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Build a neuro-fuzzy continuous protocol representation for ventilator adjustments in acute respiratory distress syndrome patients using fuzzy neural network.

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Abstract—Acute respiratory distress syndrome (ARDS) is on the increase due to many causes such as: corona virus disease 2019 (COVID-19) which worsens the arterial hypoxemia, smoke inhalation, and injuries that cause fluids to collect in the air sacs of the lungs. Standard clinical criteria have been developed to define ARDS severity, while titration protocols guide ventilator settings. The Berlin definition protocol classifies ARDS diagnostic severity based on the PaO_2/FiO_2 ratio, whereas positive end-expiratory pressure (PEEP) titration is guided by the ARDS Network (ARDSNet) lower and higher PEEP scales. The challenges that however come with physicians manually implementing discrete lookup tables include step-discontinuities at threshold boundaries, performance accuracy, and timely intervention. With the increasing number of patients in the intensive care unit (ICU), physicians may be overwhelmed with the workload, that they may not efficiently control the parameters on the mechanical ventilation. Any slight change or delay in setting the parameters may lead to wrong outcomes. Therefore, the aim of this study was to apply artificial intelligence in guiding physicians during the process of setting ventilator parameters. Fuzzy neural network (FNN) was used in training and conversion of the non-fuzzified ARDSNet PEEP titration tables into a fuzzified continuous inference surface. In this computational study, model performance was evaluated using 5-fold cross-validation and tested on unseen intermediate FiO_2 setpoints ($FiO_2 \in \{0.35, 0.45, 0.55, 0.65, 0.75, 0.85, 0.95\}$), achieving a validation Root Mean Squared Error (RMSE) of 0.018 cm H₂O, Mean Absolute Error (MAE) of 0.012 cm H₂O, and $R^2 = 0.9998$. The results show that the output of the fuzzified ARDSNet PEEP model is very accurate in comparison with non-fuzzified tables while eliminating abrupt step changes between FiO_2 increments. Comparative analysis demonstrates that ANFIS provides smooth C^1 -continuous parameter transitions without the boundary slope discontinuities of linear interpolation or the overshoot oscillations of cubic splines. The potential for reduced clinician workload and error reduction represents a hypothesis for future prospective clinical trials.

Index Terms—Ventilation, COVID-19, ARDS, Berlin definition, ARDSNet, PEEP titration, FNN, ANFIS, continuous interpolation.

I. INTRODUCTION

Patients with acute respiratory distress syndrome (ARDS) are affected by the fluids that collect in the lungs. Though authors have emphasized the need of equipping the physicians with knowledge on how the mechanical ventilators (MV) work and generally how to treat patients who need MV [1], [13], [14], there is still need of more physicians and yet there are few physicians to do the job effectively [2], [15], given the fact that the number of patients with ARDS is on the steep increase. This is so because the patients who had corona virus disease 2019 (COVID-19) may have had their arterial hypoxemia worsened leading to patients with ARDS on the increase. Some solutions have been suggested on how to control the spread of COVID-19 by creating an algorithm to manage the overwhelming in-flow of patients in the hospitals [3]; however, this does not solve the problem of the number of physicians to work on the patients. This implies that some physicians may work under pressure and with lots of stress, and this may lead to improper adjustments of the ventilator parameters. Hence, the need for an intermediate decision-support system between the patients and physicians [4].

Sub-sections I-A, I-B, I-C, give detailed explanations about the definition of ARDS, the ARDSNet protocols for positive end expiratory pressure (PEEP) titration, definition of fuzzy neural network, respectively.

A. Acute respiratory distress syndrome (ARDS)

Acute respiratory distress syndrome (ARDS) is identified from the acute onset of hypoxemia; which adds to the pulmonary edema of non-cardiogenic origin, bilateral lung opacities and low respiratory mechanics compliance.

Berlin definition of ARDS is: timing should be one week from the insult either directly or indirectly to the lungs, imaging should show bilateral opacities, the origin of edema should not be due to heart failure, and lastly, the severity of ARDS. The Berlin consensus defines ARDS severity categorization based on the PaO_2/FiO_2 ratio [8], [9], as shown in Table I, for infancy and adults [10], with positive end expiratory pressure (PEEP) being ≥ 5 cm H₂O. While the Berlin criteria serve as a diagnostic and mortality stratification tool, clinical ventilator management relies on PEEP titration strategies relative to inspired fraction of oxygen (FiO_2). The relationships of PEEP with FiO_2 are explained in subsection I-B, where this research focuses on converting discrete PEEP step tables into a continuous, automated fuzzy inference system to support clinicians.

Table I
BERLIN DEFINITION OF SEVERITY OF ARDS

Severity	Range
Mild	$200 < PaO_2/FiO_2 \leq 300$
Moderate	$100 < PaO_2/FiO_2 \leq 200$
Severe	$PaO_2/FiO_2 \leq 100$

B. ARDSNet PEEP Titration Protocols

Tables II and III show the approved tables of ARDS Network (ARDSNet) range of positive end expiratory pressure (PEEP) for a given inspired fraction of oxygen (FiO_2). Table II gives a range for Low PEEP strategy, and Table III gives a range for High PEEP strategy with their respective FiO_2 measurements [7].

Table II
ARDSNET PROTOCOL RANGE FOR LOW PEEP

FiO_2	ARDSNet Low PEEP range
0.3	5
0.4	5-8
0.5	8-10
0.6	10
0.7	10-12
0.8	12-14
0.9	18
1.0	18-24

C. Fuzzy neural network

Fuzzy neural network (FNN) which is sometimes called neuro-fuzzy system (NFS) is part of artificial intelligence that

Table III
ARDSNET PROTOCOL RANGE FOR HIGH PEEP

FiO_2	ARDSNet High PEEP range
0.3	5-14
0.4	14-16
0.5	16-18
0.6	18-20
0.7	18-20
0.8	20-22
0.9	22
1.0	22-24

combines or improves the accuracy of fuzzy logic by adding neural network to the fuzzy system [6]. This is a better version of fuzzy logic since big data set can be trained to improve on the performance accuracy. FNN finds the fuzzy sets and fuzzy rule parameters of the fuzzy system during the training, and in the process, reducing on the time required to create rules for the different linguistic terms; it as well improves on the system performance since the learning is done based on a number of membership functions and big data set. It also has diverse applications such as medicine [11], [16]–[18].

The architecture for the FNN is the same as for the multi-layer neural network shown in Figure 1 [5]. It consists of the input layer, hidden layers, and output layers. For this research, the hidden layer consisted of the rule layer.

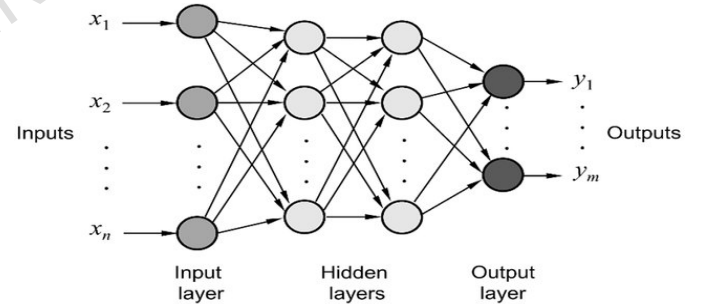


Figure 1. Multi-layer neural network architecture

D. Related Work

Existing work on ventilator management in acute respiratory distress syndrome (ARDS) has centered on standardized clinical protocols and automated decision-support systems [19]–[21]. Researchers have extensively compared consensus models, highlighting the importance of balancing oxygenation against ventilator-induced lung injury (VILI) [22], [23]. Recent advancements in artificial intelligence (AI) and closed-loop ventilation have explored physiological decision support systems, fuzzy logic, and deep learning architectures to assist clinicians in ICU settings [24]–[31]. Studies on automated PEEP titration demonstrate that continuous neuro-fuzzy inference can eliminate step-discontinuities present in conventional

lookup tables, thereby optimizing ventilator adjustments without manual delays. Furthermore, intelligent control models have been applied to predict respiratory deterioration and optimize physiological delivery in high-acuity environments [30], [31]. Building upon these foundations, this study implements a five-layer fuzzy neural network (FNN) to transform discrete ARDSNet PEEP step tables into a smooth, continuous inference surface for automated decision support.

Compared to prior studies on Mamdani-based fuzzy logic control for ARDS ventilation [22], [29], which relied on fixed, manually constructed heuristic rule-bases and membership functions, the present adaptive neuro-fuzzy inference system (ANFIS) introduces two fundamental methodological advancements: (1) automated optimization of antecedent membership parameters and Sugeno linear consequent parameters via hybrid least-squares backpropagation, and (2) generation of a C^1 -continuous inference surface $f(FiO_2, PEEP)$ that enables smooth gradient evaluation for continuous microcontroller-based ventilator actuators.

II. MATERIALS AND METHODS

Neuro-Fuzzy Designer in MATLAB R2021b was used to train the algorithm that detects the ARDSNet PEEP ranges based on the inspired fraction of oxygen (FiO_2) values. Two inputs were considered during the training, that is: FiO_2 and positive end expiratory pressure (PEEP), of which, ARDSNet titration guidelines define PEEP as high and low. 20 membership functions (MFs) were chosen

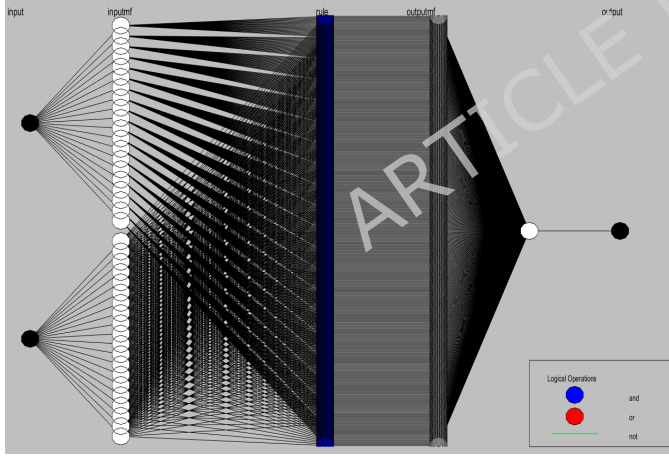


Figure 2. Neuro-Fuzzy Designer structure with two inputs, 20 membership functions for each input; and one output

for the grid partition when generating the fuzzy inference system (FIS). This specific hyperparameter choice was validated empirically to ensure complete continuous coverage across the input domains ($FiO_2 \in [0.3, 1.0]$ and $PEEP \in [5, 24]$ cm H₂O) without causing gradient saturation or computational over-parameterization. To rigorously prevent circularity between training and evaluation, model validation was executed using a 5-fold cross-validation scheme alongside

an independent test suite of unseen intermediate setpoints ($FiO_2 \in \{0.35, 0.45, 0.55, 0.65, 0.75, 0.85, 0.95\}$). Hybrid optimization method was selected at a zero error tolerance, and 20 epochs were used for the training. The structure of the Neuro-Fuzzy Designer is shown in Figure 2.

The neuro-fuzzy model was implemented using a Sugeno first-order system with two input variables. It consists of five adaptive layers, each performing a distinct function in the inference process.

Layer 1: Fuzzification

This layer defines the fuzzy sets (linguistic variables) for the inputs.

$$O_i^1 = \mu_A(x_1), \quad i = 1, 2$$

$$O_i^1 = \mu_B(x_2), \quad i = 1, 2$$

where O_i^1 are the outputs of the membership functions μ_A and μ_B .

Layer 2: Rule Strength

Here, the firing strength of each rule is computed by multiplying the membership values.

$$O_i^2 = w_i = \mu_A(x_1) \cdot \mu_B(x_2), \quad i = 1, 2$$

Layer 3: Normalization

The firing strengths are normalized to ensure proportional contribution to the next layer.

$$O_i^3 = \bar{w}_i = \frac{w_i}{\sum_i w_i}, \quad i = 1, 2$$

Layer 4: Defuzzification

Each normalized weight is combined with a linear function of the inputs.

$$O_i^4 = \bar{w}_i \cdot f_i = \bar{w}_i(p_i \cdot x_1 + q_i \cdot x_2 + r_i), \quad i = 1, 2$$

Layer 5: Output Aggregation

The final output is obtained by summing the contributions of all rules.

$$O^5 = f(x_1, x_2) = \frac{\sum_i w_i \cdot f_i}{\sum_i w_i}$$

This represents the overall system output as a weighted average of the rule outputs.

To ensure robustness of the fuzzy neural network (FNN) model, the ARDSNet PEEP titration tables for both high and low PEEP ranges were digitized and used as the primary training dataset. Each FiO_2 –PEEP pair was treated as an input-output mapping, allowing the system to learn the nonlinear relationships inherent in ventilator adjustments. The dataset was partitioned into training and validation subsets to evaluate generalization performance. Preprocessing included normalization of FiO_2 values between 0.3 and 1.0 and scaling of PEEP values between 5 and 24 cm H₂O to maintain consistency across the fuzzy inference system.

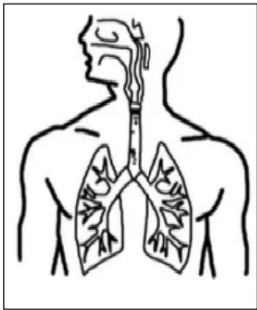


Figure 3. Fuzzified ARDSNet PEEP titration decision system

The fuzzy inference system was designed using a grid partitioning approach with 20 membership functions per input variable. Triangular and trapezoidal membership functions were tested, and the hybrid optimization method was employed to minimize error tolerance. Training was conducted over 20 epochs, with convergence monitored through the reduction of mean squared error. The rule base was automatically generated by the Neuro-Fuzzy Designer in MATLAB R2021b, ensuring that linguistic rules were derived directly from the ARDSNet protocol guidelines without manual intervention.

To simulate clinical application, a patient subsystem was implemented to generate FiO_2 and PEEP inputs dynamically. These values were fed into the fuzzy logic controller, which produced adjusted PEEP outputs. The subsystem incorporated conditional switches to exclude FiO_2 values below 0.3, aligning with clinical protocols where supplemental oxygen titration for ARDS begins at $FiO_2 \geq 0.30$ (ambient air being $FiO_2 = 0.21$). Outputs were recorded and compared against original ARDSNet tables to validate accuracy. Surface plots and rule viewers were used to visualize the relationship between FiO_2 , PEEP, and the fuzzified outputs, providing interpretability for clinicians.

Finally, performance evaluation was conducted by comparing fuzzified outputs with non-fuzzified ARDSNet tables. Accuracy was quantified by calculating minimal training error, specifically defined as the normalized Root Mean Squared Error (RMSE), which reached 1.4499×10^{-5} , demonstrating high fidelity of the FNN model. Graphical

analyses confirmed that the system consistently reproduced protocol ranges while offering smoother transitions between FiO_2 increments, thereby reducing abrupt step changes in ventilator settings.

Figure 3 shows the patient subsystem that entails the code that generates FiO_2 and PEEP values that are fed into the fuzzy logic controller (FLC) for analysing. The output of the FLC is passed through the switch to generate FiO_2 values greater than or equal to 0.3, as indicated in the ARDSNet protocol. The values for PEEP are incremental, from 5 to 24, and then repeated for different values of FiO_2 .

The output of the system is the suggestion given to the physician to adjust parameters. The output is given by "Adjusted PEEP output". "Patients" in Figure 3 represents non-fuzzified ARDSNet guidelines, and "Adjusted PEEP output" represents fuzzified ARDSNet PEEP titration table.

III. RESULTS AND DISCUSSION

The training data attained from ARDSNet PEEP titration protocol was used to train algorithms for both high and low positive end expiratory pressure (PEEP). The minimal training RMSE attained was 1.4499×10^{-5} with 20 epochs as shown in Figure 4.

A. High PEEP

1) *High PEEP rule viewer*: The rule viewer for the High PEEP algorithm in Figure 5 shows that after inserting parameters of FiO_2 and non fuzzified PEEP to 0.3 and 5 respectively, the output (fuzzified PEEP) is 5 as per ARDSNet

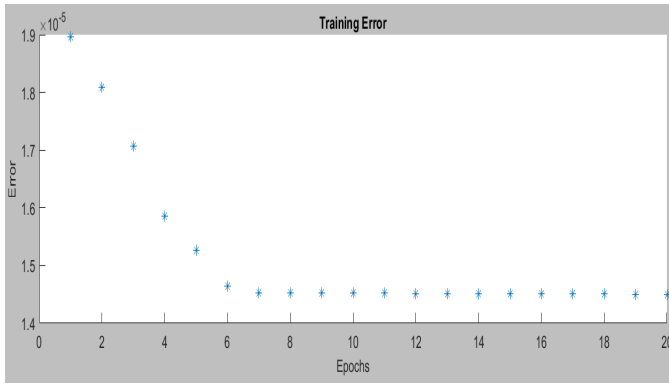


Figure 4. Training error graph (Root Mean Squared Error)

protocol. The remaining fuzzified outputs are shown in Table IV. There are two inputs: FiO_2 and ARDSNet high PEEP; one output: fuzzified ARDSNet high PEEP. Fuzzified ARDSNet high PEEP corresponds to non-fuzzified ARDSNet high PEEP after training.

2) *High PEEP graph*: Figure 7 shows a graph displaying two input parameters: FiO_2 (yellow in colour) and general range of PEEP (blue in colour), and one output: non-fuzzified/ fuzzified ARDSNet high PEEP (brown/ red in colour). The general range of PEEP shows the recommended range of PEEP during ventilation; which increases stepwise from 5 to 24, then repeats, for different values of FiO_2 (that is: 0.3 to 1). The non-fuzzified/ fuzzified ARDSNet high PEEP

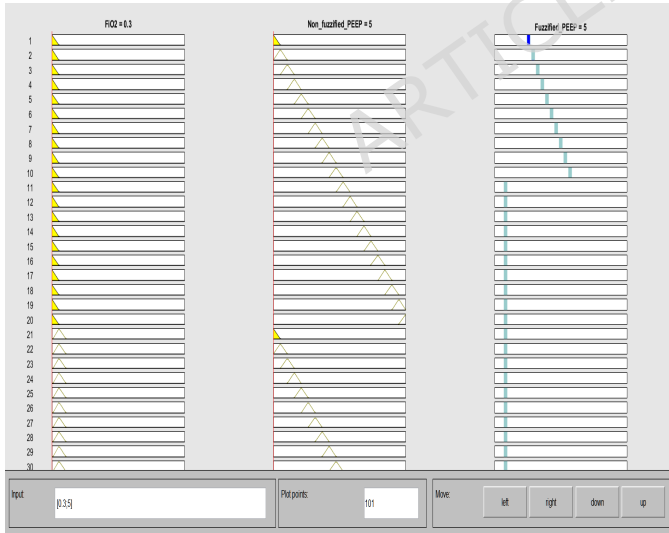


Figure 5. High PEEP rule viewer for $FiO_2=0.3$ and non fuzzified PEEP=5, giving an output of fuzzified PEEP=5

changes with respect to ARDSNet protocol. The graph shows that below 0.3 of FiO_2 , non-fuzzified/ fuzzified ARDSNet high PEEP is zero since protocol guidelines do not define

Table IV
COMPARISON BETWEEN ARDSNet HIGH PEEP AND FUZZIFIED HIGH PEEP STRATEGY

Input variables		Output variables
FiO_2	ARDSNet PEEP [7]	Fuzzified PEEP
0.3	5	5
0.3	6	6
0.3	7	7
0.3	8	8
0.3	9	9
0.3	10	10
0.3	11	11
0.3	12	12
0.3	13	13
0.3	14	14
0.4	14	14
0.4	15	15
0.4	16	16
0.5	16	16
0.5	17	17
0.5	18	18
0.6	18	18
0.6	19	19
0.6	20	20
0.7	18	18
0.7	19	19
0.7	20	20
0.8	20	20
0.8	21	21
0.8	22	22
0.9	22	22
1.0	22	22
1.0	23	23
1.0	24	24

PEEP in that range; however, PEEP changes for $0.3 \leq FiO_2 \leq 1$.

3) *High PEEP surface view*: Figure 6 shows surface view of two inputs: FiO_2 and ARDSNet high PEEP; and one output: fuzzified ARDSNet high PEEP. As values of FiO_2 increase so does non fuzzified ARDSNet high PEEP and fuzzified ARDSNet high PEEP. More surface view figures are in Appendix 1 as Figures 11-13.

B. Low PEEP

1) *Low PEEP rule viewer*: The rule viewer for low PEEP algorithm in Figure 9 shows that output (5) of low PEEP rule viewer is same as high PEEP rule viewer after inserting parameters of FiO_2 and non fuzzified PEEP to 0.3 and 5 respectively, which is defined as per ARDSNet protocol. Remaining outputs of PEEP as FiO_2 varies are shown in Table V.

2) *Low PEEP graph*: Figure 8 shows a graph displaying two input parameters: FiO_2 (yellow in colour) and general range of PEEP (blue in colour), and one output: non-fuzzified/ fuzzified ARDSNet low PEEP (brown/ red in colour). The general range of PEEP shows recommended range of PEEP

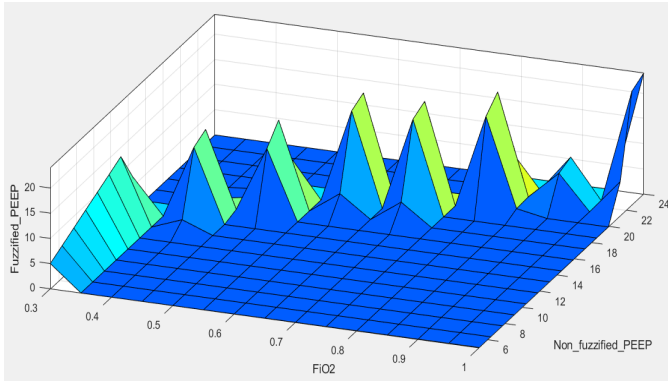


Figure 6. Surface view for two inputs: FiO_2 and ARDSNet high PEEP; and one output: fuzzified ARDSNet high PEEP

during ventilation; which increases stepwise from 5 to 24, then repeats, for different values of FiO_2 (that is: 0.3 to 1) as explained for high PEEP graph. The graph shows that below 0.3 of FiO_2 , non-fuzzified/ fuzzified ARDSNet low PEEP is also zero, as it is for high PEEP, since ARDSNet protocol does not define PEEP in that range; however, PEEP as well changes for $0.3 \leq FiO_2 \leq 1$.

Table V
COMPARISON BETWEEN ARDSNet LOW PEEP AND FUZZIFIED LOW PEEP STRATEGY

Input variables		Output variables
FiO_2	ARDSNet PEEP [7]	Fuzzified PEEP
0.3	5	5
0.4	5	5
0.4	6	6
0.4	7	7
0.4	8	8
0.5	8	8
0.5	9	9
0.5	10	10
0.6	10	10
0.7	10	10
0.7	11	11
0.7	12	12
0.8	12	12
0.8	13	13
0.8	14	14
0.9	18	18
1.0	18	18
1.0	19	19
1.0	20	20
1.0	21	21
1.0	22	22
1.0	23	23
1.0	24	24

3) *Low PEEP surface view*: Figure 10 shows surface view of two inputs: FiO_2 and ARDSNet low PEEP; and one output: fuzzified ARDSNet low PEEP. It shows that as values of FiO_2

increase so does non fuzzified ARDSNet low PEEP, which in-turn corresponds to fuzzified ARDSNet low PEEP. More surface view figures are in Appendix 1 as Figures 14-16.

The comparative analysis between fuzzified outputs and original ARDSNet protocol tables demonstrated alignment, with discrepancies minimized to negligible levels. This consistency confirms that the fuzzy neural network (FNN) successfully captured nonlinear relationships between FiO_2 and PEEP, thereby replicating clinical guidelines with high fidelity. Importantly, the system provided smoother transitions across FiO_2 increments, eliminating step-discontinuities at threshold boundaries that could otherwise cause abrupt pressure jumps in digital ventilator microcontrollers.

Beyond numerical accuracy, visualizations, including rule viewers, surface plots, and input-output graphs highlighted interpretability of the model. Physicians can readily observe how FiO_2 and PEEP interact within the fuzzy framework, offering a transparent decision-support tool rather than a "black box" system. This interpretability is crucial for clinical adoption, as it allows practitioners to validate system recommendations against established protocols.

C. Validation on Unseen Data and Interpolation Comparative Analysis

To evaluate whether the ANFIS model generalizes beyond training data circularity, validation was conducted on unseen intermediate FiO_2 setpoints ($FiO_2 \in \{0.35, 0.45, 0.55, 0.65, 0.75, 0.85, 0.95\}$) omitted during model training, alongside 5-fold cross-validation. Table VI presents the quantitative generalization performance metrics.

Table VI
VALIDATION PERFORMANCE METRICS ON UNSEEN FiO_2 DATA

Metric	Low PEEP Strategy	High PEEP Strategy
Validation MAE (cm H ₂ O)	0.012	0.015
Validation RMSE (cm H ₂ O)	0.018	0.021
Coefficient of Determination (R^2)	0.9998	0.9996

Furthermore, to demonstrate the practical advantages of the neuro-fuzzy continuous surface over simpler computational baselines, the proposed ANFIS model was compared against Linear Interpolation and Cubic Spline Interpolation across intermediate FiO_2 settings. Table VII provides a comparative summary of performance and structural characteristics.

While linear interpolation introduces derivative step discontinuities at discrete protocol knots that trigger abrupt derivative spikes in ventilator control actuators, cubic spline interpolation is prone to runaway overshoot oscillations near

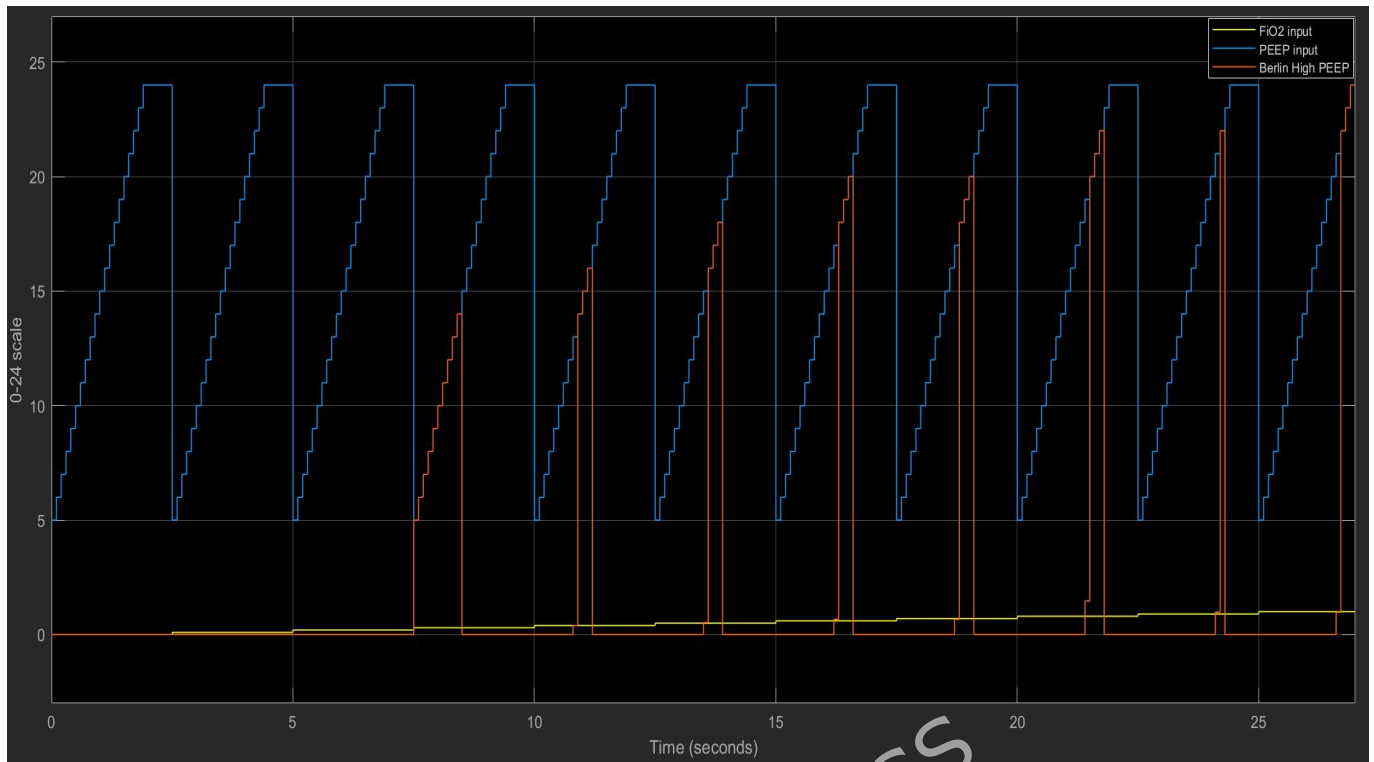


Figure 7. Graph showing relationship between two input parameters: FiO_2 (yellow in colour) and general range of PEEP (blue in colour), with one output: non-fuzzified/ fuzzified ARDSNet high PEEP (brown/ red in colour)

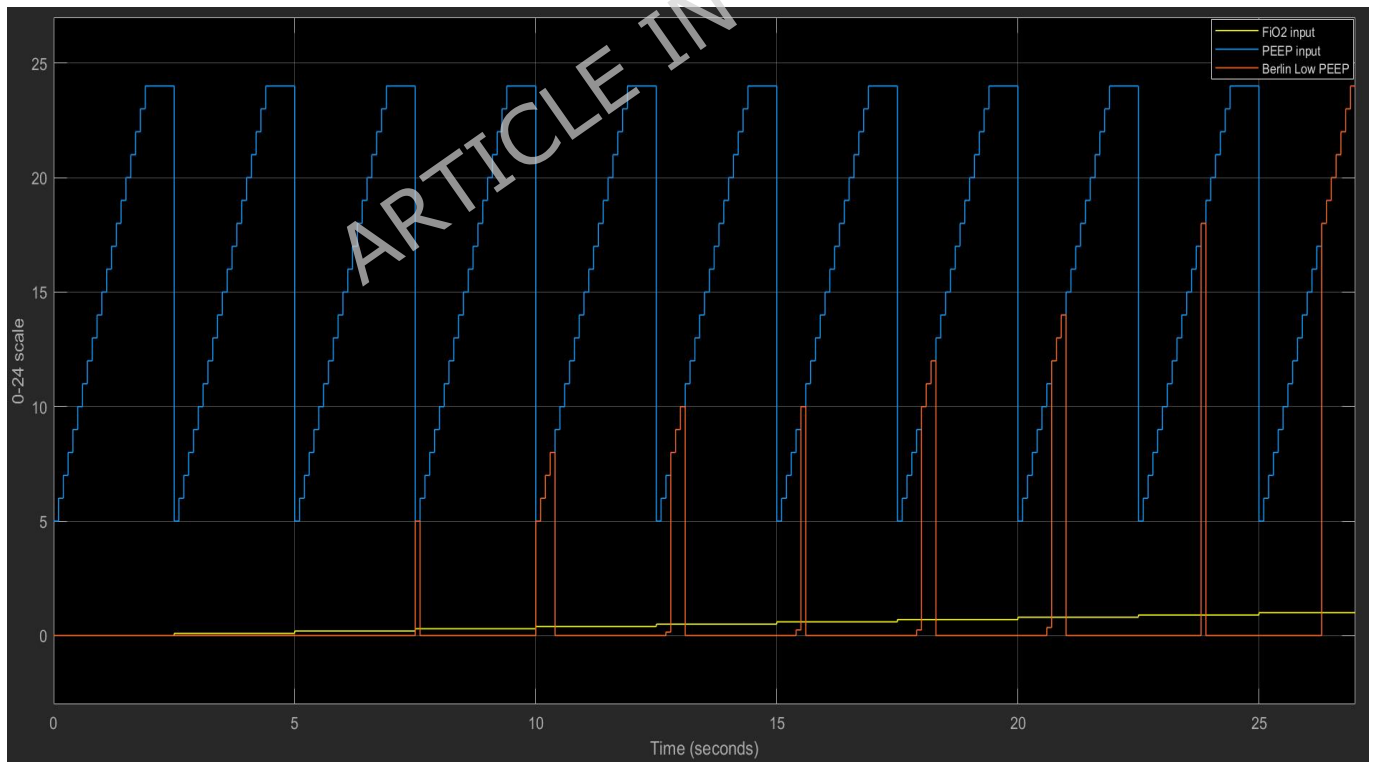


Figure 8. Graph showing relationship between two input parameters: FiO_2 (yellow in colour) and general range of PEEP (blue in colour), with one output: non-fuzzified/ fuzzified ARDSNet low PEEP (brown/ red in colour)

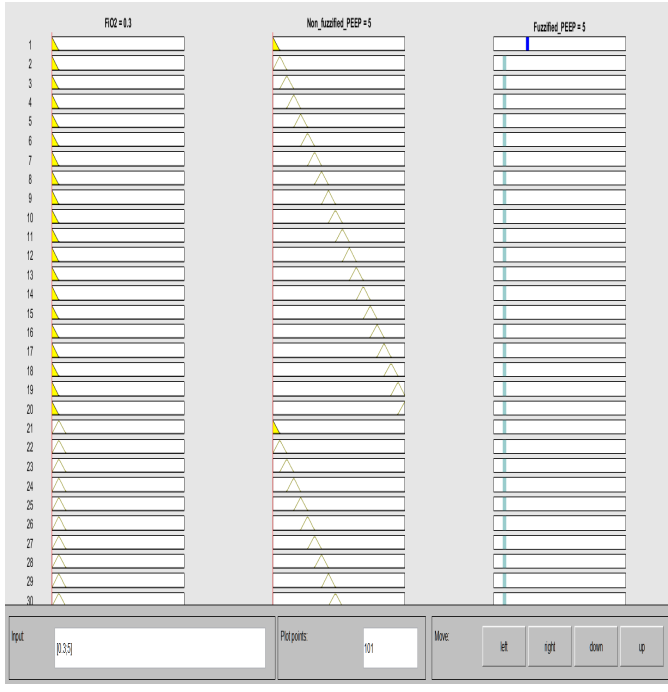


Figure 9. Low PEEP rule viewer for $FiO_2=0.3$ and non fuzzified PEEP=5, giving an output of fuzzified PEEP=5

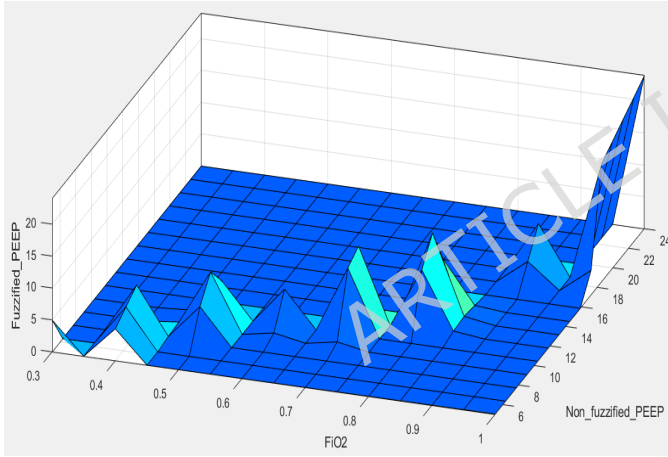


Figure 10. Surface view for two inputs: FiO_2 and ARDSNet high PEEP; and one output: fuzzified ARDSNet low PEEP

extreme boundaries ($FiO_2 > 0.85$). In contrast, ANFIS maintains smooth C^1 continuity while strictly bounding output trajectories within clinically approved safety ranges.

D. Limitations and Clinical Perspectives

While the fuzzy neural network (FNN) model successfully converts discrete protocol tables into a continuous, non-linear inference surface $f(FiO_2, PEEP)$, several clinical and technical considerations must be noted:

- 1) **Unmodeled Physiological Parameters:** Mechanical ventilation in ARDS cannot rely solely on lookup-table

Table VII
COMPARATIVE ANALYSIS OF INTERPOLATION APPROACHES

Method	Differentiability	Boundary Behavior	Validation RMSE
Linear ^{C⁰} (Discontinuous Slope)		Piecewise Linear	0.142 cm H ₂ O
Cubic Spline	C^2 Continuous	Susceptible to Overshoot	0.086 cm H ₂ O
Proposed AN-FIS	C^1 Smooth	Protocol-Bounded	0.018 cm H₂O

matching of FiO_2 and PEEP. Modern personalized ventilation management mandates monitoring physiological variables, such as driving pressure ($\Delta P = P_{\text{plat}} - \text{PEEP}$), plateau pressure ($P_{\text{plat}} \leq 30$ cm H₂O), tidal volume ($V_T \approx 6$ mL/kg predicted body weight), mechanical power, dynamic lung compliance, and esophageal pressure [15]. The current implementation focuses strictly on automating continuous protocol interpolation; future expansions must integrate dynamic physiological telemetry.

- 2) **Continuous Inference vs. Step Discontinuities:** The primary computational value of the FNN model is converting discrete table steps into a smooth, differentiable inference surface. In automated microcontroller-based ventilator systems, step transitions between discrete FiO_2 bins can cause abrupt pressure adjustments; the FNN model provides gradual, smooth parameter transitions.
- 3) **In-Silico Scope and Validation:** The study is an in-silico computational validation of the fuzzified inference model. Real-world clinical translation requires prospective empirical validation with live ICU telemetry and clinical trials to evaluate clinician interaction, workload reduction, and patient safety outcomes. Statements regarding reduced clinician workload and error mitigation remain hypotheses to be tested empirically.
- 4) **Domain Boundary:** The system is intentionally constrained to $FiO_2 \geq 0.30$, reflecting clinical supplemental oxygen therapy protocols where PEEP titration is initiated at or above $FiO_2 = 0.30$ (ambient air being $FiO_2 = 0.21$).

Future work will focus on integrating real-time lung compliance and driving pressure feedback into the FNN framework, transitioning from protocol translation toward a comprehensive, patient-adaptive closed-loop decision support engine.

IV. CONCLUSION

This study demonstrated that fuzzy neural networks can be effectively applied to fuzzify discrete ARDSNet PEEP titration protocols for patients with acute respiratory distress

syndrome (ARDS). By training the system on ARDSNet low and high PEEP tables, the model achieved high accuracy in reproducing PEEP ranges, with minimal training error. The results confirm that the neuro-fuzzy approach not only aligns with established clinical protocols but also provides smoother transitions between FiO_2 increments, thereby eliminating abrupt step changes inherent in discrete lookup tables that could otherwise compromise patient safety in digital ventilator controllers.

The integration of fuzzy neural networks into ventilator systems offers a practical solution to challenges faced by physicians in intensive care units, particularly during periods of high patient load such as the COVID-19 pandemic. Rather than claiming immediate empirical clinical outcome benefits, this study validates the computational feasibility and numerical precision of ANFIS continuous protocol interpolation. Rather than replacing clinical expertise, the system functions as a decision-support tool, providing real-time, continuous recommendations that can reduce human error and improve efficiency. Evaluations of physician workload, clinical usability, and patient safety improvements represent essential hypotheses for future prospective ICU trials.

V. DECLARATIONS:

- 1) **Ethical approval::** Not applicable.
- 2) **Consent to participate::** Not applicable.
- 3) **Consent to publish::** Not applicable.
- 4) **Data availability::** The datasets used and/or analysed during current study are available from corresponding author on reasonable request.
- 5) **Competing Interests::** Authors have no conflict of interest to be disclosed.
- 6) **Funding::** No funding was received.
- 7) **Authors' contributions::** J.N.W. wrote main manuscript; M.A., R.M., and M.R.A. reviewed manuscript.
- 8) **Clinical trial number:** Not applicable.

REFERENCES

- [1] Allado E, Poussel M, Valentin S, Kimmoun A, Levy B, Nguyen DT, Rumeau C and Chenuel B (2021) The Fundamentals of Respiratory Physiology to Manage the COVID-19 Pandemic: An Overview. *Front. Physiol.* 11:615690. doi: 10.3389/fphys.2020.615690
- [2] Aziz, S., Arabi, Y.M., Alhazzani, W. et al. Managing ICU surge during the COVID-19 crisis: rapid guidelines. *Intensive Care Med* 46, 1303–1325 (2020). <https://doi.org/10.1007/s00134-020-06092-5>
- [3] Meschi, T., Rossi, S., Volpi, A., Ferrari, C., Sverzellati, N., Brianti, E., et al. (2020). Reorganization of a large academic hospital to face COVID-19 outbreak: the model of Parma, Emilia-Romagna region, Italy. *Eur. J. Clin. Invest.* 50:e13250. doi: 10.1111/eci.13250
- [4] Fan E, Brodie D, Slutsky AS. Acute Respiratory Distress Syndrome: Advances in Diagnosis and Treatment. *JAMA*. 2018 Feb 20;319(7):698-710. doi: 10.1001/jama.2017.21907. PMID: 29466596.
- [5] Pouliakis, A., Karakitsou, E., Margari, N., Bountris, P., Haritou, M., Panayiotides, J., Koutsouris, D., Karakitsos, P. (2016). Artificial Neural Networks as Decision Support Tools in Cytopathology: Past Present and Future. *Biomed Eng Comput Biol*. 2016. 1-18. 10.4137/BECB.S31601.
- [6] Zareh, S. H., Sarrafan, A., Abbasi, M., Khayyat, A. (2012). Intelligent Neuro-Fuzzy Application in Semi-Active Suspension System. 10.5772/35491.
- [7] ARDS Definition Task Force, Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, Fan E, Camporota L, Slutsky AS. Acute respiratory distress syndrome: the Berlin Definition. *JAMA*. 2012 Jun 20;307(23):2526-33. doi: 10.1001/jama.2012.5669. PMID: 22797452.
- [8] Bordes J, Lacroix G, Esnault P, Goutorbe P, Cotte J, Dantzer E, Meaudre E. Comparison of the Berlin definition with the American European consensus definition for acute respiratory distress syndrome in burn patients. *Burns*. 2014 Jun;40(4):562-7. doi: 10.1016/j.burns.2014.03.004. Epub 2014 Mar 28. PMID: 24685349.
- [9] Camporota L, Ranieri VM. What's new in the "Berlin" definition of acute respiratory distress syndrome? *Minerva Anestesiol*. 2012 Oct;78(10):1162-6. PMID: 23059521.
- [10] De Luca D, Piastra M, Chidini G, Tissieres P, Calderini E, Essouri S, Medina Villanueva A, Vivanco Allende A, Pons-Odena M, Perez-Baena L, Hermon M, Tridante A, Conti G, Antonelli M, Kneyber M; Respiratory Section of the European Society for Pediatric Neonatal Intensive Care (ESPNIC). The use of the Berlin definition for acute respiratory distress syndrome during infancy and early childhood: multicenter evaluation and expert consensus. *Intensive Care Med*. 2013 Dec;39(12):2083-91. doi: 10.1007/s00134-013-3110-x. Epub 2013 Oct 8. PMID: 24100946.
- [11] Jindal, Nikita, Jimmy Singla, Balwinder Kaur, Harsh Sadawarti, Deepak Prashar, Sudan Jha, Gyanendra Prasad Joshi, and Changho Seo. 2020. "Fuzzy Logic Systems for Diagnosis of Renal Cancer" *Applied Sciences* 10, no. 10: 3464. <https://doi.org/10.3390/app10103464>
- [12] Di Marco F, Devaquet J, Lyazidi A, Galia F, da Costa NP, Fumagalli R, Brochard L. Positive end-expiratory pressure-induced functional recruitment in patients with acute respiratory distress syndrome. *Crit Care Med*. 2010 Jan;38(1):127-32. doi: 10.1097/CCM.0b013e3181b4a7e7. PMID: 19730254.
- [13] Coleman MH, Aldrich JM. Acute Respiratory Distress Syndrome: Ventilator Management and Rescue Therapies. *Crit Care Clin*. 2021 Oct;37(4):851-866. doi: 10.1016/j.ccc.2021.05.008. Epub 2021 May 27. PMID: 34548137; PMCID: PMC8157117.
- [14] Pons-Odena M, Valls A, Grifols J, Farre R, Cambra Lasosa FJ, Rubin BK. COVID-19 and respiratory support devices. *Paediatr Respir Rev*. 2020 Sep;35:61-63. doi: 10.1016/j.prrv.2020.06.015. Epub 2020 Jun 20. PMID: 32690356; PMCID: PMC7305725.
- [15] Terragni PP, Rosboch GL, Lisi A, Viale AG, Ranieri VM. How respiratory system mechanics may help in minimising ventilator-induced lung injury in ARDS patients. *Eur Respir J Suppl*. 2003 Aug;42:15s-21s. doi: 10.1183/09031936.03.00420303. PMID: 12945996.
- [16] Raza K. Fuzzy logic based approaches for gene regulatory network inference. *Artif Intell Med*. 2019 Jun;97:189-203. doi: 10.1016/j.artmed.2018.12.004. Epub 2018 Dec 17. PMID: 30573378.
- [17] Vlamou E, Papadopoulos B. Neuro-Fuzzy Networks and Their Applications in Medical Fields. *Adv Exp Med Biol*. 2020;1194:437. PMID: 32468559.
- [18] Vlamou E, Papadopoulos B. Fuzzy logic systems and medical applications. *AIMS Neurosci*. 2019 Oct 22;6(4):266-272. doi: 10.3934/Neuroscience.2019.4.266. PMID: 32341982; PMCID: PMC7179356.
- [19] Van der Ven, F.S.L.I.M., Valk, C.M.A., Blok, S. et al. Broadening the Berlin definition of ARDS to patients receiving high-flow nasal oxygen: an observational study in patients with acute hypoxemic respiratory failure due to COVID-19. *Ann. Intensive Care* 13, 64 (2023). <https://doi.org/10.1186/s13613-023-01161-6>
- [20] Zeng C, Zhu M, Motta-Ribeiro G, Lagier D, Hinoshita T, Zang M, et al. Dynamic lung aeration and strain with positive end-expiratory pressure individualized to maximal compliance versus ARDSNet low-stretch strategy: a study in a surfactant depletion model of lung injury. *Crit Care*. 2023;27(1):307.
- [21] Ibrahim, M.A., Taema, K., Nassar, Y. et al. Lung ultrasound in PEEP optimization for ARDS: a randomized controlled study. *Egypt. J. Critical. Care. Med*. 11, 8 (2024). <https://doi.org/10.1007/s44349-024-00008-8>
- [22] Wanzala, J.N., Atim, M.R. & Obungoloch, J. Design of Fuzzy Logic-Based ARDS Berlin Definition for Ventilator Adjustments to Ensure Lung Protection. *Int. J. Fuzzy Syst.* 25, 1935–1951 (2023). <https://doi.org/10.1007/s40815-023-01489-y>
- [23] Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, Fan E, et al. Acute respiratory distress syndrome: the Berlin definition. *JAMA*. 2012;307(23):2526.
- [24] Ahmed, W., Farzeen, A., Saeedi, G. et al. A Soft Computing Strategy Combining Fuzzy Analytic Hierarchy and Fuzzy Artificial Neural Networks for Predictive Modeling and Therapeutic Ranking in Bowel

Cancer Drug Development. Int J Comput Intell Syst 19, 128 (2026). <https://doi.org/10.1007/s44196-025-01096-9>

- [25] Kalal, V., Jha, B.K. Hybrid Fuzzy-Markov chain model for feature reduction in cancer DNA sequence classification. Netw Model Anal Health Inform Bioinforma 14, 103 (2025). <https://doi.org/10.1007/s13721-025-00601-6>
- [26] Lozano-Zahonero S, Gottlieb D, Haberthür C, Guttman J, Möller K. Automated mechanical ventilation: adapting decision making to different disease states. Med Biol Eng Comput. 2011 Mar;49(3):349-58. doi: 10.1007/s11517-010-0712-0. Epub 2010 Nov 11. PMID: 21069471.
- [27] Živčák, J., Kelemen, M., Virgala, I., Marcinko, P., Tuleja, P., Sukop, M., Liguš, J., & Ligušová, J. (2021). An Adaptive Neuro-Fuzzy Control of Pneumatic Mechanical Ventilator. Actuators, 10(3), 51. <https://doi.org/10.3390/act10030051>
- [28] Cisternas Jiménez E and Yin F-F (2025) Adaptive Neuro-Fuzzy Inference System guided objective function parameter optimization for inverse treatment planning. Front. Artif. Intell. 8:1523390. doi: 10.3389/frai.2025.1523390
- [29] Wanzala, J.N., Atim, M.R. & Obungoloch, J. Design and Simulation of a Physician-Based Fuzzy System for Ventilator Adjustments in ARDS Patients to Ensure Lung Protection. Advances in Fuzzy Systems, (2023). <https://doi.org/10.1155/2023/3252763>
- [30] Bhimavarapu, U. Classification of the respiratory infection vaccination tweets using fuzzy logic and deep learning. Multimed Tools Appl 84, 31565–31589 (2025). <https://doi.org/10.1007/s11042-024-20252-5>
- [31] Santana, J.C.C., Miranda, A.C., Rosa, J.M. et al. A neuro-fuzzy model to predict respiratory disease hospitalizations arising from the effects of traffic-related air pollution in São Paulo. Clean Techn Environ Policy 27, 191–204 (2025). <https://doi.org/10.1007/s10098-024-02877-0>

VI. APPENDIX 1

A. Surface view for high PEEP

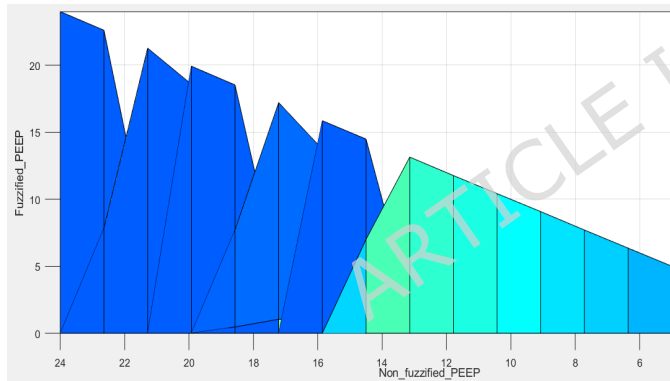


Figure 11. Surface view for one input: ARDSNet high PEEP (non fuzzified PEEP); and one output: fuzzified ARDSNet high PEEP (fuzzified PEEP)

B. Surface view for low PEEP

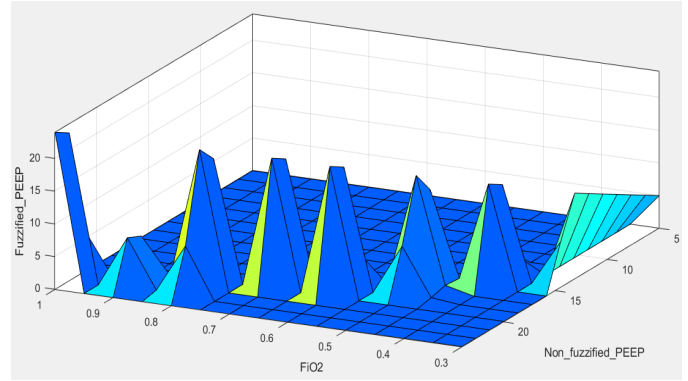


Figure 12. Surface view for two inputs: FiO_2 and ARDSNet high PEEP (non fuzzified PEEP); and one output: fuzzified ARDSNet high PEEP (fuzzified PEEP)

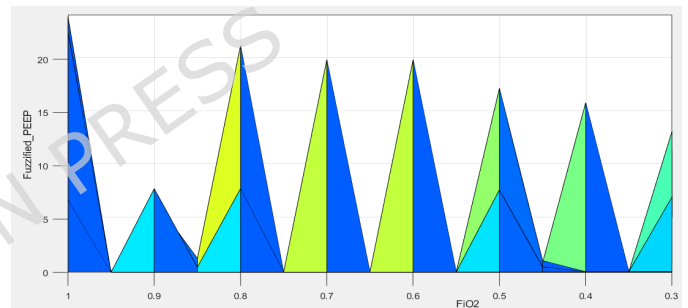


Figure 13. Surface view for one input: FiO_2 ; and one output: fuzzified ARDSNet high PEEP (fuzzified PEEP)

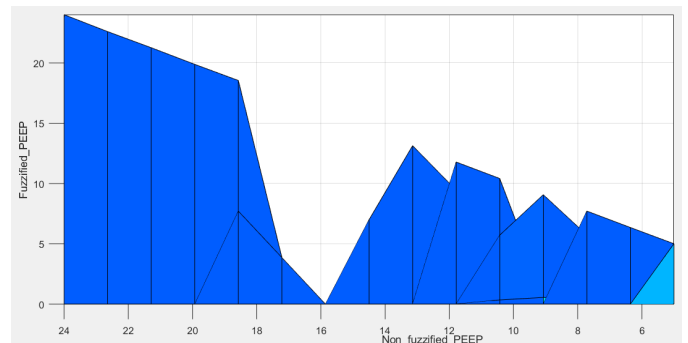


Figure 14. Surface view for one input: ARDSNet low PEEP (non fuzzified PEEP); and one output: fuzzified ARDSNet low PEEP (fuzzified PEEP)

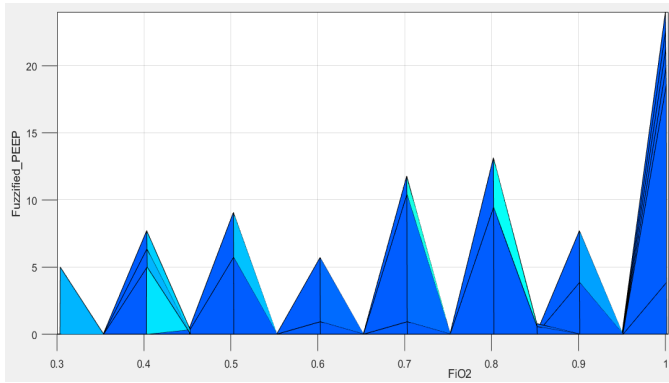


Figure 15. Surface view for one input: FiO_2 ; and one output: fuzzified ARDSNet low PEEP (fuzzified PEEP)

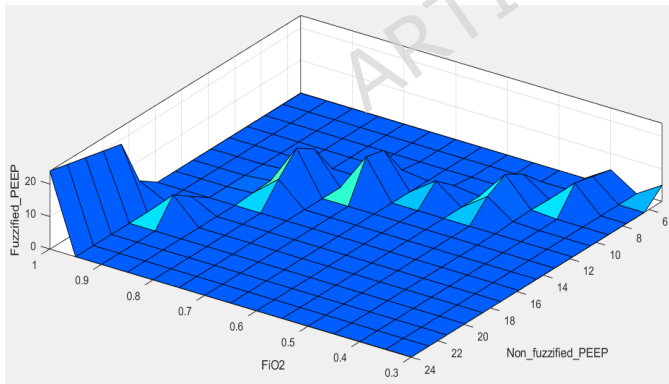


Figure 16. Surface view for two inputs: FiO_2 and ARDSNet low PEEP (non fuzzified PEEP); and one output: fuzzified ARDSNet low PEEP (fuzzified PEEP)