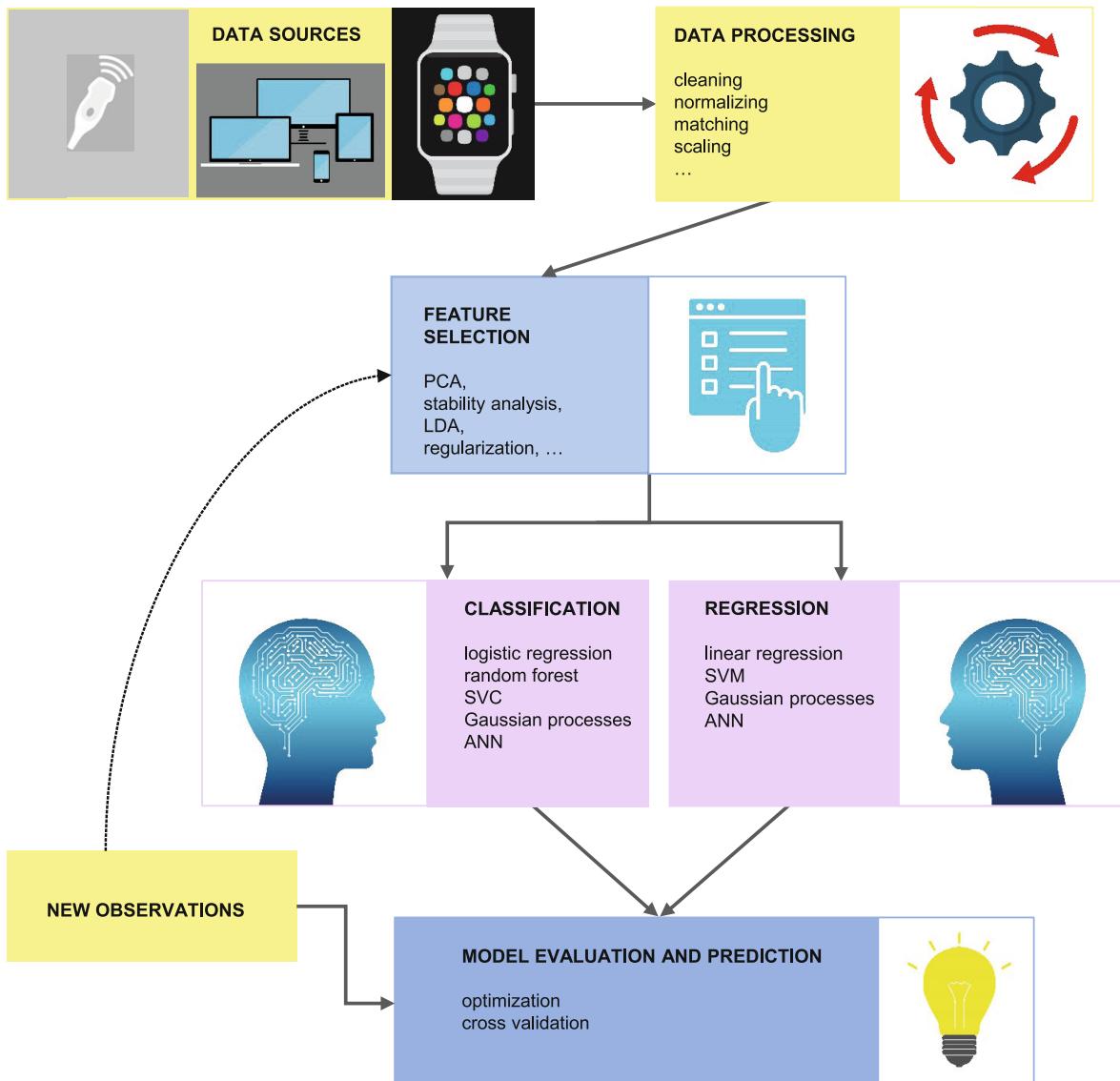


Fig. 1. Typical ML workflow: from data to predictions. An illustration of typical machine learning workflow, from data acquisition, preprocessing and cleaning, to the feature selection, the modeling itself (classification or regression), and model evaluation and prediction. When the researcher acquires new observations, new data might be included alongside the original data to retrain the model and increase its performance.

put vector to the output based on the example of input-output pairs provided to the learning algorithm (13). A supervised learning algorithm analyses the training data and produces an inferred function. In an optimal scenario, the algorithm will correctly determine the output for unseen input vectors, hence will generalize reasonably.

We can subdivide supervised ML into two distinct types: classification and regression. Fundamentally, classification algorithms are trying to predict the correct discrete label (typically dichotomous labels, but of course, multi-label problems exist), while regression algorithms predict a continuous quantity (14).

In particular, cardiology benefits from classification ML algorithms (15, 16). The typical workflow, in this case, consists of gathering the dataset (clinical risk factors, biological data such as

protein expressions, epigenome, microbiome and others), performing a feature selection in order to find relevant variables (for more details on feature selection, see the next section), training the ML model, and finally validating the model on unseen data in order to assess its performance properly (Fig. 1). The most important supervised ML algorithms are summarized in Figure 2.

Feature Selection

Any researcher willing to implement an ML model should take specific care when deciding on which variables to use in the model. This step is commonly referred to as feature selection. Fitting a model (e.g., basic logistic regression) is in fact, mathemati-

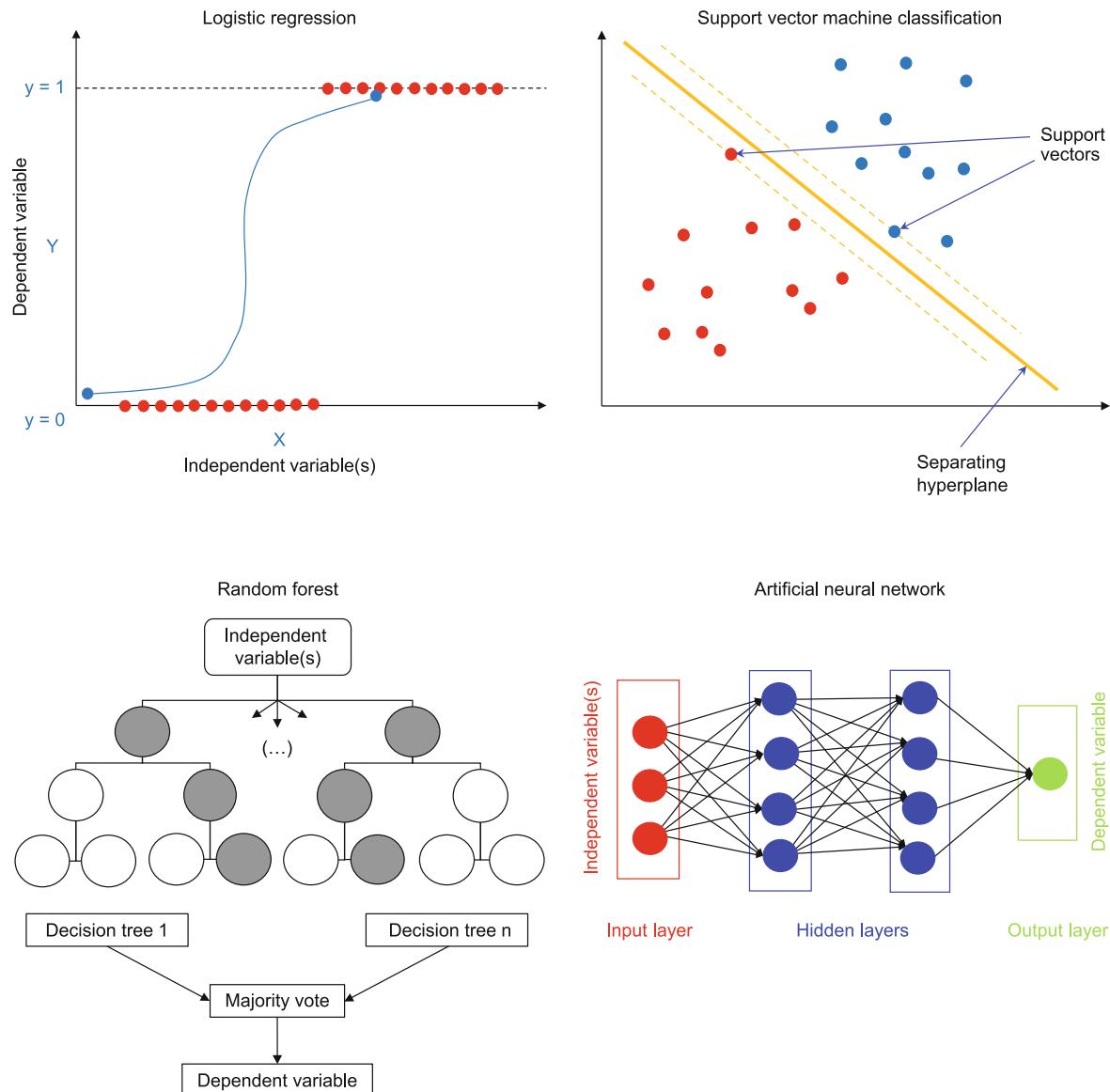


Fig. 2. Most important ML algorithms. Sketches of selected ML algorithms for classification: logistic regression (linear model with output sigmoidal nonlinearity), random forest (an ensemble of decision trees where the final classification comes from the majority vote), Support Vector Machine Classifier (kernel trick is used to separate linearly inseparable data with a hyperplane), and an artificial neural network (input is passed through several nonlinear layers that encode the hidden structure within the dataset and final sigmoid outputs the predicted label).

cally impossible when one has more independent variables than observations (input–output pairs). Techniques such as pairwise selection, forward or backward stepwise regression are often used in practice, however, they often lead to models that do not generalize well (17, 18). Furthermore, complex interactions between variables might lead to underperforming of the model.

The ML algorithms might also help here: several feature selection methods exist in both realms – supervised and unsupervised. The simplest way is to use regularization (i.e. shrinking the coefficient towards zero), which is the main feature in algorithms like LASSO (19) or Elastic Net (a mix of L1 and L2 regularization)

(20) or more complex methods like stability selection with gradient boosting (21), in which the main idea is to inject more noise into the original problem by generating bootstrap samples (stability selection) (22) and then use the base feature selection algorithm (gradient boosting classifier) (23).

From the unsupervised methods, let us briefly mention the principal component analysis (change of basis in the data where the explained variance sorts the components) (24) and linear discriminant analysis (statistically, a close relative of ANOVA, albeit with continuous independent samples and categorical class label) (25).

Unsupervised machine learning

As mentioned earlier, unsupervised machine learning focuses on uncovering the underlying structure in the (typically) high-dimensional datasets. The landmark of unsupervised learning techniques is clustering, which is a task of grouping a set of data points so that points in the same group are more similar to each other than to other groups. This is usually achieved by minimizing some objective function that encodes “similarity”. There exist a plethora of algorithms for clustering, e.g. k-means (26), DBSCAN (27), independent component analysis (ICA) (28) to name a few.

Dimensionality reduction is not strictly an ML technique, as many of the methods were invented before ML emerged. However, it slowly became an integral part of almost any ML-related analysis pipeline. Its goal is simple: to transform high-dimensional data into a low dimensional space so that the low-dimensional representation retains some meaningful properties. Apart from the methods already mentioned (PCA, ICA, LDA), there exist more complex, typically nonlinear methods such as t-SNE (nearest neighbor embedding) (29), uniform manifold approximation and projection – UMAP (30), or autoencoders (31). Shortly, t-SNE constructs a probability distribution over pairs of high-dimensional objects based on similarity and then minimizes a Kullback-Leibler divergence between high-dimensional and its low-dimensional map. UMAP is similar in its workings to t-SNE, but it assumes uniformly distributed data on a manifold. Finally, autoencoders are a specific class of artificial neural networks. Its goal is to learn a, typically, low-dimensional representation for a given dataset. It consists of encoder and decoder parts and a hidden layer with a low number of units in between, conveying the low dimensional representation. The autoencoders are trained so that both input and output are the same dataset, and thus, while training, the autoencoder has to learn an effective intermediate representation of the dataset in its hidden middle layer.

Caveats and challenges

Naturally, ML is not an omnipotent tool, and it has limitations and challenges researchers need to keep in mind. Even the best models are limited by the magnitude and quality of the input data. As an example, Frizzell et al (32) found that ML algorithms were unable to predict 30-day readmission better than basic logistic regression based on a massive dataset with more than 250 variables. All findings based on ML approaches are potentially limited by a dataset, especially when the dataset does not contain any strong predictors. However, this is true for all statistical approaches, not just ML algorithms.

Another big problem with the ML approach is the potential to overfit. Overfitting refers to a model that models the input data too well, albeit cannot generalize. This can happen when the model learns the relevant signal and all the noisy details in the dataset. In general, overfitting is more likely to occur with nonparametric and nonlinear methods that have more flexibility when learning a target. Fortunately, there are many ways and approaches to limit overfitting. One can use a resampling technique like *k*-fold cross-

validation, which trains and tests ML model *k* times on different subsets of data and estimates the performance on an unseen dataset (33).

Next potential pitfall of ML (but again, not limited to ML) is so-called dichotomania (34). Clinicians typically want a dichotomized output (yes or no); however, framing scientific questions like this might be imprecise and might lead to decreased performance of the predictive model (3).

The last point we want to mention in this context is a bias in ML. Typically bias refers to a model giving too much importance to some of its features. At first sight, it might seem like a good thing (and it indeed might be), but the problem occurs when the assumptions for a more generalized algorithm produce systematically prejudiced results. After all, the best model is only as good as the data it was trained on, ultimately depending on the research building that model (35).

Application of ML in cardiology

The human brain consists of approximately 100 billion neurons, in contrast to computers biological components capable of plasticity (36). Computational power of even the most advanced computers nowadays is incomparably lower than a human brain. This is responsible for the failure of ML in solving complex cardiological problems. On the other hand, there are many narrowly defined areas where ML outperforms the traditional statistical approach and cardiologists or provides new insight into a specific problem. We summarize some of the examples.

Preventive cardiology

Assessing cardiovascular risk is the cornerstone of the diagnostic and therapeutic approach in cardiology. Most used risk scores like the Framingham risk score (37) and SCORE (38) rely on several traditional risk factors, e.g. age, gender, arterial hypertension, smoking or blood cholesterol. However, many more risk factors contribute to the complexity of prognosis, which is impossible to predict via standard statistical approaches like classical logistic regression. ML can overcome this obstacle leading to better risk prediction (39), which could be reflected in optimization of drug treatment (40). In order to translate these novel ML approaches to clinical practice, broader validation on independent cohorts is necessary.

Electrocardiology

Electrocardiology is probably the most developed field in ML. We already know that a computer is comparable to a cardiologist in ECG reading (41). However, the capabilities of ML go beyond human capabilities. Thanks to data mining, computers are able to extract new information from ECG recordings that is hidden to human interpretation. For instance, convolutional neural networks could identify patients with atrial fibrillation from ECGs acquired in sinus rhythm with remarkable predictive value (AUC of 90 % after internal validation) (42). Furthermore, ML was able to identify

left ventricular dysfunction from the ECG. Interestingly, this algorithm was also able to predict left ventricular deterioration (43).

Cardiovascular imaging

Computer vision is an important application of ML algorithms in general. Because interpretation of cardiovascular images is challenging and requires long term expertise, ML might bring revolution into this field. Echocardiography is the most used imaging modality in cardiology. Therefore, it is no surprise that the biggest interest of computer vision algorithms in cardiovascular medicine is focused there. Several trials showed that ML-based assessment of left ventricular ejection fraction and wall motion abnormalities is precise (44, 45). Thanks to the development of speckle tracking, AI could be useful in more difficult scenarios, e.g., distinguishing between hypertrophic cardiomyopathy vs athletic heart (46) or constrictive vs restrictive pericarditis (47). The biggest obstacle in the widespread use of the mentioned algorithms are different machine vendors, image processing and image quality. It is important to remind that performance of AI is only as good as the quality of the dataset. Therefore, skilled personnel will always be needed to acquire high-quality images for the analysis. Nuclear cardiology is another fast-expanding field in terms of AI application. Indeed, many ML techniques are incorporated in the routine single photon emission computer tomography or positron emission tomography (48). Thanks to these developments, not only does myocardial ischemia quantification gets improved, but prognosis assessment and revascularization strategy could be optimized (49).

Precision medicine

Precision medicine aims for the highest possible personalization of diagnostic and therapeutic approaches. For this purpose, omics is used (e.g., genomics, proteomics, metabolomics etc.). However, omics examination provides large datasets that are difficult, even impossible, to interpret via standard statistical methods. ML enables a true innovation here by enabling analysis of these complex datasets. The synergy between omics and ML is probably one of the most important factors in the future development of medicine. The combination of precise data with sophisticated analysis should improve medical care significantly. Evidence-based medicine in this field is also promising, and we already know that ML-based analysis of proteomic or genomic examination provides better prognosis prediction than standard methods (16, 50).

Conclusion

Artificial intelligence is here to stay. It is not a future anymore, it is the present, and the field of cardiology is no exception. There are many particular problems in cardiology that are already being solved via ML and many more are to come. AI cannot solve complex questions yet, and probably this will not change in the upcoming years. Therefore, cardiologists do not have to be afraid that computers will replace them. However, cardiologists who will not be able to use ML algorithms in their clinical practice will be

replaced by those who will. Therefore, understanding the basics of ML seems to be an essential part of clinical cardiology knowledge.

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Received July 5, 2021.
Accepted August 16, 2021.