Artificial Intelligence In Medicine 151 (2024) 102869

Contents lists available at ScienceDirect

Artificial Intelligence In Medicine

journal homepage: www.elsevier.com/locate/artmed

Harnessing machine learning for EEG signal analysis: Innovations in depth of anaesthesia assessment

Thomas Schmierer *, Tianning Li, Yan Li

School of Mathematics, Physics and Computing, University of Southern Queensland, Australia

ARTICLE INFO

Keywords:
Machine learning
Electroencephalography
Deep learning
Signal analysis
Anaesthesia
Artificial intelligence

ABSTRACT

Anaesthesia, crucial to surgical practice, is undergoing renewed scrutiny due to the integration of artificial intelligence in its medical use. The precise control over the temporary loss of consciousness is vital to ensure safe, pain-free procedures. Traditional methods of depth of anaesthesia (DoA) assessment, reliant on physical characteristics, have proven inconsistent due to individual variations. In response, electroencephalography (EEG) techniques have emerged, with indices such as the Bispectral Index offering quantifiable assessments. This literature review explores the current scope and frontier of DoA research, emphasising methods utilising EEG signals for effective clinical monitoring. This review offers a critical synthesis of recent advances, specifically focusing on electroencephalography (EEG) techniques and their role in enhancing clinical monitoring. By examining 117 high-impact papers, the review delves into the nuances of feature extraction, model building, and algorithm design in EEG-based DoA analysis. Comparative assessments of these studies highlight their methodological approaches and performance, including clinical correlations with established indices like the Bispectral Index. The review identifies knowledge gaps, particularly the need for improved collaboration for data access, which is essential for developing superior machine learning models and real-time predictive algorithms for patient management. It also calls for refined model evaluation processes to ensure robustness across diverse patient demographics and anaesthetic agents. The review underscores the potential of technological advancements to enhance precision, safety, and patient outcomes in anaesthesia, paving the way for a new standard in anaesthetic care. The findings of this review contribute to the ongoing discourse on the application of EEG in anaesthesia, providing insights into the potential for technological advancement in this critical area of medical practice.

1. Introduction

Anaesthesia, essential for modern surgical practice, enables controlled, temporary loss of sensation and consciousness, aiding in pain-free procedures [1]. Traditional depth of anaesthesia (DoA) assessment methods, based on physical characteristics, is often inconsistent due to individual variations. Objective techniques, such as electroencephalography (EEG), have emerged, with indices like the Bispectral Index (BIS) providing quantifiable assessments. The complexity of determining the ideal DoA, influenced by factors like age and health, has led to the development of diverse devices and techniques, including machine learning algorithms, to enhance precision and safety in anaesthesia care. The current literature focuses on the scope of EEG analysis for the DoA, emphasising machine learning applications, and strives to improve technology to reduce variability and improve patient outcomes.

This literature review critically evaluates the landscape of EEG-based Depth of Anaesthesia (DoA) analysis, focusing on the integration of emerging methods and the comparative effectiveness of different approaches. The objective of this review is to provide a comprehensive analysis of the latest methodologies in anaesthesia and consciousness research, with a primary focus on EEG-based techniques. It examines recent advancements in technical model building and feature extraction for assessing cognitive states during induced unconsciousness, drawing from papers published in the last five years to incorporate the most current and pertinent findings. The review methodically analyses each stage of model design, as outlined in Section 2.2 comparing the performance of developed algorithms with existing methods regarding accuracy, reliability, and computational efficiency.

The primary research question guiding this literature review is: How

* Corresponding author at: UniSQ Toowoomba, 487-535 West St, Darling Heights, QLD 4350, Australia.
E-mail addresses: Thomas.Schmierer@usq.edu.au (T. Schmierer), Tianning.li@usq.edu.au (T. Li), Yan.li@usq.edu.au (Y. Li).

https://doi.org/10.1016/j.artmed.2024.102869
Received 28 September 2023; Received in revised form 31 January 2024; Accepted 3 April 2024
Available online 4 April 2024

do current EEG-based methods for Depth of Anaesthesia (DoA) analysis, particularly those involving machine learning, compare in terms of accuracy, reliability, and computational efficiency? This review is structured around several key objectives, which collectively aim to address the primary research question:

1. To critically evaluate and summarise the current landscape of EEG-based DoA analysis.
2. To provide a comprehensive analysis of the latest methodologies in anaesthesia and consciousness research, focusing primarily on EEG-based techniques.
3. To assess recent advancements in model building and feature extraction in EEG signal processing.

The following sections of this literature address these objectives by examining recent advancements in EEG-based DoA methods. The sections of this paper are organized as follows; 2. Background of EEG-based DoA analysis, 3. Literature review selection and methodology, 4. Latest Algorithms for each DoA assessment stage, 5. Limitations and future direction.

2. Background

Anaesthesia is crucial in surgery, offering benefits like amnesia, pain relief, muscle relaxation, and autonomic reflex regulation. Effective Depth of Anaesthesia (DoA) monitoring improves patient outcomes, minimizes intraoperative awareness, and aids quicker recovery [2,3]. However, excessive anaesthetic doses can lead to postoperative complications like nausea and cognitive issues [1,4,5]. EEG monitoring plays a vital role in assessing DoA by analysing cortical feedback suppression, which affects complex information processing in the brain. Anaesthetists typically evaluate DoA by observing physiological responses and estimating the effects of anaesthetic drugs. EEG signals from the frontal cortex, reflecting cortical and subcortical brain states, can indicate consciousness levels [6,7]. This method encounters challenges such as the lack of standardised EEG indices and variability in response to different anaesthetic agents and between patients. This variability highlights the need for effective evaluation of current methodologies and further development of EEG-based DoA analysis methods. The rapid advancements in signal processing and machine learning have opened new avenues for extracting valuable insights from complex data that are shown to provide substantiative contributions to the field of DoA analysis.

2.1. The role of EEG in determining the DoA

Traditional methods to assess the depth of anaesthesia (DoA) use simple biological indicators such as muscle reflexes, pulse rate, and blood pressure. However, their reliability is limited due to patient variability in response to anaesthetics. The electrical activity of the brain, measured by EEG, reflects the effects of anaesthetic agents on the primary target, the brain. Thus, EEG provides a direct, non-invasive assessment of anaesthetic states, more accurate than other methods [8,9]. EEG signals exhibit characteristic changes in their frequency, amplitude, and complexity as the depth of anaesthesia increases or decreases. For instance, during the transition from wakefulness to unconsciousness, the EEG typically shows a shift from low-amplitude, high-frequency activity to high-amplitude, low-frequency activity [5]. The key benefit of the use of EEG in determining the DoA lies in its ability to provide a direct, real-time, and continuous measure of brain activity during anaesthesia. While there are limitations and challenges to overcome, recent advancements in the field have led to improved EEG-based monitoring systems that can enhance patient safety and optimize anaesthesia management in clinical practice [6,9].

2.2. General process of determining the DoA from EEG

The general approach to DoA evaluations can be visualised in Fig. 1. Typically, the initial stage is the collection of raw EEG data from the patient, which is then denoised and subjected to feature extraction. Using supervised machine learning, changes in the EEG are associated with anaesthetic states. The feature extraction and index design processes often lead to variations among different DoA estimation methods. Section 4 of this review paper offers an overview of prevailing research trends in these domains, which are feature extraction, model building, and evaluation and testing.

Various commercially available devices utilise EEG to assess the anaesthetic effect, each outputting unique indices; these include the SedLine, BIS vista, Narcotrend Monitor, NeuroSENSE, and qCON 2000 monitor. These monitors have been found to generally correlate with alertness assessments and reduce anaesthetic use and emergence time [10]. The BIS is seen to be the most popular device in clinical settings with a recent study indicating that 81 % of clinicians used the BIS with 68.5 % indicating their indication that it is the most reliable DoA application on the market [11]. Despite the popularity of the BIS index known limitations include age dependence [12], drug dependence [13], time delay and vulnerability to noise [14,15]. Consequently, innovation in EEG-derived DoA estimation algorithm design is a critical area of research.

3. Literature review method

3.1. Search strategy

This literature review provides a comprehensive and unbiased synthesis of existing research on EEG analysis for determining the depth of anaesthesia (DoA). The literature employed a structured approach following the PRISMA guidelines, as illustrated in the accompanying flowchart, Fig. 3. The search was initiated with a comprehensive query across five major databases: PubMed, Cochrane, Scopus, CINAHL, and Google Scholar to ensure a wide coverage of potential literature, spanning various disciplines and research scopes. The search focused on papers published within the last 5 years to build upon and complement existing reviews in this field [13,15–17], ensuring the inclusion of the most recent and relevant findings. A breakdown of the publication date range for the included papers is included in Fig. 2. The search terms were structured around the following concepts: “anaesthesia or anaesthetist” and “consciousness monitors, monitor, depth of anaesthesia, machine learning, or artificial intelligence” and “electroencephalography or Bispectral index”.

3.2. Study selection

From the initial 2839 records identified, we systematically removed duplicates ($n = 810$) and those not meeting our initial screening criteria ($n = 302$), resulting in 1727 articles for detailed screening. Articles not retrieved ($n = 58$) and those excluded after a thorough review of the full texts ($n = 120$) for various reasons such as lack of relevance to the research question, insufficient methodological quality, or data incompleteness, were documented at each stage. This process is transparently depicted in Fig. 3. The 295 full-text articles assessed for retrieval underwent a rigorous eligibility evaluation, focusing on the study’s relevance to the research question, methodological soundness, and the applicability of the findings. Ultimately, 117 studies met our inclusion criteria, which specified that selected works must be peer-reviewed, published in English, focused on human subjects, utilise EEG as the primary assessment tool for DoA, and be published within the last five years. This final cohort of articles forms the basis of our comprehensive review. Each included study was subjected to a quality assessment using standardised checklists appropriate for the study design to ensure the reliability and validity of our synthesis. Data extraction was performed

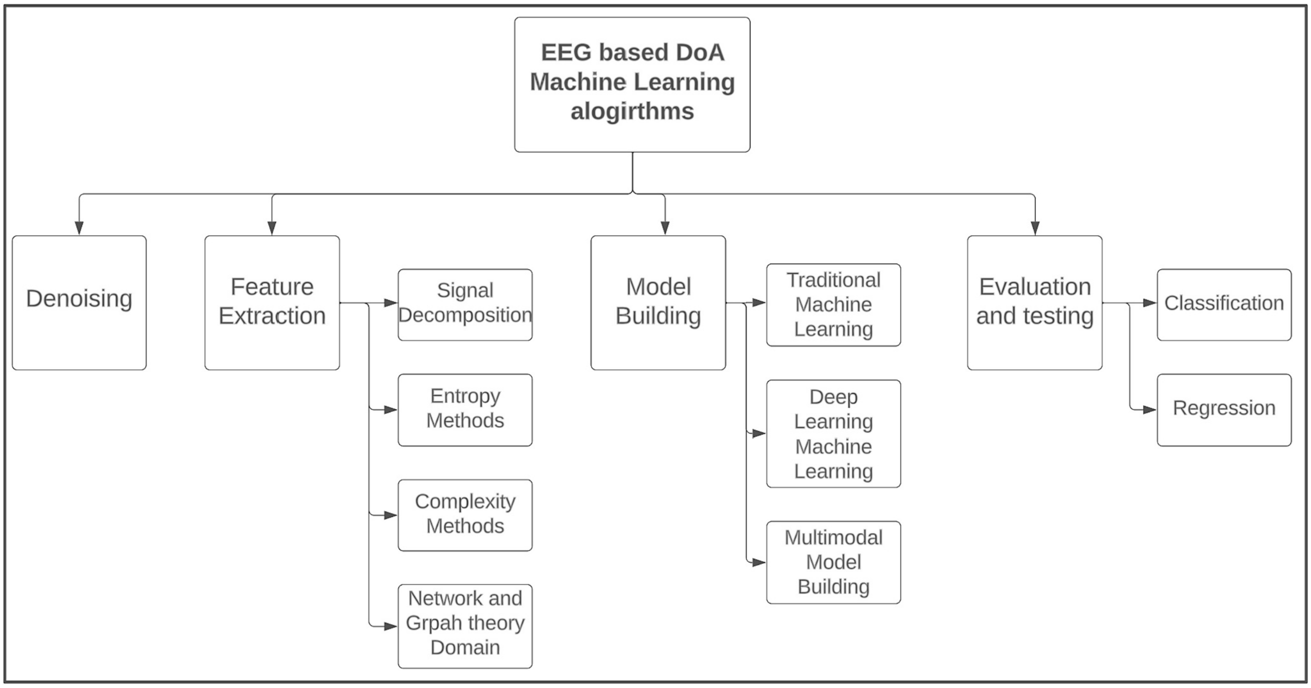

Fig. 1. The general process of a DoA index design based on EEG signals. Current advances in each of these areas are discussed in this work.

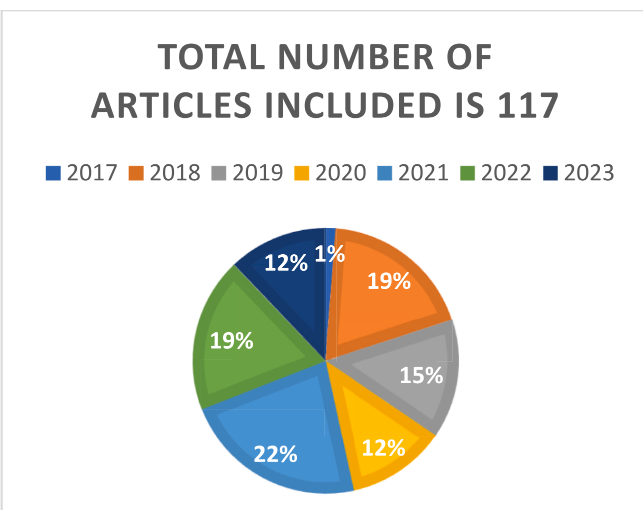

Fig. 2. Articles referenced by publication year.

systematically, with information regarding study design, participant demographics, EEG methodologies, and key findings being collated using a predefined template.

4. The latest algorithms for each DoA assessment stage

The following sections highlight the current leading algorithms for the DoA assessment at each of the identified stages, as outlined in Fig. 1. The initial stage of denoising and artifact removal is fundamentally essential to EEG analysis due to the prevalence of electrical interference in EEG signals. The most common initial step in the preprocessing of EEG signals are temporal filtering using bandpass filters [14,18–48], typically between 0.5 Hz and 47 Hz [18]. Those methods occurred in approximately 70 % of the reviewed methodologies that implemented denoising. Other denoising methods seen in the literature include Non-Local Means (NLM) [49,50], Wavelet-based denoising [51,52], surrogates-Based Artifact Removal (SuBAR) method [53], and Sparse Denoising Autoencoder (SDAE) [54]. In some cases, the use of the Signal Quality Index (SQI) is available to assist in ensuring the data presented is of suitable clarity for analysis and model building [49,55–57].

4.1. Feature extraction methods

One of the key steps in signal analysis is feature extraction (FE) which involves examining EEG signals to isolate characteristics that are associated with the level of cognition. Four categories are used in this paper to identify FE methods based on the purpose of the feature extraction technique; these are signal decomposition methods, entropy methods, complexity methods, and network and graph theory feature extraction methods. EEG signal analysis often uses non-linear methods due to the non-linear nature of state transitions, as evidenced in the literature [58]. Signal decomposition methods include all time, frequency, and time-domain frequency decomposition techniques. Entropy and complexity measures, which often use non-linear techniques, are common to observe underlying consciousness dependent information in EEG signals. A rising trend is using raw EEG with deep learning, eliminating initial feature extraction, and showcasing advancements in EEG-based DoA analysis.

4.1.1. Signal decomposition based methods

Signal decomposition is a technique in signal analysis to divide an observed signal into components or subsets to reduce the complexity of a signal for analysing and improving model building. The general classification for signal decomposition methods includes frequency, time, and time-frequency domain methods. The transformation of a signal from the time domain to the frequency domain using Fourier transform (FT) is a popular tool in EEG analysis for the DoA assessment [23,30,41,42,45,54,59–65]. A range of papers consider features extracted from ratios of relative frequency bands such as alpha or beta bands. Alpha band power is considered of particular significance to the DoA estimation [64,66,46] and refers to the amount of electrical activity or power within the alpha band is typically defined as the frequency range between 8 Hz and 12 Hz. Another popular analysis method is spectral edge frequency (SEF) [29,44,68,69]. The ordinal power spectral

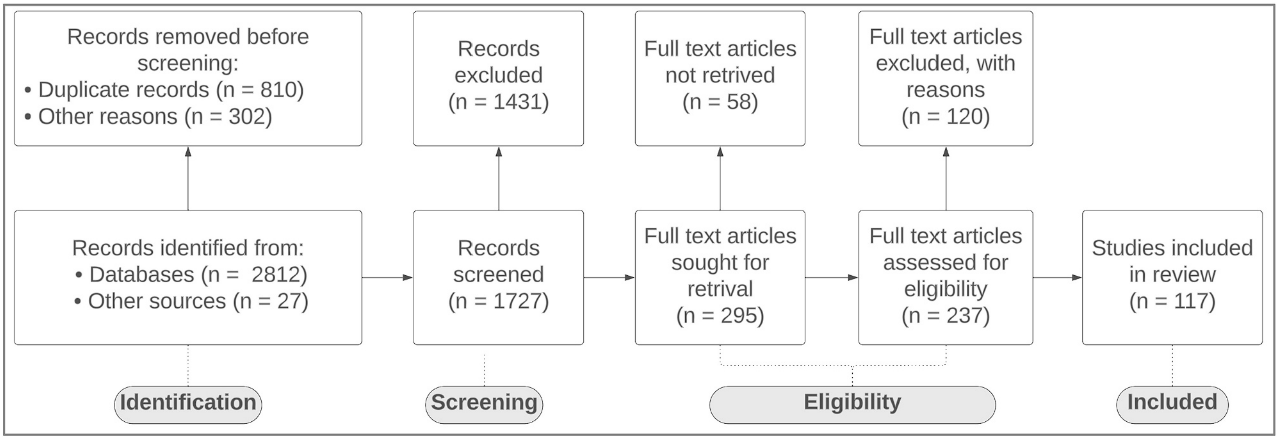

Fig. 3. Preferred reporting items for systematic reviews and meta-analyses diagram of screening and evaluation process.

density (O-PSD) is demonstrated to capture spectral trends across frequency bands and correlates strongly (Spearman's correlation of 0.821) with clinical DoA assessments [70]. Recent analysis concludes that the alpha-wave amplitude and slow-wave-frequency modulatory processes can effectively track the transition between states of unconsciousness and burst suppression in anaesthetised patients [64]. Burst suppression is a deep state of unconsciousness that has been associated with post-operative cognitive disorders [71].

The wavelet transform is a popular signal decomposition method in the reviewed literature; decomposing a signal into a set of scaled and translated wavelets. Discrete wavelet transform (DWT) is a computationally efficient version of the wavelet transform used in EEG analysis for the DoA analysis [19,72–74]. It uses a set of discrete wavelets that are derived from a single mother wavelet by dilations and translations [19]. DWT is more rigid and less flexible than other forms of wavelet transformation which may be a drawback of this method. Alternatively, continuous wavelet transform (CWT) allows for the extraction of a continuous family of wavelets, leading to a two-dimensional representation of the signal (time and scale) [75,76]. This method is more computationally intense yet more flexible than DWT. A variety of other wavelet transformations are seen in the literature, including spectral graph wavelet transformation (SQWT), stationary wavelet transform (SWT) [77–79] and empirical wavelet transform (EWT) [57]. These methods all serve a similar purpose of deconstructing a signal into packets for convenient analysis.

Principal component analysis (PCA) is utilised extensively due to its ability to reduce the dimensionality of the data while retaining most of the original variance [23,24,51,80–83]. Other time domain signal decomposition techniques employed include non-linear PCA [20], and independent component analysis (ICA) [20,23,39,53,84,85]. Other decomposition methods employed include empirical mode decomposition (EMD), alongside its multivariate empirical mode decomposition (MEMD) [86], and EEG variability (EEGV) [69].

4.1.2. *Entropy based methods*

Entropy-based measures quantify the unpredictability or randomness in the EEG signals; various entropy metrics are employed to assess the randomness and predictability in the EEG data [41]. Permutation entropy (PEn) is a robust and efficient tool that quantifies the complexity of a time series [42]. In the reviewed literature, permutation entropy was seen as a popular method of feature extraction [29,35,42,48,52,54,63,69,72]. This method is particularly useful for analysing dynamic changes in EEG signals by evaluating the order relations between values. Permutation entropy is considered advantageous due to the method's noise tolerance and robustness [87]. Despite the popularity of this method, permutation entropy was observed to be significantly influenced by patient age in all settings except for narrow-band EEG activity [88]. Spectral entropy (SE) was implemented in the reviewed literature effectively decomposing EEG signals to extract features from frequency bands of EEG signals for the effective DoA assessment [41,57,63]. Ra et al. [41] illustrated in a study involving 24 patients, the PE showed a high correlation (the highest $R^2 = 0.793$) with the BIS index, however, the SE presented an improved correlation (the highest $R^2 = 0.846$). Several other entropy measures are seen in the reviewed literature including wave entropy [54], hierarchical dispersion entropy (HDE) [49], sample entropy [35,52,54,46,69,89], Hurst entropy [52,63], singular value decomposition entropy [79], and fuzzy entropy [34,52].

4.1.3. *Complexity based methods*

The intricate relationship between the complexity of EEG signal and state of awareness lends to the implementation of non-linear signal analysis. Lempel-Ziv Complexity (LZC) is a non-parametric method used to quantify the complexity or randomness of a finite sequence and has been used successfully in the DoA applications with EEG in the past [62,63] to quantify the complexity or irregularity of the EEG signal. Changes in LZC have been associated with various neurological conditions and cognitive states [14,22,90], making LZC a useful tool for EEG-based diagnosis and monitoring. It was observed that brain activity complexity, when measured by LZC, may produce inconsistent associations with propofol concentration [22]. In a study of age dependency in EEG-based DoA estimators, Biggs et al. [14] observed that LZC also showed an age bias, underestimating the depth of hypnosis in elderly patients. An extension of LZC, permutation Lempel-Ziv Complexity (PLZC) is a method for analysing signal complexity. Unlike the traditional LZC, PLZC is more resilient to noise because it is based on the relative amplitude of the signal due [35,91].

In addition, detrended fluctuation analysis (DFA) operates by examining the fluctuations within a time series scale with a size of the observation window. Compared to other non-linear analysis methods, DFA offers advantages such as fewer stringent assumptions about signal stationarity and increased accuracy in correlation estimates allowing this feature to effectively illustrate features associated with levels of consciousness [35,45,62,63,92,93]. Other methods for measuring complexity include the second order difference plot (SODP) [57] and fractal dimension [20,30,42,75,77,78,90,94–96,98]. EEG signals often display fractal or self-similar characteristics, where their structure looks alike at various scales, a phenomenon that can be quantified using fractal dimension. In one study examining EEG characteristics of 36 anaesthesia patients, the fractal dimension showed a strong association with the clinical assessment of the DoA, achieving an area under the curve (AUC) of 0.74 without remifentanil [98]. Several techniques exist for estimating the fractal dimension of EEG signals, such as the Higuchi, Katz, and Petrosian fractal dimensions.

4.1.4. Network & graph theory approaches for feature extraction

The application of network and graph theory feature extraction methods has gained traction in the study of EEG based DoA assessment, particularly with the increasing availability of high-density EEG data. These mathematical frameworks facilitate the representation of intricate brain activity as a complex network, where the complex interactions between different brain regions can be systematically analysed (Table 1).

Functional connectivity (FC) is a statistical measure that describes the dependencies or correlations between neurophysiological events in different regions of the brain. It quantifies the synchrony or correlation between these regions and can be measured using various methods, including correlation, coherence, and phase-locking value. FC has become an essential tool in understanding the neural mechanisms underlying consciousness and anaesthesia, particularly in the context of the loss and recovery of consciousness [26,99]. Recent studies have further explored the role of FC in anaesthesia, focusing on the changes in brain network properties and community structure during the loss of consciousness (LOC) and recovery of consciousness (ROC). Findings reveal a breakdown of FC under anaesthesia, leading to impaired connectivity between brain areas. Bi et al. [99] illustrated the effectiveness of sparse representation modelling with network parameters in detecting significant FC differences in the frontal, occipital cortices, and the whole brain network. These results were obtained with a 256-channel high-density EEG and tested across three different General anaesthesia agents. Phase amplitude coupling (PAC) measures the interaction between the phase of a low-frequency oscillation and the amplitude of a high-frequency oscillation and is thought to play a key role in coordinating neural activity. Specific PAC patterns in theta-alpha and alpha-beta observed in certain brain regions represented information processing on multiple spatial scales and reflected cross-frequency coordination in different frequency bands and functional regions [24]. In addition, PAC feature extraction is noted as a valid FE method for cerebral hemodynamic variables [103]. Furthermore, the PAC between delta-alpha frequency bands is associated with a consciousness state in adults and children [65].

Table 1
Network and graph feature extraction methods.

Method	Channels	Authors
Community detection	19 channel EEG	Dong et al. [26]
Mutual information	7 channel EEG	Dong et al. [27]
Sparse representation (SR)	256 channel EEG	Bi et al. [99]
Directed coherence	32 channel EEG	Lioi et al. [36]
Long-range temporal correlation (LRTC)	64 channel EEG	Thiery et al. [45]
Spatiotemporal dynamics	60 channel EEG	Lee et al. [33]
Posteriorization/anteriorization index (P/A index)	5 channel EEG	Baron Shahaf et al. [21]
Gray-level co-occurrence matrix (GLCM)	15 channel EEG	Mousavi et al. [100]
Characteristic path length (CPL)	128 channel EEG	Li et al. [34]
Common spatial pattern (CSP)	128 channel EEG	Rimbert et al. [61]
Microstate analysis	16 channel EEG	Lapointe et al. [31]
	128 channel EEG	Si et al. [101]
	91 channel EEG	Liu et al. [38]
Occipital delta power	256 channel EEG	Casey et al. [23]
Phrasal relationship	19 channel EEG	Dong et al. [24].
	19 channel EEG	Xiao et al. [102]

Directed coherence is a measure of the directionality of the information flow between different brain regions [36]. Changes in temporal dynamics of neuronal oscillations are shown to be associated with consciousness. Long-range temporal correlations (LRTC) refer to a statistical phenomenon where the values of a time series are correlated over a wide range of time lags. Beta LRTC combined with alpha amplitude provides the highest observed classification accuracy (above 80 %) for consciousness state prediction [45]. Changes in the characteristic path length (CPL) may reflect disruption in functional connectivity. The disruptions in CPL were observed with a multi-channel method utilising a time-varying fuzzy entropy. This approach identified specific disruptions in connectivity, including frontal-occipital connectivity during the early LOC stage and inner-frontal connectivity during the later LOC stage [34]. The functional relationship between brain regions was illustrated with the posteriorizing/anteriorization (P/A) index and was effective at determining recall under sedation [21]. This index is calculated based on the ratio between the strongest posterior activity and the strongest anterior activity. For each segment, the number of valid (non-noisy) epochs where the posterior/anterior ratio was greater than 1 was counted, indicating that the alpha posterior activity exceeded the alpha anterior activity. This count of greater posterior activity was then divided by the total number of valid epochs per segment to derive the P/A index. This index was found to differentiate between patients with or without recall under sedation in a study involving 26 sedated patients. In comparison with the BIS index, both indexes were effective in distinguishing between patients with and without recall. However, while the BIS differentiation appeared to be sensitive to the specific sedation drug used (midazolam vs. propofol), the P/A index did not exhibit similar drug-based sensitivity. The P/A index showed a statistically significant difference under sedation between patients who had recall (median 66.75) and those who did not (median 22) [21].

Microstate analysis involves segmenting the EEG signal into a series of quasi-stable states typically 40 to 100 milliseconds in duration. These microstates may be considered representative of basic building blocks of brain activity and represent periods of scalp activity that manifest as spatially organized topographical maps. In one study involving 22 adult surgical patients, 6-channel EEG recordings were taken throughout the perioperative period to observe microstate transitions. Most notably, during surgical anaesthesia, patients demonstrated increased mean duration and, consequently, a reduction in the occurrence of microstates when compared to both preoperative baseline and PACU admission [31]. In a separate study, microstate analysis combined with the Hidden Markov Model (HMM) was used to accurately estimate the DoA state based on 128-channel EEG [101]. Global field power and global interpretation variance were generated to examine the characteristics of corresponding microstate sequences; the accuracy in distinguishing between the baseline and moderate sedation states was found to be 80.16 % [38].

4.2. Model building methods

Model building processes typically follows the extraction of relevant features from the EEG signal that encapsulates its essential characteristics. Model building for the DoA analysis typically employs supervised machine learning techniques with few exceptions [51,101]. In most cases, training is based on the label provided by industry models (for example the BIS), or clinical assessment of the DoA state (CAD) for index design, and classification models respectively. Methods in this review are grouped according to the model-building methodology employed with information about the feature extraction technique implemented.

4.2.1. Traditional machine learning methods

Traditional Machine Learning methods employed in the literature include regression techniques (such as the Gaussian process, linear and logistical), support vector machines, decision trees, random forests, and k-NN algorithms). These methods are grouped according to the evaluation metrics with classification and regression methods presented separately (Table 2).

Studies have achieved variable success with Linear Regression modelling based on the effectiveness of the feature extraction method and sample size examined [41,72,104]. Linear regression models exhibit relatively low computational intensity, making them potentially more feasible for real-time analysis [87]. However, their performance is often overshadowed by more complex models like SVM, which demonstrate higher accuracy but may require more computational resources.

The review reveals machine learning models like Gaussian process regression and SVM tend to show high correlation with BIS index, indicating strong potential for clinical application. However, the variation in correlations across studies suggests a significant influence of feature extraction methods and sample sizes on model performance. The use of spectral graph wavelet transforms achieved a high correlation of 0.95681 with the BIS, underscoring the importance of advanced feature extraction techniques [50]. However, this also implies a trade-off between model complexity and interpretability.

Huang et al. [52] illustrated Gaussian process regression models' ability to model complex, non-linear relationships, which achieved a correlation of 0.9491 with the BIS in a study involving 73 patients. Support vector machine (SVM) have seen validity in both classification and regression cases. A correlation of 0.834 and Cohen's Kappa of 0.809 with the BIS was observed with this method utilising non-linear features based on Empirical Wavelet Transformation [57] (Table 3).

K-Nearest Neighbours ($K-$NN) algorithm, used in various studies, showed high accuracy (ranging from 91 % to 95.32 %) in smaller patient cohorts [30,100]. In the largest of these studies, Nguyen-Ky et al. [74] achieved 93 % accuracy in a 25-patient study with power spectral density (PSD) and Hurst method denoising. However, these high accuracies raise questions about the model's performance in larger, more diverse populations.

Decision tree classifiers have shown promising results when applied to SEF95 alongside spectral beta power ratio, and energy in four frequency bands achieved a classification accuracy of 92.2 % and latency of 1 second (s) [44]. This outcome was substantiated in a large study involving two EEG databases with a total of 95 patients [73] with sensitivity and specificity of 95.4 % and 97.7 % respectively.

Extending this concept, random forest is an ensemble learning method that builds multiple decision trees and combines their predictions to reduce overfitting. In a recent study utilising a large number of time-series features, random forest classification methods outperformed other classification algorithms, including support vector classifier, XG boost classifier, gradient boost classifier and decision trees, in estimating the DoA states [106]. This study observed a classification accuracy of 83 %.

Table 2
Traditional model building methods for index design/regression.

Method	FE method	Author	Outcome
Gaussian process regression	Range of entropy features including fuzzy entropy	Huang et al. [52]	Correlation = 94.91 (BIS)
Linear regression	FFT with spectral entropy	Ra et al. [41]	Correlation = 0.9196 (BIS)
	Spectral graph wavelet transform (SGWT) with average energy of wavelets and scale coefficients	Diykh et al. [50]	Correlation = 0.95681 (BIS)
	DWT with standard deviation, entropy, median, root mean square of coefficients	Diykh et al. [72]	Correlation = 0.798 (BIS)
SVM regression	EWT with SODP and SE	Schmierer et al. [57]	Correlation = 0.834, Choen's Kappa of 0.809 (BIS)

Table 3
Traditional model building methods for classification.

Method	FE method	Author	Outcome
Decision tree (DT)	DWT with a range of temporal and spectral features	Khan & Saadeh [73]	Sensitivity: 95.4 %, Specificity: 97.7 % (CAD)
	FFT with a range of temporal and spectral features	Khan et al. [60]	79 % accuracy (CAD)
	FFT with SEF, beta ratio, and four bands of spectral energy (FBSE)	Saadeh et al. [44]	92.2 % accuracy (CAD)
Genetic algorithm SVM	Permutation and sample entropy, permutation Lempel-Ziv complexity measure (PLZC), DFA	Liang et al. [35]	92.3 % accuracy (CAD)
K-NN	Range of time-domain, spectral-domain, and entropy features.	Kashkooli et al. [30]	91 % accuracy (CAD)
	PSD features in each epoch. Max PSD and standard deviation of PSD	Nguyen-Ky et al. [74]	93 % accuracy (BIS mapping to DoA state)
	15-Channel EEG with gray-level co-occurrence matrix (GLCM)	Mousavi et al. [100]	95.32 % accuracy (BIS mapping to DoA state)
Logistic regression	Range (44) of time-domain, spectral-domain, and entropy features.	Ramaswamy et al. [42]	AUC = 0.83 (0.17) (CAD)
SVM	Atomic decomposition	Nagaraj et al. [39]	AUC = 0.9 (CAD)
	256-Channel EEG with occipital delta power and power spectrum density (PSD)	Casey et al. [23]	AUC = 0.622 (CAD)
	32-Channel EEG with directed coherence	Lioi et al. [36]	95 % accuracy (CAD)
	EEG and AEP with a range (10) of spectral-domain and entropy-domain features extracted.	Tacke et al. [63]	Prediction Probability = 0.935 (CAD)
Linear discriminant analysis	128-Channel EEG to generate brain topography based on common spatial pattern (CSP) features	Rimbert et al. [61]	Accuracy = 74 % (CAD)
Random Forrest classifier	19-Channel EEG with phasal relationship	Xiao et al. [102]	Accuracy = 93.88 % (based on 2 states, CAD)
	Range of time series features (63) extracted	Anand et al. [106]	Accuracy = 83 % (based on 2 states BIS)

Studies employing high-density EEG and advanced feature extraction methods, like functional connectivity, show promise but also underscore the challenges in interpreting complex EEG data. Xiao et al. [102] demonstrated the potential to create a brain connection network system by employing functional connectivity (FC) characteristic parameters of 19 channel EEG signals. Utilising graph theory features, including phase locking value and phase lag index, in conjunction with a random forest model, the researchers were able to assess the state of anaesthesia with an accuracy of 93.88 %.

In a 10-patient study, the graded changes in EEG directional connectivity relative to propofol effect-site concentrations were assessed. Using a 32-channel system and directed coherence feature extraction methods with an SVM classifier, 95 % accuracy was observed [36]. Tacke et al. [63] achieved a prediction probability of 0.935 with this modelling method utilising both EEG and auditory evoked potential (AEP) signals. Applying functional connectivity (FC) with SVM classification from 256-channel high-density EEG monitoring AUC 0.97 was observed [23]. The study identified that sensory disconnection was characterized by extensive spatial and spectral changes, whereas unconsciousness was typically marked by localised decreases in activity in the anterior and posterior cingulate cortices. A genetic SVM method achieved 92.3 % accuracy in estimating the DoA state based on clinical assessment when measured on a sample of 18 patients using single-channel EEG [35].

Logistic regression [42] and linear discriminant analysis (LDA) [95] for both regression and classifications were observed in the literature with varied effectiveness. The variability in the effectiveness of logistic regression and LDA suggests a need for more nuanced model selection and feature engineering strategies.

While these models show promise, their clinical relevance remains a subject for further investigation. The reliance on high-accuracy models in small-scale studies highlights a gap in current research methodologies. Some models, particularly those using high-dimensional feature sets, may be prone to overfitting, especially in studies with limited sample sizes. The applicability of these models in diverse clinical settings, considering factors like patient variability and different anaesthetic regimes, requires further assessment. Additionally, there is a need for real-time processing capabilities to make these models viable in clinical settings. Exploring hybrid models that combine the simplicity of linear regression with the accuracy of more complex models might also be a worthwhile direction. There is a critical need for larger-scale studies to validate these findings and for methodologies that can handle the complexity of EEG data while being applicable in diverse clinical settings.

4.2.2. Deep learning machine learning methods

Various model-building methods based on deep learning was present in recent literature. These methods have been employed to model the complex and non-linear relationships between EEG signals and the DoA based on EEG signal analysis. A new development in the DoA research space has involved the implementation of DL models with no discrete FE stages, instead, simply utilising the capacity of different DL algorithms for both FE and model building based on raw EEG signals (Table 4).

Deep learning models, such as artificial neural networks (ANN), can extract complex features from EEG signals and learn hierarchical representations, which can be instrumental in accurately determining the DoA [29]. This group of methods may require substantial data and computational resources and may prone to overfitting [107]. Alsafy & Diykh [49] achieved an average coefficient of determination of 0.965 using a DNN with a 15-patient study, indicating a strong predictive power of the model. The potential for overfitting must be critically evaluated in these models, especially in scenarios with limited training data. In classification models, the ANN achieved an accuracy of 89.2 % in clinical assessment of the DoA [90]. These results demonstrate the potential of ANNs and DNNs in providing accurate and reliable DoA estimation based on EEG signals.

Feed forward neural networks (FFNNs) and multilayer perceptron (MLP) demonstrate high effectiveness in estimating the DoA from raw EEG signals as observed with a correlation of 0.94 with the BIS [32]. When utilising SWT with a combination of features including fractal, spectral and non-linear features MLP regressor network achieved an accuracy of ∼97 % in the clinical assessment of the DoA [78,79] (Table 5).

Convolutional Neural Networks (CNN) excel at handling data with grid-like topology, such as image data, and can automatically and adaptively extract hierarchical features. However, they require substantial computational resources, posing challenges in some applications [111]. CNNs have been employed successfully as a classification method [43,109]. In a 50-patient study without a discreet feature extraction method, a CNN model achieved an average accuracy of 97.90 % [108]. When implemented on a broad range of features extracted following a wavelet transformation, a deep residual shrinkage network (DRSN) combined with a 1×1 convolution network reported a Spearman's rank correlation coefficient of 0.9344 (PSI), indicating a strong positive association [68]. However, the small patient sample size, ($n = 18$) suggests further investigation to ensure model generalisability in larger studies may be needed. A correlation of 0.872 with the perturbational complexity index (PCI) was found using a CNN model [33] that employed network and graph properties to analyse 60-channel EEG signals. The 3D EEG signal was initially transformed into 2D meshes based on spatial data and a 1D vector for temporal information.

Comparing CNNs with LSTM models, the latter's ability to effectively learn and remember long sequences is advantageous in utilising the temporal features of EEG signals. In a 56-patient, single-channel EEG study, long short-term memory (LSTM) modelling was observed to achieve a correlation of 0.70 and an area under the curve (AUC) of 0.93 based on the BIS [55] demonstrating the potential of this approach in temporal data analysis. For a two-state classification assessment of the DoA based on clinical assessment, LSTM modelling achieved an accuracy of 98.5 % [110]. These methods effectively learn and remember

Table 4
Deep learning model building methods for index design/regression.

Method	FE method	Author	Outcome
3-stage DNN: 1. CNN, 2. RNN	No FE	Afshar et al. [18]	$R^2 = 81.55$, Accuracy = 88.71 %. (BIS)
Artificial neural network	Hierarchical dispersion entropy (HDE) with WT	Alsafy & Diykh [49]	Average coefficient of determination = 0.965 (BIS)
	PEn with SEF	Gu et al. [29]	Correlation = 0.892 (BIS)
Feed Forward neural network	No FE	Lee et al. [32]	Correlation = 0.94 (BIS)
Long short-term memory	EEG variability and EEG analysis with a range of spectral-domain and entropy-domain features	Chen et al. [55]	Correlation = 0.70, AUC = 0.93 (BIS). Correlation = 0.80, AUC = 0.93 (CAD)
Convolutional neural network	60-Channel EEG with spatiotemporal dynamics	Lee et al. [33]	Correlation = 0.872 (perturbational complexity index)
Deep residual shrinkage network (DRSN) & 1×1 CNN	WT with 14 features extracted including SEF and Sample Entropy	Shi et al. [68]	Spearman's rank correlation coefficient = 0.9344 (PSI)

Table 5
Deep learning model building methods for classification.

Method	FE method	Author	Outcome
Adaptive neuro-fuzzy Inference system with linguistic hedges	Range (11) of spectral-domain and entropy-domain features including DFA	Shalbaf et al. [62]	Accuracy = 93 % (2 state CAD)
CNN	No FE	Ferreira et al. [108]	Accuracy = 97.90 %
		Liu et al. [37]	Accuracy = 93.50 % (CAD)
		AlMeer & Abbod [109]	Accuracy = 97 % (2 state CAD)
Long short-term memory (LSTM)	No FE	Gupta & Kalla [110]	Accuracy = 98.5 % (2 states CAD)
		Wang et al. [47]	Accuracy = 81.8 % (CAD)
	Range of spectral domain and entropy domain features	Li et al. [54]	Pk value of 0.8556 (Drug concentration)
Multilayer perceptron regressor network	Stationary wavelets transform (SWT) with fractal, non-linear and spectral features.	Dutt & Saadeh [78]	Accuracy = 96.8 % (CAD)
		Dutt & Saadeh [79]	Accuracy = 97.1 %, $R^2 = 0.9$, MAE = 1.5

over long sequences making use of the temporal features present in the EEG signal. A three-stage DNN without the need for FE demonstrated an r^2 of 0.82 [18] in a 176 patient study.

While deep learning models have shown promising results in DoA assessment, achieving high accuracy and correlation with BIS, their reliance on substantial datasets and computational resources poses a challenge. This highlights a trade-off between model complexity and practicality in clinical settings. Comparing the performance of deep learning models with traditional machine learning methods, it is evident that while deep learning models can achieve higher accuracy, they often require more complex feature extraction and larger datasets. This necessitates a careful consideration of the balance between accuracy and feasibility in clinical practice regarding operational requirements and the clinical workflow. The potential impact on clinical decision-making processes, particularly in real-time monitoring, needs further exploration. The diverse methodologies employed, from network and graph properties analysis to 3D EEG signal transformation, indicate a wide range of approaches within CNN applications. However, the varying degrees of correlation and accuracy across studies raise questions about the generalisability of these models to different patient groups and EEG signal types. Future research should explore ways to reduce the computational intensity of deep learning models without compromising their accuracy.

4.2.3. Multimodal monitoring of the DoA

Multimodal monitoring of the DoA represents a cutting-edge approach that integrates various physiological signals to provide a comprehensive and accurate assessment of a patient's anaesthetic state. By considering signals such as electrocardiogram (ECG) and near-infrared spectroscopy (NIRS) alongside EEG, clinicians can simultaneously evaluate the cardiac activity and cerebral oxygenation for association with the DoA. The following section outlines key innovations in the space of multimodal monitoring of DoA. For most methods presented, the concepts are in their infancy and represent high value features for implementation in future work.

HRV-derived features in the time and frequency domain combined with a deep neural network were able to classify the DoA state with an accuracy of 90.1 % in a 23-patient study [112]. The combination of EEG and ECG was able to predict interoperative events such as hypotension with an AUC of 0.935 based on 3-, 5-, 10- and 15-minute prediction windows [113]. The variations in the local regularity of EEG relative to HRV reflect the interaction of autonomic and central nervous system activities during anaesthesia [20]. Time-frequency ridge mapping applied to the combined information from joint EEG-ECG recordings on the same data set yielded strong classification results for the DoA states [114]. These features achieved a precision of 94.14 % and a prediction time of 0.28 s [19]. In a study of eighty patients, heart rate variability (HRV) was assessed using spectral analysis and short-term Detrended Fluctuation Analysis (DFAα1). It was found that light general anaesthesia increased short-term fractal correlations in heart rate dynamics, whereas deep general anaesthesia disrupted these fractal properties. This indicates that ECG-derived features could enhance existing EEG-based Depth of Anaesthesia (DoA) assessment methods [93].

The brain, while only 2.5 % of body weight, disproportionately consumes 20 % of the body's oxygen and receives 15 % of cardiac output. General anaesthesia reduces the brain's glucose and oxygen metabolic rates, observable via positron emission tomography. Anaesthetics also influence cerebral blood flow and the vascular responses in regions like the prefrontal cortex, measurable through changes in haemoglobin concentrations using NIRS techniques. Moreover, anaesthesia impacts neurovascular coupling—the relationship between neurons, support cells, and vascular cells—dampening the usual correlation between neuronal activation, metabolism, and local blood flow. Consequently, effective monitoring of brain oxygenation levels can distinguish anaesthetic states [115]. The sample entropy based on NIRS demonstrated statistical consistency between the BIS index during the complete anaesthesia process [116]. Brain oxygenation can be assessed noninvasively using near-infrared spectroscopy and has been associated with the DoA estimation in recent research [46,103,115,117]. The association between the phase-amplitude coupling of different frequency NIRS signals and the EEG signal are capable of effectively discriminating between the DoA states. It was found that the AUC of BIS was 0.9856 ± 0.0252, which was higher than that of Modulation Index (MI) (0.9760 ± 0.0143). Suggesting that MI is comparable to BIS in its ability to distinguish between the periods of anaesthesia maintenance and awake [103]. In addition, it is suggested that this technology could also be employed to gauge the autoregulation of cerebral blood flow, assisting in the individualised titration of arterial blood pressure, and enabling bedside diagnosis of disrupted autoregulation [118]. Ha et al. [117] proposes a multimodal head-patch system that represents innovation in the field by simultaneously measures EEGs and NIRS on the frontal lobe to improve the responsiveness and noise tolerance of the DoA monitoring devices. In a clinical trial, the combined signals of clinically important transition from the awake to deep state are observed that the BIS could not detect suggesting the viability of this multimodal index for further investigation.

Despite the slower dynamics associated with the calcium signal, there exists a strong correlation between EEG signal and two-photon signals obtained from the neuropil outside neuronal somata. These findings indicate that calcium signals alone may be sufficient to identify activity patterns like slow oscillations, and thereby evaluate the brain state and level of anaesthesia [119].

4.3. Evaluation and testing methods

A range of evaluation and performance metrics in both index and classification scenarios were present in the reviewed literature. Typically, classification evaluation methods were employed with comparisons to anaesthesiologist observations of the DoA states during the surgical procedure. A variety of metrics were employed to provide different perspectives on the performance of a classification model. The most popular classification evaluation metric observed in the literature was accuracy due to its simplicity and understandability. Additionally, the area under the receiver operating characteristic curve (AUC) provides a comprehensive view of the performance across thresholds and due to the information density of the AUC, it is considered the gold standard of evaluation metrics for this model type [120]. Prediction probability (PK) quantifies the ability of a predictive model to correctly classify two randomly chosen observations. It is typically chosen in the case of binary prediction or estimation. On the other hand, index or regression models were compared to known industry benchmarks, most often the BIS. Correlation, r, and coefficient of determination, r^2, assess the linear relationship between variables and were the most popular metrics used in these cases. The mean squared error (MSE) and root mean squared error (RMSE) quantify the differences between predicted and actual values and provide a measure of how well the model's predictions match the overall variation in the data. In general, these evaluation methods were employed during feature selection and were not often used to evaluate final models. In addition to these metrics, a range of visualisations were employed successfully to evaluate the performance of features and models. The most popular visualisation metrics employed were time-domain plot and scatter plots. Q-Q plots and Poincaré plots were used to explain feature associations and justify feature selections. Alternatively, heat maps are popular to convey information related to functional connectivity when observed with high-density EEG signals.

5. Limitations and future direction

In the evolving landscape of depth of anaesthesia (DoA) research, several limitations, and prospective research directions warrant attention. In the reviewed studies, most work uses single or dual-channel EEG data. The effect of functional connectivity and relational dynamics within brain chemistry is well known, and the limited signal source may represent a potential oversight of the nuanced spatial information that could be obtained from multiple channels. Even research employing high-density EEG often does not effectively utilise channel selection strategies to optimize the feature set for the DoA assessment. Future studies should prioritize the optimization of EEG channel selection, exploring the impact of utilising multi-channel data to capture the comprehensive spatial dynamics of brain activity during anaesthesia. A rigorous examination of channel selection methods, paralleling the current depth of feature selection, can enhance DoA indicator accuracy.

Additionally, to combat the issue of data source limitations, a concerted effort is needed to create a consortium for data sharing. This could involve establishing agreements between research institutions and private entities to standardize the sharing of EEG datasets. A multi-phased initiative could be developed, beginning with the creation of a shared database protocol, followed by the integration of diverse datasets from global sources to foster a more representative and robust body of data. Currently, a scant proportion of the literature—less than 20 %—indicates the availability of their datasets for public use or upon request. It is, therefore, a priority to bolster the sharing and transparency of research databases to facilitate effective comparison and validation of findings, leading to advancements in the field of EEG-based DoA analysis. Enhancing collaboration among data centres is pivotal for broadening access to diverse training and testing datasets, which is essential for the development of more sophisticated machine learning models. Such collaborative efforts should be aimed at improving the modelling and evaluation processes to ensure that the resulting models are robust and reliable across various patient demographics and anaesthetic types. An essential step in this direction includes the initiation of pilot studies to validate the efficacy of proposed models and the establishment of partnerships with clinical practitioners for real-world testing. Additionally, this work should account for the known limitations of current indices like BIS, aiming to either improve upon these standards or develop alternative metrics that could offer more reliable and comprehensive DoA assessments.

The current state of the DoA research often focuses on classification models that use limited states, such as ‘awake’, ‘light anaesthesia’, and ‘deep anaesthesia’. This approach may misrepresent the granularity of the DoA states and could potentially lead to misleading evaluation metrics. The complexity of anaesthetic states is not discrete but exists on a continuum. Some of the most novel developments in the DoA research in the reviewed work were for classification models. In response to the limitation of existing DoA classification models, future research should embrace the development of more sophisticated algorithms. These should be capable of identifying a wider spectrum of anaesthetic states, moving beyond binary or ternary classifications to incorporate multi-class or continuous output models. This nuanced approach will require the establishment of new evaluation metrics that consider the continuum of DoA states, potentially redefining industry standards. Effective development of new models should consider both the detail of continuous models based on industry standard indexes and the meaningfulness of classification models based on clinical assessment of anaesthesia.

Additionally, a notable gap in the existing literature is in the development of the DoA prediction algorithms. This area holds particular interest for anaesthetists and clinicians, as forecasting the DoA states based on EEG and other vital signs could offer substantial benefits to patient care. Future research should focus on predictive analytics. Such studies should integrate multimodal data analysis, combining EEG signals with other physiological parameters to develop predictive models. This calls for the adoption of advanced machine learning techniques and cross-disciplinary collaboration to refine predictive accuracy and clinical utility.

In summary, the future trajectory of DoA research should be characterized by an integrated approach that includes optimizing EEG channel selection strategies, expanding, and standardizing data sources, refining classification models to more accurately reflect the DoA continuum, and advancing the development of predictive algorithms. Addressing these focus areas will significantly contribute to the precision and clinical relevance of DoA assessments, with the goal of enhancing patient outcomes in anaesthetic care.

6. Conclusion

The effective and comprehensive monitoring of anaesthetic state is crucial for effective patient management during surgery. In this review paper, we review the state-of-the-art anaesthesia monitoring methodologies with a principle focus on EEG signal analysis techniques. These methods can be categorised into three principal stages: feature extraction, model building, and evaluation. The feature extraction stage often employs signal decomposition techniques such as Fourier or wavelet transformation methods. Notably, the extraction of complexity and entropy features has emerged as significant due to its reliability and computational efficiency. Traditional model building methods such as linear regression and SVMs persist in their popularity due to their simplicity and transparency. These methods highlight the effectiveness of novel feature extraction methods employed. While these models show promise, their clinical relevance remains a subject for further investigation. The reliance on high-accuracy models in small-scale studies highlights a gap in current research methodologies. Some models, particularly those using high-dimensional feature sets, may be prone to overfitting, especially in studies with limited sample sizes. Specifically, models employing complex, high-dimensional features are at risk of overfitting, a concern amplified in research with constrained sample sizes.

It was apparent that with the advancement of deep learning techniques and artificial intelligence a shift towards integrating these advanced techniques with existing feature extraction methods is leading to great improvements in model’s quality and robustness. Furthermore, with the growing ability of machine learning algorithms to manage increasingly complex data, the analysis of high-dimensional signals using networks and graph theory is gaining further prominence. When assessing deep learning models against traditional machine learning approaches, it becomes clear that although deep learning can yield more accurate results, it typically demands more elaborate feature extraction and extensive datasets. This situation calls for a judicious balance between achieving high accuracy and maintaining practical feasibility in clinical settings. Future developments are anticipated to refine and integrate these methods with established feature extraction techniques, enhancing the effectiveness of DoA estimation indices.

Moving forward, research in DoA should adopt a holistic approach, encompassing the optimization of EEG channel selection, broadening and standardizing data sources, and refining classification models for a more precise representation of the DoA spectrum. Additionally, the progression of predictive algorithms will be crucial. Concentrating on these key areas is expected to substantially enhance the accuracy and clinical applicability of DoA evaluations, ultimately aiming to improve patient outcomes in anaesthesia management.

In summary, this paper reviews, evaluates and classifies the leading DoA analysis methods with an emphasis on the recent studies in this research area. The insights from this review not only shed light on the current landscape of the DoA analyses but also highlight promising avenues for future research and innovation in this critical aspect of anaesthetic research.

CRediT authorship contribution statement

Thomas Schmierer: Conceptualization, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Tianning Li:** Supervision, Writing – review & editing. **Yan Li:** Supervision, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] Bowdle A, "Can We Prevent Recall During Anesthesia?," in *Evidence-Based Practice of Anesthesiology*, 2022, pp. 309–315.

[2] Chew WZ, Teoh WY, Sivanesan N, Loh PS, Shariffuddin, II, Ti LK, *et al.* "Bispectral index (BIS) monitoring and postoperative delirium in elderly patients undergoing surgery: a systematic review and Meta-analysis with trial sequential analysis," (in eng), J Cardiothorac Vasc Anesth, vol. 36, no. 12, pp. 4449–4459, Dec 2022, doi: doi:https://doi.org/10.1053/j.jvca.2022.07.004.

[3] Chan MTV, Hedrick TL, Egan TD, García PS, Koch S, Purdon PL, et al. American Society for Enhanced Recovery and Perioperative Quality Initiative Joint Consensus Statement on the role of Neuromonitoring in perioperative outcomes: electroencephalography. Anesthesia and Analgesia, Article 2020;130(5): 1278–91. https://doi.org/10.1213/ANE.0000000000004502.

[4] Berger M, Eleswarpu SS, Cooter Wright M, Ray AM, Wingfield SA, Heflin MT, *et al.* "developing a real-time electroencephalogram-guided anesthesia-management curriculum for educating residents: a single-center randomized controlled trial," (in eng), Anesth Analg, vol. 134, no. 1, pp. 159–170, Jan 1 2022, doi: doi:https://doi.org/10.1213/ane.0000000000005677.

[5] Shander A, Lobel GP, Mathews DM. Brain monitoring and the depth of anesthesia: another goldilocks dilemma. Anesthesia and Analgesia, Article 2018;126(2): 705–9. https://doi.org/10.1213/ANE.0000000000002383.

[6] Nsugbe E, Connelly S. Multiscale depth of anaesthesia prediction for surgery using frontal cortex electroencephalography. Healthcare Technology Letters 2022;9(3):43–53.

[7] Schmierer T, Li T, Li Y. "A novel empirical wavelet SODP and spectral entropy based index for assessing the depth of anaesthesia," *Health Information Science and Systems,* Article vol. 10, no. 1, 2022, Art no. 10, doi: doi:https://doi.org/10.1007/s13755-022-00178-8.

[8] Lee KH, Egan TD, Johnson KB. "raw and processed electroencephalography in modern anesthesia practice: a brief primer on select clinical applications," (in eng), Korean J Anesthesiol, vol. 74, no. 6, pp. 465–477, Dec 2021, doi: doi:https://doi.org/10.4097/kja.21349.

[9] Lobo FA, Saraiva AP, Nardiello I, Brandão J, Osborn IP. Electroencephalogram monitoring in anesthesia practice. Current Anesthesiology Reports, Review 2021; 11(3):169–80. https://doi.org/10.1007/s40140-021-00461-6.

[10] Eagleman SL, Drover CM, Li X, MacIver MB, Drover DR. "offline comparison of processed electroencephalogram monitors for anaesthetic-induced electroencephalogram changes in older adults," *BJA: the*. Br J Anaesth 2021;126 (5):975–84. https://doi.org/10.1016/j.bja.2020.12.042.

[11] Zhan J, Yi T-T, Wu Z-X, Long Z-H, Bao X-H, Xiao X-D, *et al.* "A survey of current practices, attitudes and demands of anaesthesiologists regarding the depth of anaesthesia monitoring in China," BMC Anesthesiol, vol. 21, no. 1, p. 294, 2021/11/23 2021, doi: doi:https://doi.org/10.1186/s12871-021-01510-7.

[12] Obert DP, Schweizer C, Zinn S, Kratzer S, Hight D, Sleigh J, et al. The influence of age on EEG-based anaesthesia indices. J Clin Anesth 2021;73. https://doi.org/10.1016/j.jclinane.2021.110325 [pp. N.PAG-N.PAG].

[13] Al-Kadi MI, Reaz MBI, Ali MAM. Evolution of electroencephalogram signal analysis techniques during anesthesia. Sensors 2013;13(5):6605–35.

[14] Biggs D, Boncompte G, Pedemonte JC, Fuentes C, Cortinez LI. The effect of age on electroencephalogram measures of anesthesia hypnosis: a comparison of BIS, alpha power, Lempel-Ziv complexity and permutation entropy during propofol induction. Front Aging Neurosci 2022;14:1–9. https://doi.org/10.3389/fnagi.2022.910886.

[15] Hajat Z, Ahmad N, Andrzejowski J. The role and limitations of EEG-based depth of anaesthesia monitoring in theatres and intensive care. Anaesthesia 2017;72: 38–47.

[16] Li T-N, Li Y. Depth of anaesthesia monitors and the latest algorithms. Asian Pac J Trop Med 2014;7(6):429–37.

[17] Hashimoto DA, Witkowski E, Gao L, Meireles O, Rosman G. Artificial intelligence in anesthesiology: current techniques, clinical applications, and limitations. Anesthesiology 2020;132(2):379–94.

[18] Afshar S, Boostani R, Sanei S. "a combinatorial deep learning structure for precise depth of anesthesia estimation from EEG signals," (in eng), IEEE J Biomed Health Inform, vol. 25, no. 9, pp. 3408–3415, Sep 2021, doi: doi:https://doi.org/10.1109/jbhi.2021.3068481.

[19] Bahador N, Kortelainen J. "a robust bimodal index reflecting relative dynamics of EEG and HRV with application in monitoring depth of anesthesia," (in eng). IEEE Trans Neural Syst Rehabil Eng 2021;29:2503–10. https://doi.org/10.1109/tnsre.2021.3128620.

[20] Bahador N, Jokelainen J, Mustola S, Kortelainen J. Multimodal spatio-temporal-spectral fusion for deep learning applications in physiological time series processing: a case study in monitoring the depth of anesthesia. Information Fusion, Article 2021;73:125–43. https://doi.org/10.1016/j.inffus.2021.03.001.

[21] Baron Shahaf D, Hare GMT, Baker AJ, Chenosia V, Priven L, Mistry N, *et al.* "A new index of coordinated posterior and anterior evoked EEG to detect recall under sedation - a pilot study," (in eng), *Sci Rep,* vol. 9, no. 1, p. 17859, Nov 28 2019, doi: doi:https://doi.org/10.1038/s41598-019-54270-3.

[22] Boncompte G, Medel V, Cortínez LI, Ossandón T. "brain activity complexity has a nonlinear relation to the level of propofol sedation," (in eng), Br J Anaesth, vol. 127, no. 2, pp. 254–263, Aug 2021, doi: doi:https://doi.org/10.1016/j.bja.2021.04.023.

[23] Casey CP, Tanabe S, Farahbakhsh Z, Parker M, Bo A, White M, et al. "distinct EEG signatures differentiate unconsciousness and disconnection during anaesthesia and sleep," *BJA: the*. Br J Anaesth 2022;128(6):1006–18. https://doi.org/10.1016/j.bja.2022.01.010.

[24] Dong K, Zhang D, Wei Q, Wang G, Huang F, Chen X, *et al.* "intrinsic phase-amplitude coupling on multiple spatial scales during the loss and recovery of consciousness," (in eng), Comput Biol Med, vol. 147, p. 105687, Aug 2022, doi: doi:https://doi.org/10.1016/j.compbiomed.2022.105687.

[25] Dong H, Li N, Sun Z. "the effect of anesthesia depth on radiofrequency catheter ablation of ventricular tachycardia: a retrospective study," (in eng), BMC Anesthesiol, vol. 21, no. 1, p. 285, Nov 15 2021, doi: doi:https://doi.org/10.1186/s12871-021-01503-6.

[26] Dong K, Wei Q, Zhang D, Zhang L, Wang G, Chen X, et al. Recovery of brain network integration and segregation during the loss and recovery of consciousness induced by sevoflurane. IEEE Transactions on Neural Systems and Rehabilitation Engineering, Article 2023;31:304–15. https://doi.org/10.1109/TNSRE.2022.3221965.

[27] Dong K, Zhang D, Wei Q, Wang G, Chen X, Zhang L, *et al.* "an integrated information theory index using multichannel EEG for evaluating various states of consciousness under anesthesia," (in eng), Comput Biol Med, vol. 153, p. 106480, Feb 2023, doi: doi:https://doi.org/10.1016/j.compbiomed.2022.106480.

[28] Dong K, Zhang D, Wei Q, Wang G, Huang F, Chen X, "Intrinsic phase–amplitude coupling on multiple spatial scales during the loss and recovery of consciousness," Computers in Biology and Medicine, Article vol. 147, et al. Art no. 2022:105687. https://doi.org/10.1016/j.compbiomed.2022.105687.

[29] Gu Y, Liang Z, Hagihira S. "Use of Multiple EEG Features and Artificial Neural Network to Monitor the Depth of Anesthesia," (in eng), *Sensors (Basel),* vol. 19, no. 11, May 31 2019, doi: doi:https://doi.org/10.3390/s19112499.

[30] Kashkooli K, Polk SL, Hahm EY, Murphy J, Ethridge BR, Gitlin J, *et al.* "improved tracking of sevoflurane anesthetic states with drug-specific machine learning models," (in eng), J Neural Eng, vol. 17, no. 4, p. 046020, Aug 4 2020, doi: doi: https://doi.org/10.1088/1741-2552/ab98da.

[31] Lapointe AP, Li D, Hudetz AG, Vlisides PE. "microstate analyses as an indicator of anesthesia-induced unconsciousness," (in eng), Clin Neurophysiol, vol. 147, pp. 81–87, Mar 2023, doi: doi:https://doi.org/10.1016/j.clinph.2023.01.007.

[32] Lee HC, Ryu HG, Chung EJ, Jung CW. Prediction of bispectral index during target-controlled infusion of propofol and remifentanil. Anesthesiology, Article 2018;128(3):492–501. https://doi.org/10.1097/ALN.0000000000001892.

[33] Lee M, Sanz LRD, Barra A, Wolff A, Nieminen JO, Boly M, *et al.* "Quantifying arousal and awareness in altered states of consciousness using interpretable deep learning," (in eng), *Nat Commun,* vol. 13, no. 1, p. 1064, Feb 25 2022, doi: doi:https://doi.org/10.1038/s41467-022-28451-0.

[34] Li F, Li Y, Zheng H, Jiang L, Gao D, Li C, et al. "identification of the general anesthesia induced loss of consciousness by cross fuzzy entropy-based brain network," (in eng). IEEE Trans Neural Syst Rehabil Eng 2021;29:2281–91. https://doi.org/10.1109/tnsre.2021.3123696.

[35] Liang Z, Shao S, Lv Z, Li D, Sleigh JW, Li X, *et al.* "constructing a consciousness meter based on the combination of non-linear measurements and genetic algorithm-based support vector machine," (in eng), IEEE Trans Neural Syst Rehabil Eng, vol. 28, no. 2, pp. 399–408, Feb 2020, doi: doi:https://doi.org/10.1109/tnsre.2020.2964819.

[36] Lioi G, Bell SL, Smith DC, Simpson DM. Measuring depth of anaesthesia using changes in directional connectivity: a comparison with auditory middle latency response and estimated bispectral index during propofol anaesthesia. Anaesthesia 2019;74(3):321–32. https://doi.org/10.1111/anae.14535.

[37] Liu Q, Cai J, Fan SZ, Abbod MF, Shieh JS, Kung Y, "Spectrum Analysis of EEG Signals Using CNN to Model Patient's Consciousness Level Based on Anesthesiologists' Experience," IEEE Access, Article vol. 7, pp. 53731-53742, et al. Art no. 2019:8695791. https://doi.org/10.1109/ACCESS.2019.2912273.

[38] Liu Z, Si L, Xu W, Zhang K, Wang Q, Chen B, et al. "characteristics of EEG microstate sequences during Propofol-induced alterations of brain consciousness states," (in eng). IEEE Trans Neural Syst Rehabil Eng 2022;30:1631–41. https://doi.org/10.1109/tnsre.2022.3182705.

[39] Nagaraj SB, McClain LM, Boyle EJ, Zhou DW, Ramaswamy SM, Biswal S, *et al.* "Electroencephalogram Based Detection of Deep Sedation in ICU Patients Using Atomic Decomposition," *IEEE Transactions on Biomedical Engineering,* Article vol. 65, no. 12, pp. 2684–2691, 2018, Art no. 8307456, doi: doi:https://doi.org/10.1109/TBME.2018.2813265.

[40] Patlatzoglou K, Chennu S, Boly M, Noirhomme Q, Bonhomme V, Brichant JF, *et al. Deep neural networks for automatic classification of anesthetic-induced unconsciousness, International Conference on Brain Informatics, BI* 2018, vol. 11309 LNAI, pp. 216–225, 2018.

[41] Ra JS, Li T, Li Y. "a novel spectral entropy-based index for assessing the depth of anaesthesia," (in eng), *brain* Inform, vol. 8, no. 1, p. 10, May 12 2021, doi: doi:https://doi.org/10.1186/s40708-021-00130-8.

[42] Ramaswamy SM, Kuizenga MH, Weerink MAS, Vereecke HEM, Struys M, Nagaraj SB. "Novel drug-independent sedation level estimation based on machine learning of quantitative frontal electroencephalogram features in healthy volunteers," (in eng), Br J Anaesth, vol. 123, no. 4, pp. 479–487, Oct 2019, doi: doi:https://doi.org/10.1016/j.bja.2019.06.004.

[43] Roy Chowdhury M, Madanu R, Abbod MF, Fan SZ, Shieh JS. "Deep learning via ECG and PPG signals for prediction of depth of anesthesia," Biomedical Signal

Processing and Control, Article vol. 68. Art no. 2021:102663. https://doi.org/10.1016/j.bspc.2021.102663.

[44] Saadeh W, Khan FH, Altaf MAB. "design and implementation of a machine learning based EEG processor for accurate estimation of depth of anesthesia," (in eng), IEEE Trans Biomed Circuits Syst, vol. 13, no. 4, pp. 658–669, Aug 2019, doi: doi:https://doi.org/10.1109/tbcas.2019.2921875.

[45] Thiery T, Lajnef T, Combrisson E, Dehgan A, Rainville P, Mashour GA, *et al.* "Long-range temporal correlations in the brain distinguish conscious wakefulness from induced unconsciousness," (in eng), Neuroimage, vol. 179, pp. 30–39, Oct 1 2018, doi: doi:https://doi.org/10.1016/j.neuroimage.2018.05.069.

[46] Vijayakrishnan Nair V, Kish BR, Yang HCS, Yu Z, Guo H, Tong Y, et al. Monitoring anesthesia using simultaneous functional near infrared spectroscopy and electroencephalography. Clinical Neurophysiology, Article 2021;132(7): 1636–46. https://doi.org/10.1016/j.clinph.2021.03.025.

[47] Wang Q, Liu F, Wan G, Chen Y. "inference of brain states under anesthesia with Meta learning based deep learning models," (in eng). IEEE Trans Neural Syst Rehabil Eng 2022;30:1081–91. https://doi.org/10.1109/tnsre.2022.3166517.

[48] Zhang W, Yu H, Duan Z, Yu T, Li X. Anesthesia depth evaluation algorithm based on permutation and combination entropy. Neural Computing and Applications, Article 2022;34(9):6647–60. https://doi.org/10.1007/s00521-021-06030-6.

[49] Alsafy I, Diykh M. "developing a robust model to predict depth of anesthesia from single channel EEG signal," (in eng), Phys Eng Sci Med, vol. 45, no. 3, pp. 793–808, Sep 2022, doi: doi:https://doi.org/10.1007/s13246-022-01145-z.

[50] Diykh M, Li Y, Wen P, Li T. "complex networks approach for depth of anesthesia assessment," *measurement: journal of the international measurement confederation*. Article 2018;119:178–89. https://doi.org/10.1016/j.measurement.2018.01.024.

[51] Haghighi SJ, Komeili M, Hatzinakos D, Beheiry HE. "40-Hz ASSR for measuring depth of Anaesthesia during induction phase," (in eng), IEEE J Biomed Health Inform, vol. 22, no. 6, pp. 1871–1882, Nov 2018, doi: doi:https://doi.org/10.1109/jbhi.2017.2778140.

[52] Huang Y, Wen P, Song B, Li Y. "Real-Time Depth of Anaesthesia Assessment Based on Hybrid Statistical Features of EEG," (in eng), *Sensors (Basel),* vol. 22, no. 16, Aug 15 2022, doi: doi:https://doi.org/10.3390/s22166099.

[53] Chavez M, Grosselin F, Bussalb A, De Vico Fallani F, Navarro-Sune X. Surrogate-based artifact removal from single-channel EEG. IEEE Transactions on Neural Systems and Rehabilitation Engineering, Article 2018;26(3):540–50. https://doi.org/10.1109/TNSRE.2018.2794184.

[54] Li R, Wu Q, Liu J, Wu Q, Li C, Zhao Q. "monitoring depth of anesthesia based on hybrid features and recurrent neural network," (in eng). Front Neurosci 2020;14: 26. https://doi.org/10.3389/fnins.2020.00026.

[55] Chen YF, Fan SZ, Abbod MF, Shieh JS, Zhang M. "Nonlinear Analysis of Electroencephalogram Variability as a Measure of the Depth of Anesthesia," IEEE Transactions on Instrumentation and Measurement, Article vol. 71. Art no. 2022: 4004413. https://doi.org/10.1109/TIM.2022.3167793.

[56] Chowdhury MH, Eldaly ABM, Agadagba SK, Cheung RCC, Chan LLH. "machine learning based hardware architecture for DOA measurement from mice EEG," (in eng), IEEE Trans Biomed Eng, vol. 69, no. 1, pp. 314–324, Jan 2022, doi: doi:https://doi.org/10.1109/tbme.2021.3093037.

[57] Schmierer T, Li T, Li Y. "a novel empirical wavelet SODP and spectral entropy based index for assessing the depth of anaesthesia," (in eng), Health Inf Sci Syst, vol. 10, no. 1, p. 10, Dec 2022, doi: doi:https://doi.org/10.1007/s13755-022-00178-8.

[58] García PS, Kreuzer M, Hight D, Sleigh JW. "effects of noxious stimulation on the electroencephalogram during general anaesthesia: a narrative review and approach to analgesic titration," *BJA: the*. Br J Anaesth 2021;126(2):445–57. https://doi.org/10.1016/j.bja.2020.10.036.

[59] Kashkooli K, Polk SL, Chamadia S, Hahm E, Ethridge B, Gitlin J, *et al.* "drug-specific models improve the performance of an EEG-based automated brain-state prediction system," in *41st annual international conference of the IEEE engineering in medicine and biology society, EMBC* 2019, 2019, pp. 5808–5811, doi: https://doi.org/10.1109/EMBC.2019.8856935.

[60] Khan FH, Ashraf U, Bin Altaf MA, Saadeh W. "a patient-specific machine learning based EEG processor for accurate estimation of depth of anesthesia," in *2018 IEEE biomedical circuits and systems conference*. BioCAS 2018;2018. https://doi.org/10.1109/BIOCAS.2018.8584828.

[61] Rimbert S, Guerci P, Gayraud N, Meistelman C, Bougrain L. "Innovative brain-computer interface based on motor cortex activity to detect accidental awareness during general anesthesia," in *2019 IEEE International Conference on Systems, Man and Cybernetics, SMC 2019*, 2019, vol. 2019-October, pp. 3931–3936, doi: https://doi.org/10.1109/SMC.2019.8914666.

[62] Shalbaf A, Saffar M, Sleigh JW, Shalbaf R. "monitoring the depth of anesthesia using a new adaptive Neurofuzzy system," (in eng), IEEE J Biomed Health Inform, vol. 22, no. 3, pp. 671–677, May 2018, doi: doi:https://doi.org/10.1109/jbhi.2017.2709841.

[63] Tacke M, Kochs EF, Mueller M, Kramer S, Jordan D, Schneider G. "machine learning for a combined electroencephalographic anesthesia index to detect awareness under anesthesia," (in eng). PloS One 2020;15(8):e0238249. https://doi.org/10.1371/journal.pone.0238249.

[64] Adam E, Kwon O, Montejo KA, Brown EN. Modulatory dynamics mark the transition between anesthetic states of unconsciousness. Proceedings of the National Academy of Sciences of the United States of America, Article 2023;120 (30):e2300058120. https://doi.org/10.1073/pnas.2300058120.

[65] Zakaria L, Desowska A, Berde CB, Cornelissen L. Electroencephalographic delta and alpha oscillations reveal phase-amplitude coupling in paediatric patients undergoing sevoflurane-based general anaesthesia. British Journal of Anaesthesia, Article 2023;130(5):595–602. https://doi.org/10.1016/j.bja.2023.01.025.

[66] Park SH, Jung IY, Shin HC. "spectral asymmetry of EEG signals in transition from conscious to unconscious state," in *9th international conference on information and communication technology convergence, ICTC* 2018, 2018, pp. 963–966, doi: https://doi.org/10.1109/ICTC.2018.8539628.

[68] Shi M, Huang Z, Xiao G, Xu B, Ren Q, Zhao H. "Estimating the depth of anesthesia from EEG signals based on a deep residual shrinkage Network," (in eng), *Sensors (Basel),* vol. 23, no. 2, Jan 15 2023, doi: doi:https://doi.org/10.3390/s23021008.

[69] Chen YF, Fan SZ, Abbod MF, Shieh JS, Zhang M. "electroencephalogram variability analysis for monitoring depth of anesthesia," (in eng), J Neural Eng, vol. 18, no. 6, Nov 17 2021, doi: doi:https://doi.org/10.1088/1741-2552/ac3316.

[70] Choi HI, Noh GJ, Shin HC. "Measuring the Depth of Anesthesia Using Ordinal Power Spectral Density of Electroencephalogram," IEEE Access, Article vol. 8, pp. 50431-50438. Art no. 2020:9034018. https://doi.org/10.1109/ACCESS.2020.2980370.

[71] Mahanna-Gabrielli E, Schenning KJ, Eriksson LI, Browndyke JN, Wright CB, Culley DJ, *et al.* "state of the clinical science of perioperative brain health: report from the American Society of Anesthesiologists Brain Health Initiative Summit 2018," (in eng), Br J Anaesth, vol. 123, no. 4, pp. 464–478, Oct 2019, doi: doi:https://doi.org/10.1016/j.bja.2019.07.004.

[72] Diykh M, Miften FS, Abdulla S, Saleh K, Green JH. Robust approach to depth of anaesthesia assessment based on hybrid transform and statistical features. IET Science, Measurement and Technology, Article 2020;14(1):128–36. https://doi.org/10.1049/iet-smt.2018.5393.

[73] Khan FH, Saadeh W. "An EEG-Based Hypnotic State Monitor for Patients during General Anesthesia," *IEEE Transactions on Very Large Scale Integration (VLSI) Systems,* Article vol. 29, no. 5, pp. 950–961, 2021, Art no. 9360837, doi: doi:https://doi.org/10.1109/TVLSI.2021.3058047.

[74] Nguyen-Ky T, Tuan HD, Savkin A, Do MN, Van NTT. "real-time EEG signal classification for monitoring and predicting the transition between different Anaesthetic states," (in eng), IEEE Trans Biomed Eng, vol. 68, no. 5, pp. 1450–1458, May 2021, doi: doi:https://doi.org/10.1109/tbme.2021.3053019.

[75] Altes J, Valencia JF, Jaramillo S, Gambes PL. "prediction model of response to standardized painful stimulation during general anesthesia: applying machine learning to the EEG signal," in *2021 IEEE symposium series on computational intelligence*. SSCI 2021;2021. https://doi.org/10.1109/SSCI50451.2021.9660114.

[76] Guo C, Yu J, Wu L, Liu Y, Jia C, Xie Y. "Analysis and feature extraction of EEG signals induced by anesthesia monitoring based on wavelet transform," IEEE Access, Article vol. 7, pp. 41565-41575. Art no. 2019:8675269. https://doi.org/10.1109/ACCESS.2019.2907794.

[77] Dutt MI, Saadeh W. "a multilayer perceptron (MLP) Regressor network for monitoring the depth of anesthesia," in *20th IEEE international interregional NEWCAS conference*. NEWCAS 2022;2022:251–5. https://doi.org/10.1109/NEWCAS52662.2022.9842242.

[78] Dutt MI, Saadeh W. "An Accurate EEG-based Deep Learning Classifier for Monitoring Depth of Anesthesia," in *2022 IEEE International Symposium on Circuits and Systems, ISCAS 2022*, 2022, vol. 2022-May, pp. 1768-1772, doi: https://doi.org/10.1109/ISCAS48785.2022.9937408.

[79] Dutt MI, Saadeh W. Monitoring level of hypnosis using stationary wavelet transform and singular value decomposition entropy with feedforward neural network. IEEE Transactions on Neural Systems and Rehabilitation Engineering, Article 2023;31:1963–73. https://doi.org/10.1109/TNSRE.2023.3264797.

[80] Abel JH, Badgeley MA, Baum TE, Chakravarty S, Purdon PL, Brown EN. "Constructing a control-ready model of EEG signal during general anesthesia in humans," in *21st IFAC World Congress 2020*, 2020, vol. 53, 2 ed., pp. 15870–15876, doi: https://doi.org/10.1016/j.ifacol.2020.12.243.

[81] Idzhilova OS, Smirnov IV, Malyshev AY. Detection of spontaneous action potentials in extracellular recordings of visual cortex neurons using eeg predictors for a machine learning-based approach. Opera Medica et Physiologica, Article 2021;8(3):5–11. https://doi.org/10.24412/2500-2295-2021-3-5-11.

[82] Yeom SK, Kim HJ, Seo KS, Kim HJ, Lee SW. "EEG-based classification of consciousness during sedation using global spectra principal components," in *4th Asian conference on pattern recognition, ACPR* 2017, 2018, pp. 804–809, doi: https://doi.org/10.1109/ACPR.2017.57.

[83] De Faria W, Schamberg G, Brown EN. "classifying EEG of Propofol-induced unconsciousness in the presence of burst suppression," in *2020 IEEE MIT undergraduate research technology conference*. URTC 2020;2020. https://doi.org/10.1109/URTC51696.2020.9668878.

[84] Dubost C, Humbert P, Benizri A, Tourtier JP, Vayatis N, Vidal PP. "selection of the best Electroencephalogram Channel to predict the depth of anesthesia," (in eng). Front Comput Neurosci 2019;13:65. https://doi.org/10.3389/fncom.2019.00065.

[85] Dora M, Holcman D. "adaptive Single-Channel EEG artifact removal with applications to clinical monitoring," (in eng). IEEE Trans Neural Syst Rehabil Eng 2022;30:286–95. https://doi.org/10.1109/tnsre.2022.3147072.

[86] Liu Q, Chen Y-F, Fan S-Z, Abbod M, Shieh J-S, Abbod MF. EEG artifacts reduction by multivariate empirical mode decomposition and multiscale entropy for monitoring depth of anaesthesia during surgery. Med Biol Eng Comput 2017;55 (8):1435–50. https://doi.org/10.1007/s11517-016-1598-2.

[87] Li T, Sivakumar P, Tao X. *Anesthesia Assessment Based on ICA Permutation Entropy Analysis of Two-Channel EEG Signals, 12th International Conference on Brain Informatics, BI* 2019, vol. 11976 LNAI, pp. 244–253, 2019.

[88] Hight D, Obert DP, Kratzer S, Schneider G, Sepulveda P, Sleigh J, et al. Permutation entropy is not an age-independent parameter for EEG-based

anesthesia monitoring. Front Aging Neurosci 2023;15:1173304. https://doi.org/10.3389/fnagi.2023.1173304.
[89] Wang G, Liu Z, Feng Y, Li J, Dong H, Wang D, *et al.* "monitoring the depth of anesthesia through the use of cerebral hemodynamic measurements based on sample entropy algorithm," (in eng), IEEE Trans Biomed Eng, vol. 67, no. 3, pp. 807–816, Mar 2020, doi: doi:https://doi.org/10.1109/tbme.2019.2921362.
[90] Hosseini SA, Naghibi-Sistani MB. A computationally bio-inspired framework of brain activities based on cognitive processes for estimating the depth of anesthesia. Australasian Physical and Engineering Sciences in Medicine, Article 2019;42(2):465–80. https://doi.org/10.1007/s13246-019-00743-8.
[91] Tosun PD, Abásolo D, Stenson G, Winsky-Sommerer R. "Characterisation of the Effects of Sleep Deprivation on the Electroencephalogram Using Permutation Lempel–Ziv Complexity, a Non-Linear Analysis Tool," Entropy, vol. 19, no. 12, p. 673, 2017. [Online]. Available: https://www.mdpi.com/1099-4300/19/12/673.
[92] Chen X, Wen P. "a novel real-time depth of Anaesthesia monitoring method using Detrended fluctuation analysis and ANN," in *5th international conference on biomedical signal and image processing*. ICBIP 2020;2020:86–92. https://doi.org/10.1145/3417519.3419403.
[93] Lan JY, Shieh JS, Yeh JR, Fan SZ. "Fractal Properties of Heart Rate Dynamics: A New Biomarker for Anesthesia—Biphasic Changes in General Anesthesia and Decrease in Spinal Anesthesia," *Sensors,* Article vol. 22, no. 23, 2022, Art no. 9258, doi: doi:https://doi.org/10.3390/s22239258.
[94] Sai CY, Mokhtar N, Yip HW, Bak LLM, Hasan MS, Arof H, *et al.* "Objective identification of pain due to uterine contraction during the first stage of labour using continuous EEG signals and SVM," *Sadhana - Academy Proceedings in Engineering Sciences,* Article vol. 44, no. 4, 2019, Art no. 87, doi: doi:https://doi.org/10.1007/s12046-019-1058-4.
[95] Nsugbe E, Connelly S. "multiscale depth of anaesthesia prediction for surgery using frontal cortex electroencephalography," (in eng), Healthc Technol Lett, vol. 9, no. 3, pp. 43–53, Jun 2022, doi: doi:https://doi.org/10.1049/htl2.12025.
[96] Kashkooli K, Polk SL, Chamadia S, Hahm E, Ethridge B, Gitlin J, *et al.* "drug-specific models improve the performance of an EEG-based automated brain-state prediction system," (in eng), Annu Int Conf IEEE Eng Med Biol Soc, vol. 2019, pp. 5808–5811, Jul 2019, doi: doi:https://doi.org/10.1109/embc.2019.8856935.
[98] Ramaswamy SM, Kuizenga MH, Weerink MAS, Vereecke HEM, Struys MMRF, Belur Nagaraj S. Frontal electroencephalogram based drug, sex, and age independent sedation level prediction using non-linear machine learning algorithms. Journal of Clinical Monitoring and Computing, Article 2022;36(1):121–30. https://doi.org/10.1007/s10877-020-00627-3.
[99] Bi H, Cao S, Yan H, Jiang Z, Zhang J, Zou L. "resting state functional connectivity analysis during general anesthesia: a high-density EEG study," (in eng), IEEE/ACM Trans Comput Biol Bioinform, vol. 19, no. 1, pp. 3–13, Jan-Feb 2022, doi: doi:https://doi.org/10.1109/tcbb.2021.3091000.
[100] Mousavi SM, Asgharzadeh-Bonab A, Ranjbarzadeh R. "time-frequency analysis of EEG signals and GLCM features for depth of anesthesia monitoring," (in eng). Comput Intell Neurosci 2021;2021:8430565. https://doi.org/10.1155/2021/8430565.
[101] Si L, Liu Z, Wang G. "depth of anesthesia monitoring method based on EEG microstate analysis and hidden Markov model," in *2nd IEEE international conference on pattern recognition and machine learning*. PRML 2021;2021:298–303. https://doi.org/10.1109/PRML52754.2021.9520709.
[102] Xiao Z, Xu Z, Ma L. *Construction of Complex Brain Network Based on EEG Signals and Evaluation of General Anesthesia Status, 15th International Conference on Intelligent Robotics and Applications, ICIRA* 2022, vol. 13456 LNAI, pp. 747–759, 2022.
[103] Liu Z, Si L, Li J, Zhu J, Lee WH, Chen B, et al. Monitoring the depth of anesthesia based on phase-amplitude coupling of near-infrared spectroscopy signals. IEEE Transactions on Neural Systems and Rehabilitation Engineering, Article 2023;31:2849–57. https://doi.org/10.1109/TNSRE.2023.3289183.
[104] Sanjari N, Shalbaf A, Shalbaf R, Sleigh J. "assessment of anesthesia depth using effective brain connectivity based on transfer entropy on EEG signal," (in eng), *basic* Clin Neurosci, vol. 12, no. 2, pp. 269–280, Mar-Apr 2021, doi: doi:10.32598/bcn.12.2.2034.2.
[106] Anand RV, Abbod MF, Fan SZ, Shieh JS. "Depth Analysis of Anesthesia Using EEG Signals via Time Series Feature Extraction and Machine Learning," *Sci,* Article vol. 5, no. 2, 2023, Art no. 19, doi: doi:https://doi.org/10.3390/sci5020019.
[107] Srivastava N, Hinton G, Krizhevsky A, Sutskever I, Salakhutdinov R. Dropout: a simple way to prevent neural networks from overfitting. The journal of machine learning research 2014;15(1):1929–58.
[108] Ferreira AL, Vide S, Nunes CS, Neto J, Amorim P, Mendes J. Implementation of neural networks to frontal electroencephalography for the identification of the transition responsiveness/unresponsiveness during induction of general anesthesia. IRBM, Article 2021;42(5):390–7. https://doi.org/10.1016/j.irbm.2021.02.004.
[109] AlMeer MH, Abbod MF. *Deep learning in classifying depth of anesthesia (DoA), Intelligent Systems Conference, IntelliSys* 2018, vol. 868, pp. 160–169, 2018.
[110] Gupta H, Kalla S. "analysis of Micro state EEG signals through RNN classification," in *3rd IEEE international virtual conference on innovations in power and advanced computing technologies, i-PACT 2021*. 2021. https://doi.org/10.1109/i-PACT52855.2021.9696981.
[111] Krizhevsky A, Sutskever I, Hinton GE. Imagenet classification with deep convolutional neural networks. Advances in neural information processing systems 2012;25.
[112] Zhan J, Wu Z-x, Duan Z-x, Yang G-y, Du Z-y, Bao X-h, et al. Heart rate variability-derived features based on deep neural network for distinguishing different anaesthesia states. BMC Anesthesiol 2021;21(1):1–11. https://doi.org/10.1186/s12871-021-01285-x.
[113] Jo YY, Jang JH, Kwon JM, Lee HC, Jung CW, Byun S, et al. "predicting intraoperative hypotension using deep learning with waveforms of arterial blood pressure, electroencephalogram, and electrocardiogram: retrospective study," (in eng). PloS One 2022;17(8):e0272055. https://doi.org/10.1371/journal.pone.0272055.
[114] Boashash B. Time-frequency signal analysis and processing: A comprehensive reference. Academic press; 2015.
[115] Wang G, Yan X, Liu Z, Feng Y, Li J, Dong H, *et al.* "Monitoring the Depth of Anesthesia through the Use of Cerebral Hemodynamic Measurements Based on Sample Entropy Algorithm," *IEEE Transactions on Biomedical Engineering,* Article vol. 67, no. 3, pp. 807–816, 2020, Art no. 8732458, doi: doi:https://doi.org/10.1109/TBME.2019.2921362.
[116] !!! INVALID CITATION !!! (G. Wang, Liu, et al., 2020).
[117] Ha U, Lee J, Kim M, Roh T, Choi S, Yoo HJ. An EEG-NIRS multimodal SoC for accurate anesthesia depth monitoring. IEEE Journal of Solid-State Circuits, Article 2018;53(6):1830–43. https://doi.org/10.1109/JSSC.2018.2810213.
[118] Scheeren TWL, Kuizenga MH, Maurer H, Struys MMRF, Heringlake M. Electroencephalography and brain oxygenation monitoring in the perioperative period. Anesthesia and Analgesia, Article 2019;128(2):265–77. https://doi.org/10.1213/ANE.0000000000002812.
[119] Tort-Colet N, Resta F, Montagni E, Pavone F, Allegra Mascaro AL, Destexhe A. "Assessing brain state and anesthesia level with two-photon calcium signals," *Scientific Reports,* Article vol. 13, no. 1, 2023, Art no 3183, doi: doi:https://doi.org/10.1038/s41598-023-30224-8.
[120] Jaskowiak PA, Costa IG, Campello RJGB. "The area under the ROC curve as a measure of clustering quality," Data Mining and Knowledge Discovery, vol. 36, no. 3, pp. 1219–1245, 2022/05/01 2022, doi: doi:https://doi.org/10.1007/s10618-022-00829-0.