Identification of Patient Ventilator Asynchrony in Physiological Data Through Integrating Machine-Learning

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Abstract: Patient Ventilator Asynchrony (PVA) occurs where a mechanical ventilator aiding a patient's breathing falls out of synchronisation with their breathing pattern. This de-synchronisation may cause patient distress and can lead to long-term negative clinical outcomes. Research into the causes and possible mitigations of PVA is currently conducted by clinical domain experts using manual methods, such as parsing entire sleep hypnograms visually, and identifying and tagging instances of PVA that they find. This process is very labour-intensive and can be error prone. This project aims to make this analysis more efficient, by using machine-learning approaches to automatically parse, classify, and suggest instances of PVA for ultimate confirmation by domain experts. The solution has been developed based on a retrospective dataset of intervention and control patients that were recruited to a non-invasive ventilation study. This achieves a specificity metric of over 90%. This paper describes the process of integrating the output of the machine learning into the bedside clinical monitoring system for production use in anticipation of a future clinical trial.

1 INTRODUCTION

Patient Ventilator Asynchrony (PVA) occurs where a mechanical ventilator assisting a patient's breathing falls out of synchronisation with their intrinsic breathing pattern. This de-synchronisation may result in patient discomfort and can lead to long-term negative clinical outcomes. Three types of PVA that have been demonstrated to impact on a patients during non-invasive ventilation (NIV): 1) ineffective effort - where the patient tries to take a breath, but this effort fails to register with the ventilator, and it does not provide the necessary support; 2) autocycle – a small period of volatility where the patient takes several breaths in quick succession and the ventilator fails to respond to the rapid behaviour; 3) double trigger - where the patient has taken two breaths, one of which the ventilator fails to register (Hannan et al, 2019).

It has been shown that frequent PVA events during both invasive- and non-invasive ventilation can lead to many adverse consequences for a patient, ranging from reduced sleep quality to more serious outcomes such as lung injury, and an increased ICU and hospital mortality rate (Brochard et al, 2014). It is a significant burden on a variety of different patient cohorts, such as those with specific conditions like motor neuron disease (MND) or obesity

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hypoventilation syndrome (OHS), but also severely affecting those with more general chronic respiratory failure. This group forms a significant percentage of the global population.

Current practice to research and understand PVA events includes clinical domain experts manually assessing entire sleep hypnograms, along with electroencephalogram (EEG) and physiological output channels. For a single patient stay, this is often of the order of several hours of data, with a resolution of nanoseconds in some instances. The identification of PVA events such as ineffective efforts, requires a combination analysis of (for instance) the mask pressure output (*"pmask"*) channel along with signs of volatility in the EEG.

Technology used to tackle such problems at present includes integrated tools, which present all the information in one visual space that is convenient and optimised for clinical use. An example of this is the use of the *CompuMedics* sleep monitoring software (Compumedics ProFusion, Abbotsford Australia) that directly connects to the output from the ventilator. However, despite the presence of this integrated solution, given the relative frequency of events against the time resolution described, this process is highly labour-intensive and prone to error. With recent advances in artificial intelligence and machine-learning, it is clearly a process that would benefit from automated optimisation. Therefore, this project aims to integrate a machine-learning algorithm that can automate the process of PVA detection and provide clinical decision-support in the form of suggestions of PVA event labels. These can then be confirmed or rejected by the clinical domain experts.

Several challenges in this work exist, which form the basis of this paper. They include:

- integration of all data channels in an open format supporting proprietary software such as *CompuMedics*;
- reliance on hardware-accelerated processors to fully exploit machine-learning algorithms;
- the need for specialist software libraries;
- the need to maximise memory efficiency when choosing the software environment and deciding on the system architecture;
- time-sampling factors such as down-sampling of the machine learning output and the unit choices of the EDF file specification, and finally,
- the choice of presentation combined with the operation of the algorithm to maximise the utility for the clinical end-users.

2 BACKGROUND LITERATURE

Two interdisciplinary work threads have combined to lead to the development of this work: one clinical and the other from information and data science. The clinical arm of this interdisciplinary group provided the basis for this work through a randomised-controlled trial that they had conducted previously, where NIV was titrated with nocturnal polysomnography (one of the first ever controlled trials of this intervention) (Hannan, et al, 2019). One of the primary findings of this study was that polysomnography assisted optimization NIV titration resulted in increased NIV usage (hours per night), and an association was observed between fewer PVA events and increased usage. In certain patient cohorts, such as those living with motor neurone disease, cohort evidence suggests that increased usage (adherence to therapy) leads to a significant increase in long-term survival (Berlowitz, et al, 2021).

2.1 PVA and NIV

Some independent software solutions to the issue of detecting and mitigating PVA have been proposed (Dres et al, 2021), but there is a general lack of validation for these approaches and they still require intensive effort to fully implement. Other studies have focused on the storage of raw data on a long-term basis (Janssens et al., 2015; Rabec et al., 2009) but without estimations of signals and interpretation, the utility of these tools have also yet to be determined. This leads to an opportunity to explore algorithmically-centered solutions integrated with targeted software modules (as presented here).

Non-invasive ventilation (NIV) is a therapeutic method used to provide respiratory support to individuals with breathing difficulties without the need for invasive procedures such as endotracheal intubation. It delivers positive airway pressure to help keep the airways open and assist with breathing. It typically involves continuous monitoring to assess the effectiveness and the patient's response to treatment. There are different techniques used for NIV monitoring including capnography, which monitors patient's exhaled carbon dioxide (CO2) levels.

A unique way of monitoring that captures the interaction of patient and ventilator during nocturnal use is polygraphy or polysomnography (PSG). It is used in the context of sleep-related disorders, where NIV can be titrated and monitored using polysomnography. While ventilators normally only provide readings such as mask pressure, PSG can record various physiological parameters including airflow, chest and abdominal movement (Gao, et al, 2021). Such data can help identify and classify PVA events including Ineffective Effort (IE), Double Trigger (DT) and Autocycle (AC).

A randomised controlled trial conducted by (Hannan et al, 2019) suggested that using PSG to titrate NIV therapy can lead to better alignment between the patient's breathing patterns and the ventilator's settings, but it may not reduce sleep disruption. The data collected in this trial comprised information from a cohort of 58 participants, primarily individuals diagnosed with neuromuscular disorders, all of whom were receiving NIV support including the use of PSG titration.

2.2 Machine-Learning Approaches

A key unique aspect of the clinical work outlined in this paper is that it has been performed during non-invasive ventilation. This is a novel and ground-breaking approach. Previous attempts at PVA detection by other groups have always been performed during invasive ventilation, usually in an intensive care-unit. Therefore, when comparing against other ML approaches to PVA detection, in the invasive ventilation situation the available signals are easier to detect as the system is closed, not open, and thus inherently less noisy. It is in this context that other ML approaches should be considered.

Zhang et al. (2020) proposed a novel method using a two-layer neural network to detect the most frequent types of PVA, resulting in the detection of double triggering (DT) and ineffective inspiratory effort (IIE). According to the study, it was shown that ML-based approaches based on a robust database (159 patients were included) could assist in PVA recognition for clinicians.

Adams et al. (2017) explored the ventMAP platform with focus on types of double-trigger and breath stacking PVA. The algorithm proposed was rule-based, using pressure and airflow signals, including both a derivation and a validation cohort. They obtained a performance of 92.2-97.7% on the validation cohort. The algorithm helped in detecting harmful forms of off-target ventilation in critical patients.

The method developed by (Bakkes et al., 2020) provided new insights for PVA. The study conducted showed that the algorithm could detect and classify types of PVA obtaining a precision average of 97.7%. However, the study also emphasised the need for inclusion of different network architectures to address the necessary robustness of detection methods. It should be noted that both algorithms (Adams et al., 2017; Bakkes et al., 2020) faced different challenges related to the data collection. Data labelling in the (Bakkes et al, 2020) study was made by one expert only, which led to an increase in the error margin of the results. The platform ventMAP was capable of obtaining a robust amount of data, however when conducting the development and translation of the output data into clinical applications, there were a wide range of implementation issues (Adams et al., 2017).

Another approach in the PVA field has been the use of ensemble machine learning classifiers, e.g., (Rehm et al., 2018). The results suggest that high-performing ML-based models are capable of producing well-specified outputs despite the presence of clinical artefacts. Therefore, the methodology used serves as a helpful framework to guide classification of such events.

3 METHODOLOGY

Considering the range of methods in the area, the use of a data-driven approach has been embraced. (Wang et al., 2022) proposed the use of several similarity and randomness measures. This approach underpins this paper, and specifically using variants of the matrix profile (MP) algorithm. They achieved encouraging results for detecting suspected PVA with a high percentage test recall (90%+) among the reported outputs. As a potential improvement on this technique, the extension of similarity-based methods to supervised nearest-neighbour search and including techniques for ineffective effort detection has also been considered here.

3.1 ML Algorithm

We extend Wang's work (Wang et al, 2022) using an algorithm that detects contiguous repeating patterns in signals even with rhythm changes. This allows for detection of abnormal changes, as well as segmentation and feature analysis of the signals. Follow-up models based on this algorithm have been trained on an annotated non-invasive ventilation waveform dataset, which gives a specificity and sensitivity of over 90% in the context of detecting auto-triggering events from noisy waveform data.

In the first instance, the practical measure of the ML metric is simply the scalar number value representing how volatile the different input channels are (therefore, it is likely that a PVA event occurs near a spike in the ML metric). However, a further future refinement to this is to analyse the shape of the ML output and classify the type of anomaly based on that shape.

The automated method to flag the anomalous output is also based on several channels rather than manually aligning and determining a PVA presence based on the disjoint evaluation of each, which is necessary when conducting the inspection manually. The four primary channels used in the work are the pressure mask (*pmask*), abdominal (*abdo*) and thoracic (*thor*) respiratory inductance bands, and flow as output form the NIV device (*flow-tx*). This multiple channel feature is particularly useful in cases such as ineffective efforts, which would not necessarily show up on a single channel but could still be present.

3.2 Software Implementation

To integrate the output for the machine-learning algorithm, an open-source format – the European Data Format (EDF) specification (www.edfplus.info) – has been chosen for data representation and manipulation, not only because of the standardised structure and well-supported open-source community, but also to allow the portability of the output across different platforms. This open format supports the extraction in a standardised structure – of both scored labels and free-text comments, which have been added manually into the integrated bedside system. It enforces a degree of structure on data offering critical contextual data during a monitored patient sleep. Such data is usually openly structured and difficult to report in a standard way. Both scored labels and free text annotations also present a heterogeneity challenge in that there is no standardized input approach. This effect is amplified when there is more than one clinician involved in data entry.

Therefore, the first step in producing the EDF file with additional ML-output channel, is to extract the original EDF file from the integrated bedside clinical monitoring system, in this case *CompuMedics*, with one EDF file per patient per stay. The meta-data outlining the annotations accompanying that patient stay are captured in the associated XML descriptor file.

Once the original EDF has been extracted, the full data integrity of that file is checked and written to another newly created EDF file. This new file is composed of the original physiological channels chosen by the user with the addition of new channels containing the ML-generated output.

This is achieved using the python library *pyedflib*, which is a fork from the library *EDFlib* (www.teuniz.net). These libraries are used to read the EDF file's properties and values including: number of signals, channel indexes, sample frequency, and number of data records. The physiological channels are then read into this library for pre-processing, in anticipation of processing by the ML algorithm. For ease of persistent data storage, and to ease the burden of volatile memory requirements, intermediate files are written as part of these pre-processing steps. These are stored in the Apache Parquet file format (parquet.apache.org) - an open source, column-oriented data file format, which uses in-built compression for efficient data storage and retrieval.

The output of the parquet files is then fed into the ML algorithm. The operation of the algorithm involves many dependencies in both software and hardware including:

- A memory-efficient version of the Anaconda Python environment, known as **MambaForge** (mamba.readthedocs.io), which provides a setting that maximises the available underlying memory to run the memory-intensive ML algorithm.
- A library called **Signatory** that allows the calculation of a "signature transform", an operation roughly analogous to a Fourier transform that extracts information on the order and area of a given data stream.
- Underlying **GPU acceleration** at a hardware level, requiring the activation of an NVIDIA processor (if available). In this project the Azure cloud resource provides a VM within the "NC series" that provides an NVIDIA GeForce RTX 3090 chip with 24 GiB

Using this software stack, once the algorithm is fully computed, it is stored in a multi-dimensional *numpy* array type, which the EDF file format and libraries use heavily for functional operation. An anomaly list is successively generated from the *numpy* array, and this list is iterated over to produce a sub-set of values where the ML metric has gone over a user-supplied threshold number. This new subset array is written to the same output EDF file but in the form of point annotations.

In terms of timing, for each down-sampled window, a corresponding value is produced (measured in the arbitrary units of "ML-P"), along with a corresponding timing value. This timing value can be configured to be situated in the window at the beginning (value 0), the end (value 1), the middle (value 0.5), or any point in between. Due to the down-sampling of the output by a factor of 16, the ML output is rendered at a sample frequency of 2 Hz, when combined with the *pmask* output in the final

EDF. This is due to the *pmask* output having a frequency of 32 Hz (so when divided by 16, the final frequency is 2 Hz). This output is written to the final EDF using a pre-prepared buffer array of double values, written to the file at repeat intervals governed by that sample frequency. The sample frequency itself varies according to channel and this is set at the original point of first extraction of that channel from the bedside system.

The EDF file itself is then rendered using open-source tools that are freely available, again mainly supported by the work of Teuniz van Beelen (www.teuniz.net). The most popular option is *EDFBrowser*, which provides standard tools to operate and manipulate EDF files, such as varying timescale, amplitude, window, and video playback/recording. *EDFBrowser* is not entirely portable across the main consumer operating systems – for instance, installation on MacOS requires detailed configuration that is a non-trivial task for an average computer user. Therefore, an alternative is the *Polyman* application (sites.google.com/view/diegoalvarezestevez/projects/polyman), which has similar tools but less visual depth when rendering.

4 RESULTS

The presentation of the ML output was rendered using *EDFBrowser* (figures 1 and 2).

Figure 1 shows the overall output when compared between the machine-learning output (the green line) and the entire output of a *pmask* channel for a 9.5 hour patient stay (the yellow line, solid due to the high resolution viewed from overall timepoint).

As can be seen, the highest points in the ML output correspond to the largest variations in the overall output of the *pmask* channel. In physical terms, this most likely relates to the initial period where the mask was not yet fitted to the patient, and a period of adjustment that occurred midway through the sleep.

From a clinical perspective, it is often the case that the smaller, more subtle, variations in the ML output are more useful. These are the “needle in a haystack” points that the application is being used to identify, rather than the large-scale volatility that can be most easily seen on first viewing (though this helps to validate that the ML output is in fact correctly reflecting a valid physiological output). Therefore, Figure 2 shows how the ML output looks when compared against individual events in the physiological channel, in this case one of the primary PVA events: an ineffective effort.

Figure 2 also shows the annotations that are also included in the output EDF file. These include a combination of the threshold crossing notes (a threshold of 4 was chosen for this exploration), as well as the scored labels and free-text comments extracted from the original EDF file. The high number of these mean that the filtering tools available through *EDFBrowser* needs to be used to meaningfully navigate the EDF file and identify points of interest in the readout (in *EDFBrowser*, the list on the right of the window interactively corresponds to the dashed line markers that span both outputs).

5 DISCUSSION

There were a variety of issues that were encountered when attempting to bring this implementation to a production level. Many of those issues were due to the interactions between uniquely-specified software and hardware requirements that often led to unpredictable interactions.

The *Signatory* library could only be run reliably when executed on the Linux Ubuntu 22.04 operating system. Portability across other operating systems could not be guaranteed due, for instance, due to the incompatibility with the Clang C-compiler, which ships as standard on most MacOS versions.

Similarly, the Conda (Anaconda) Python environment was required to set up and run the dependency list to support the requirements for the machine learning solution. However, due to the extensive memory requirements, the larger scale *MambaForge* environment was required. There are a variety of flavours of this environment, which again constrained the stack upon which the execution could be performed.

The *Pytorch* library version – required to support the complex functions of the *Signatory* library - varied depending on whether the GPU or CPU environment was available for execution. This variation in itself created conflicting dependency and version issues, which would need to be tightly controlled before run-time, due to the need to understand the particular hardware environment.

Overall, these issues could be grouped as the requirement of pinned software versions along with libraries without consolidated community support, which is often a necessary feature of leading-edge research.

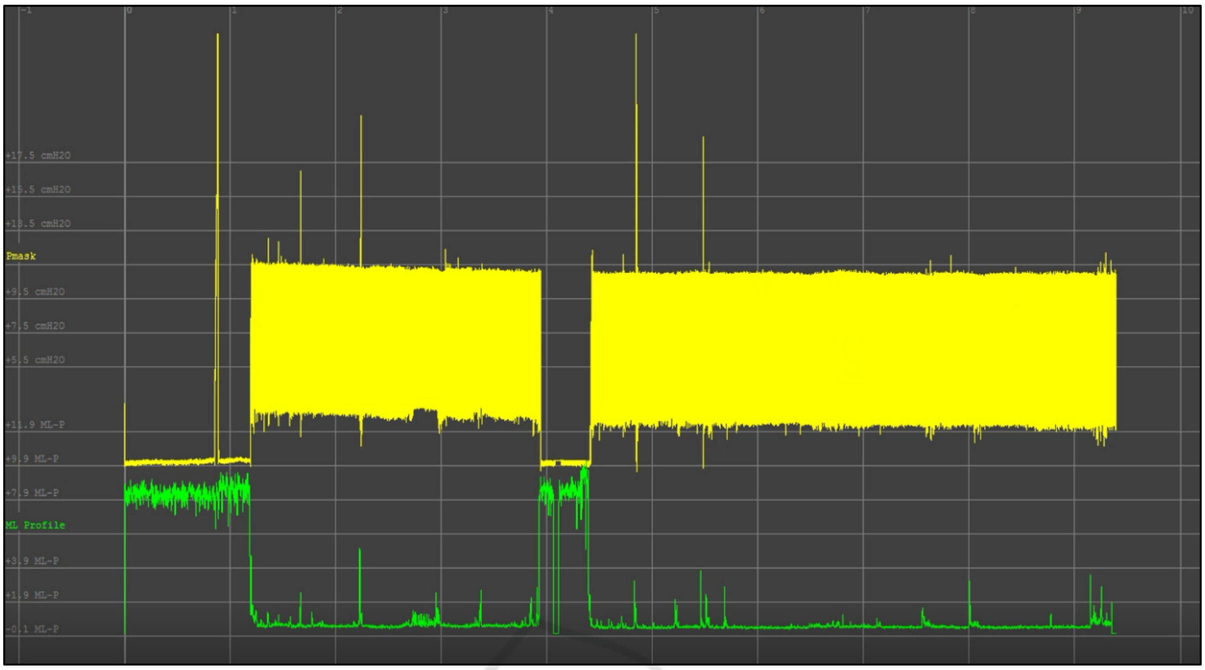


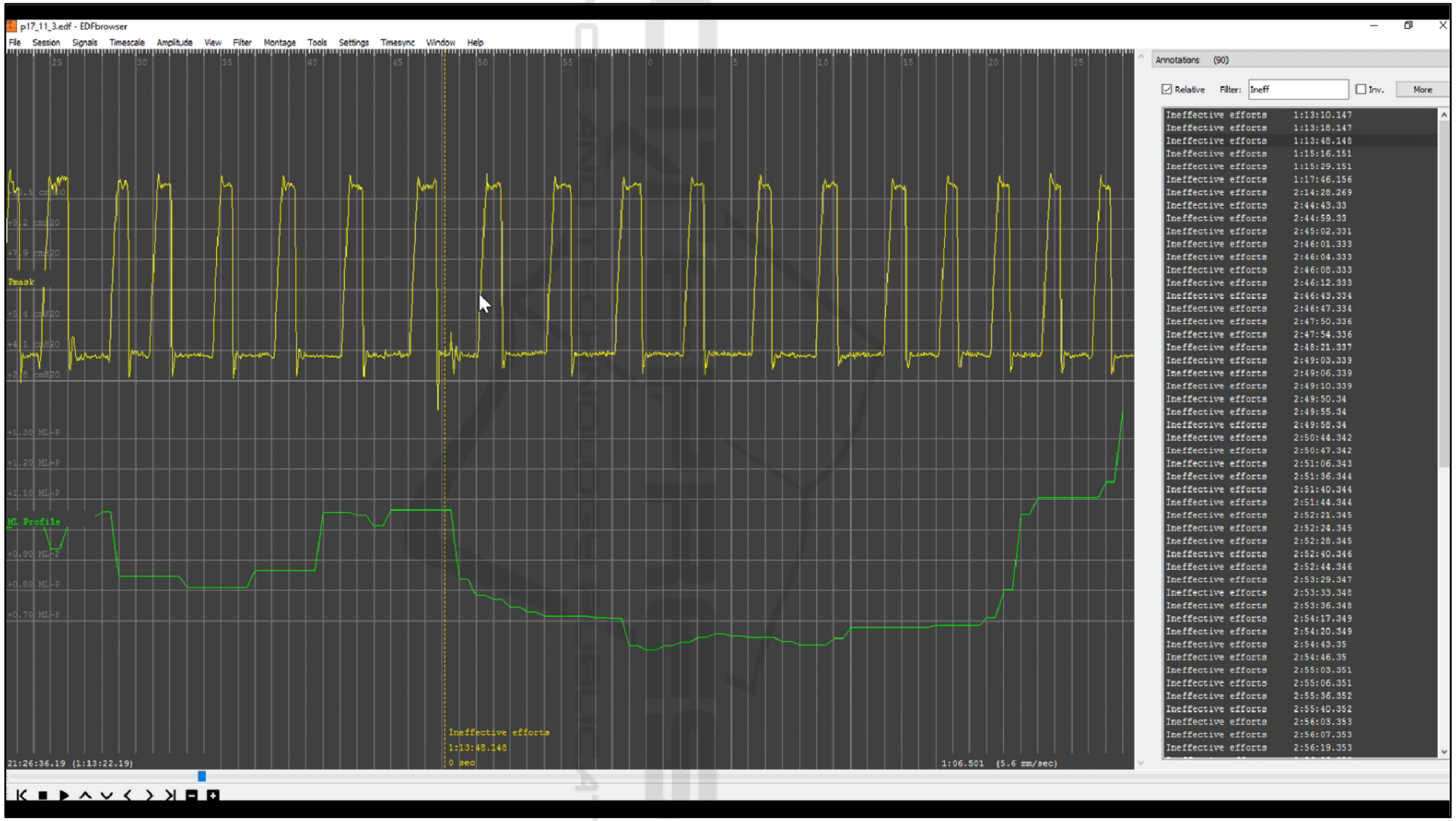
Figure 1: Overall monitored patient sleep, covering 9.5 hours. The large periods of volatility in the ML output (green) correspond to aspects of the physiological output (yellow) which are highly differentiated from the majority of that output.

GPU requirements were also extensive, with a minimum benchmark of 24 GiB in the "NC series" of Azure VMs, required to execute the application on an NVIDIA GeForce RTX 3090 processor. This was required so that the calculation could be run over a feasible timescale. There was a *batch_size* variable, specifying the size of batches of data for processing, which acted as an in-code handle and supported the calculation accuracy and controlled the execution time. But when this went over 10^6 (the minimum requirement for sufficient accuracy), the calculation time began to run to hours on a regular CPU platform.

However, again these are considerations that are not uncommon in advanced ML approaches and will inevitably become less problematic as processor powers increase and execution speeds decrease. This also has an impact on the cost-effectiveness of the solution, e.g., does the cost of using such high-end resources outweigh the cost of employing skilled workers to manually detect PVA, and at what is the trade off in accuracy? Such a cost-benefit exercise would be a next logical step in evaluation of this technology, repeated at various time intervals as the underlying hardware improves.

Output timings were also a factor that require further consideration. Due to the down-sampling of output windows, some manipulation of the annotation and ML output points was required, with a "stretching factor" of 1.97 eventually settled upon. This was also reflected in clinician feedback, where the annotation indicating threshold crossing did not directly line up with the corresponding point in the physiological output, but rather it occupied a window, pre-determined by the down-sampling rate. Though a concern, it was noted that time was only one of several factors that may have had an impact on the system stability. Other factors such as the topography of the ML output may influence the readout and allow a classification of the type and presence of a given instability. This could also help in identifying low-resolution events, not immediately drawn out when considering timing alone.

Finally, the idea of optimal presentation should be considered. To express the output in the open-source EDF format was a deliberate choice to promote portability and accessibility. When taken to further validation and downstream studies, the user-interface considerations should be evaluated, and would ultimately likely compete in terms of integration with the *in-situ* bedside monitoring systems. If this requires direct integration with the software vendor solution this could become a block to further development unless intellectual property and collaborative agreements are negotiated.



Annotations (90)

☑ Relative Filter: Ineff □ Inv. More

```
Ineffective efforts    1:13:10.147
Ineffective efforts    1:13:18.147
Ineffective efforts    1:13:48.148
Ineffective efforts    1:15:16.151
Ineffective efforts    1:15:29.151
Ineffective efforts    1:17:46.156
Ineffective efforts    2:14:28.269
Ineffective efforts    2:44:43.33
Ineffective efforts    2:44:59.33
Ineffective efforts    2:45:02.331
Ineffective efforts    2:46:01.333
Ineffective efforts    2:46:04.333
Ineffective efforts    2:46:08.333
Ineffective efforts    2:46:12.333
Ineffective efforts    2:46:43.334
Ineffective efforts    2:46:47.334
Ineffective efforts    2:47:50.336
Ineffective efforts    2:47:54.336
Ineffective efforts    2:48:21.337
Ineffective efforts    2:49:03.339
Ineffective efforts    2:49:06.339
Ineffective efforts    2:49:10.339
Ineffective efforts    2:49:50.34
Ineffective efforts    2:49:55.34
Ineffective efforts    2:49:58.34
Ineffective efforts    2:50:44.342
Ineffective efforts    2:50:47.342
Ineffective efforts    2:51:06.343
Ineffective efforts    2:51:36.344
Ineffective efforts    2:51:40.344
Ineffective efforts    2:51:44.344
Ineffective efforts    2:52:21.345
Ineffective efforts    2:52:24.345
Ineffective efforts    2:52:28.345
Ineffective efforts    2:52:40.346
Ineffective efforts    2:52:44.346
Ineffective efforts    2:53:29.347
Ineffective efforts    2:53:33.348
Ineffective efforts    2:53:36.348
Ineffective efforts    2:54:17.349
Ineffective efforts    2:54:20.349
Ineffective efforts    2:54:43.35
Ineffective efforts    2:54:46.35
Ineffective efforts    2:55:03.351
Ineffective efforts    2:55:06.351
Ineffective efforts    2:55:36.352
Ineffective efforts    2:55:40.352
Ineffective efforts    2:56:03.353
Ineffective efforts    2:56:07.353
Ineffective efforts    2:56:19.353
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Figure 2: This shows an example event of interest (an ineffective effort). The ML output corresponds to a higher-than-normal spike in volatility, and the broken vertical line indicates that the annotation lining up in time with an effort that failed to register and receive the necessary support.

6 CONCLUSIONS

In this paper, the implementation details of the integration of a machine-learning algorithm to detect PVA events, into a production version of a bedside clinical environment has been presented. The functional operation has been shown demonstrating how the automated detection of ineffective efforts, autocycles and double triggers can be achieved. We also discuss the challenges encountered during the work.

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