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Utilization of Temporal Information for Intracranial Pressure Development Trend Forecasting in Traumatic Brain Injury

Mengling Feng,[1] * Zhuo Zhang, [1] Cuntai Guan [1], David R. Hardoon, [2]
Nicolas Kon Kam King,[3] Boon Chuan Pang,[3] Beng Ti Ang, [3]

[1] Institute for Infocomm Research, Singapore.
[2] SAS, Singapore
[3] Department of Neurosurgery, National Neuroscience Institute,Singapore.

ABSTRACT

Objective. Our primary objective is to demonstrate and statistically justify that forecasting models that utilize temporal information of the historical readings of ICP and related parameters are superior, in terms of performance, compared with models that do not make use of temporal information.

Material & Method. 82 traumatic brain injuries patients, who were admitted between 2002 to 2007 and were continuously monitored on ICP for more than 24 hours, are selected for the study. Together with ICP, MAP and $PbtO_2$ were also monitored, and PRx was calculated as a moving correlation between ICP and MAP.

The development trends of ICP and the related parameters are measured by first segmenting the time-series data into multiple periodic windows. The development trend of each periodic window is then discretized into three classes — *elevate*, *stay* or *reduce* — based on the concept of "trend line". A systematic framework is developed to compare the forecast performance between the temporal and non-temporal models.

Findings. Experimental results demonstrate that the utilization of temporal information directly leads to a considerable boost in trend forecasting performance (on average 20% relative performance gain was achieved). Moreover, the performance gain is confirmed to be statistically significant (p-value < 0.0001) based on a paired t-test.

1. BACKGROUND

Traumatic Brain Injury (TBI) is a major public health problem with significant socioeconomic implications [14]. To prevent secondary ischemic brain injury, continuous monitor and optimization of intracranial pressure (ICP) through protocol-driven therapies [1, 3, 13, 17] have become the standard practice in many neurocritical care units. Research on TBI patient monitoring has been primarily focusing on predicting the patients' outcome based on the values of ICP [6, 7, 15, 16], the dynamic variability of ICP [2, 4], or the combinations of ICP and other physiological parameters, such as mean arterial pressure (MAP), brain tissue oxygenation ($PbtO_2$) and pressure reactivity index (PRx) [14].

Different from the prior works, this study focuses on forecasting the development trend of ICP. That is to say, we aim to predict, in the next time frame of monitoring, whether the ICP of the patient will rise, stay relatively stable or decrease. ICP development trend forecasting is a valuable tool to TBI patient monitoring. It can be used as an alarm for more intensive monitoring, and it allows early preparation and opens up more treatment options. We propose to forecast the development trend of ICP by utilizing the temporal information of ICP and the related parameters —MAP, $PbtO_2$ and Prx. However, in this study, we do not aim to develop an optimum forecasting model. Our primary objective is to demonstrate and statistically justify that forecasting models that utilize temporal information of the historical readings of ICP and related parameters are superior, in terms of performance, compared with models that do not make use of the temporal information. We call the former group of models "temporal" models and the latter ones "non-temporal" models.

2. MATERIAL & METHODS

Patients and Monitoring.

This analytical study was conducted based on the monitoring data of TBI patients, who were admitted to the neurocritical care unit of a tertiary hospital between January 2002 to December 2007. In particular, 82 patients, who underwent invasive monitoring of ICP, MAP and $PbtO_2$ for more than 24 consecutive hours and were connected to a bedside computerized system, were selected for the study. Local ethics committee approval was obtained prior to commencement of the study.

All 82 patients had a CT brain scan performed before their admission to the neurocritical care unit. After informed consent was obtained, intraparenchymal probes were inserted based on the CT findings. ICP was contiously monitored using a fiber-optic intraparenchymal gauge (Codman and Shurtleff, Taynham, MA), and Licox polarographic Clark-

*Corresponding Author. Email: mfeng@i2r.a-star.edu.sg

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type microcatheters (Integra Neuroscience, Plainsboro, NJ) were inserted into peri-lesional brain tissues to measure the brain temperature and $PbtO_2$. MAP was measured through an arterial line from the radial artery using a standard pressure monitoring kit (Biosensors International Pte. Ltd., The Netherlands). The continuously monitored physiological readings were sampled and recorded every 5 sec via a computerized system. The PRx was calculated as a moving correlation between the last 30 consecutive samples of ICP and MAP readings. All patients underwent multi-modality monitoring with continuous recording of clinical data on a Hewlett-Packard Carevue System.

Patients were managed in accordance to the guidelines for severe TBI management [3]. ICP of patient was optimized based on an incremental regimen to maintain ICP < 20 mmHg and CPP > 60 mmHg. First-tier ICP control treatment included elevation of bed to 30°, sedation of propofol ($2-10$mg/kg/h), and adequate analgesia (intravenous morphine 2-5 mg/h). Boluses of 20% mannitol (2 mg/kg up to a plasma osmolarity of 320 mosmoI/L) were administered, if there was an sudden increase in ICP. Second-tier measures then included paralysis, cooling of core body temperature to 36°C and institution of a barbiturate comma, which is achieved with intravenous thiopentone 250 mg boluses of over 10-20 min (up to a total dose of 500-1000 mg) with a maintenance dose of 125-500 mg/h titrated to ICP control or to maintain burst suppression on EEG. Surgical decompression was used as the final stage of therapy for scenarios where the above medical therapy failed.

ICP Development Trend Forecasting

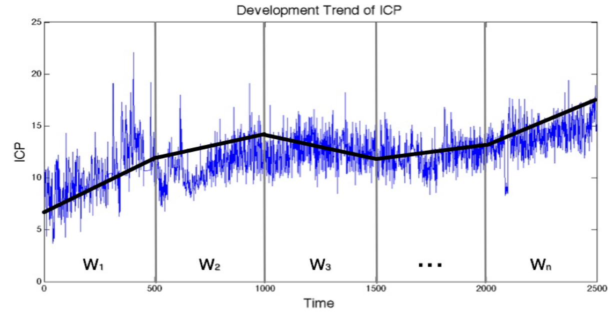
This study addresses the problem of ICP development trend forecasting. The study aims to demonstrate that models that utilize temporal information in development trend forecast are superior to non-temporal models. Continuous monitoring data of four physiological parameters — ICP, MAP, $PbtO_2$ and PRx — were collected for this study. Note that necessary medical intervention were administered to the patients to maintain their ICP to be below 20 mmHg. These interventions usually induce a sudden reduction in ICP and thus interrupts our trend study. Therefore, to minimize the effect of intervention, only data points in between two intervention were used for the study. A systematic performance evaluation framework is developed to compare the forecasting performance of "temporal" and "non-temporal" models. Before we introduce the framework, let us first discuss how the development trend is measured.

Measurement of Development Trend

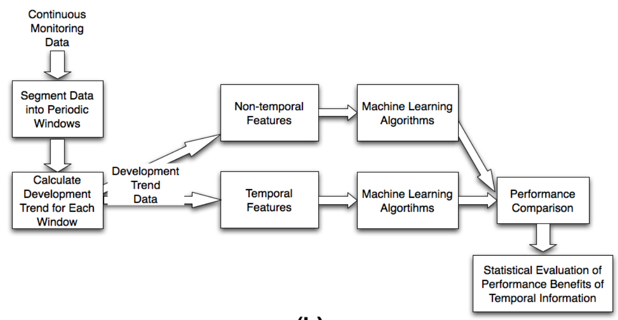
The monitoring data of ICP and related parameters, as shown in Figure 1 (a), are continuous time-series data. We measure the development trend of the time-series data by first segmenting the continuous data into multiple windows of a fix width. We call these windows the "periodic windows". In this study, the width of the window is set as one hour. After the continuous time-series data is segmented into periodic windows, we then apply a straight line to fit the data points within each periodic window. The data segmentation and trend line fitting process is graphically illustrated in Figure 1 (a). The fitting line is formulated as:

$$y = \alpha t + y_o \qquad (1)$$

where α refers to the gradient(steepness) of the line; t refers to the time points and y_o is the offset. This fitting line is known as the "trend line" [20] in financial and economical data analysis. It is widely used to describe the development trend of economic growth, price index, etc. In this study, a Linear Regression model [22] was employed to calculate the trend line of each periodic window. Based on the fitted trend line, we further discretize the development trend of a particular periodic window, w_i, into 3 classes: *elevate*, *stay* or *reduce*. The discretization follows the following formula:



(a)



(b)

Figure 1: (a) Proposed method for development trend measurement in continuous ICP monitoring data. (b) Proposed framework for evaluating the benefits of temporal information utilization in ICP development trend forecasting.

$$T_{w_i} = \begin{cases} +1 \text{ ``}\textit{elevate}\text{''} & \text{if } \alpha_{w_i} > 0 \\ 0 \text{ ``}\textit{stay}\text{''} & \text{if } \alpha_{w_i} = 0 \\ -1 \text{ ``}\textit{reduce}\text{''} & \text{if } \alpha_{w_i} < 0 \end{cases} \qquad (2)$$

Based on the above measurement, we can then transform the time-series monitoring data into development trend data, in which each record consists of the discretized trend of ICP, MAP, $PbtO_2$ and PRx. For a particular periodic window w_i, the trend record is mathematically denoted as $T_{w_i} =< T_{w_i}^{ICP}, T_{w_i}^{MAP}, T_{w_i}^{PbtO_2}, T_{w_i}^{PRx} >$.

Forecasting of Development Trend

Given the development trend data of n previous periodic windows, $\{T_{w_1}, \cdots, T_{w_n}\}$, the forecasting task is to predict the development trend of ICP at the next periodic window w_{n+1}, $T_{w_{n+1}}^{ICP}$.

Non-temporal forecasting models predict the development trend of ICP at periodic window w_{n+1}, $T_{w_{n+1}}^{ICP}$, based on the trend information of the related parameters, MAP, $PbtO_2$, PRx, at w_{n+1}. Thus, for non-temporal models, the "trend feature vector" is:

$$\mathcal{F}_{n+1} =< T^{MAP}_{w_{n+1}}, T^{PbtO_2}_{w_{n+1}}, T^{PRx}_{w_{n+1}} > \quad (3)$$

Moreover, to reflect the differences in the correlations between ICP and MAP, $PbtO_2$ and PRx, a weight vector Ω is employed, where

$$\Omega =< \omega^{MAP}, \omega^{PbtO_2}, \omega^{PRx} > \quad (4)$$

The non-temporal models then can be generically defined as:

$$T^{ICP}_{w_{n+1}} = f(\Omega \circ \mathcal{F}_{n+1}) \quad (5)$$

where $\circ$ refers to the Hadamard product (a.k.a. pairwise product) [11] and $f(.)$ refers to the prediction function, which is determined by the employed machine learning algorithm. Machine learning algorithms are applied to "learn" the optimum values for the weight vector Ω via training with the previous development trend data $\{T_{w_1}, \cdots, T_{w_n}\}$.

Simplicity is the biggest advantage of the non-temporal models. However, these models may compromise on their prediction accuracy, because they fail to capture the temporal correlation between the predicting ICP trend and the previous trends ICP and related parameters.

The temporal model that we propose, on the other hand, predicts the ICP development trend based on the heuristic that: how ICP and the other related parameters previously evolved significantly affects how ICP is going to evolve next. Guided by this heuristic, we expand the feature vector to capture the temporal information. For a periodic window w_{n+1}, the "expanded trend feature vector" is:

$$\mathcal{F}'_{n+1} =< \mathcal{F}_{n+1}, T^{ICP}_{w_n}, \mathcal{F}_n, \cdots, T^{ICP}_{w_{n+1-k}}, \mathcal{F}_{n+1-k} > \quad (6)$$

where $\mathcal{F}_i$ is the trend feature vector of w_i defined by Equation 3 and k is a user-defined parameter. As shown in the Equation 6, the expanded feature vector $\mathcal{F}'_{n+1}$ captures not only the current trend feature $\mathcal{F}_{n+1}$ but also the previous ICP development trends and trend feature vectors. Parameter k then indicates how far back the history is captured in the expanded feature vector. k is set to 3 for this study. Correspondingly, we have an expanded weight vector Ω'. The temporal forecasting model can then be expressed as:

$$T'^{ICP}_{w_{n+1}} = f(\Omega' \circ \mathcal{F}'_{n+1}) \quad (7)$$

Similar to non-temporal models, the values of the expanded weight vector Ω' are "learned" with machine learning algorithms based on the previous development trend data. Compared with non-temporal models, the temporal model is more complicated (having larger feature and weight vectors) and may requires more time for the optimum model to be "learned". However, we believe that, by capturing the temporal information, the temporal model can outperform non-temproal models in terms of trend forecasting performance.

A systematic framework is developed to compare the forecasting performance of the temporal and non-temporal models. The mechanism of the framework is graphically illustrated in Figure 1 (b). First, the time-series data was segmented into periodic windows (1 hour per window), and development trend of each window was captured based on the concept of trend line and Equation 2. Then, the non-temporal and temporal trend feature and weight vectors were formulated based on Equation 3 & 6. After that, a same set of machine learning algorithms were employed to learn both the temporal and non-temporal models. Finally, the forecasting performance of both models were compared, and the significance of the performance difference was statistically evaluated.

3. RESULTS & DISCUSSION

To evaluate the forecasting performance of both the non-temporal and temporal models, multiple machine learning algorithms are employed. The selected algorithms are representative algorithms that are widely used by the research community. These selected algorithms include: Aggregating One-Dependence Estimators (AODE) [23], Ada-Bossting with Decision Tree (AdaBoost-J48) [24, 21], Bayesian Network with K2 & TAN (BayesNet-K2/TAN) [5, 8], Lazy Bayesian Rules (LBR) [25], Logistic Regression (LogReg) [12], Naive Bayesian Classifier (Naive Bayes) [9] and Support Vector Machine (SVM) [19]. All the selected algorithms were implemented with WEKA (Waikato Environment for Knowledge Analysis) [10] and were executed using default parameters. The forecasting performance was determined by a 10-fold cross-validation and was evaluated with three metrics, including the raw predictive accuracy, the AUC (area under curve) and the F-measure.

Statistical Results

The average forecasting performance of non-temporal and temporal models are compared in Table 1 along with the relative performance gain achieved by the temporal model. The relative performance gain is calculated as:

$$Gain_{relative} = \frac{P_{temp} - P_{non-temp}}{P_{non-tem}} \times 100\% \quad (8)$$

where P_{temp} and $P_{non-temp}$ refer to the performance metric readings of the temporal and non-temporal models. It can be observed that, for the non-temporal model, the predictive accuracy is only slightly better than random guesses, i.e. 50%. On the other hand, by utilizing the temporal information of the data, the temporal model achieves a considerable higher predictive accuracy. On average, the temporal model is 16.8% better in raw accuracy, 20.5% better in AUC and 17.5% better in F-measure. The performance advantage of the temporal model is also graphically illustrated in Figure 2.

To justify that the performance gain achieved by the temporal model is not due to random chances but statistically significant, a paired t-test was conducted. The results of the paired t-test are summarized in Table 2. We observe that, for all three performance metrics, the absolute performance gains achieved by the temporal model fall within the 95% confidence interval. Moreover, we also calculated the actual p-values. As shown in Table 2, all the p-values are less than 0.0001, which implies that the performance difference between the temporal and non-temporal models are extremely significant.

Model	Non-Temporal Approach			Temporal Approach			Relvative Gain		
	Accuracy	AUC	F-measure	Accuracy	AUC	F-measure	Accuracy	AUC	F-measure
AODE	51.4%	0.488	51.8%	62.4%	0.66	62.2%	21.4%	35.2%	20.1%
AdaBoost-J48	52.7%	0.53	52%	61.5%	0.632	61%	16.7%	19.7%	17.3%
BayesNet-K2	53.3%	0.56	51.4%	62.3%	0.648	62.5%	16.9%	15.7%	21.6%
BayesNet-TAN	52.2%	0.515	52.2%	62.0%	0.644	61.7%	18.8%	25%	18.2%
LBR	56.1%	0.549	55.9%	63.3%	0.647	62.9%	12.8%	17.9%	12.5%
LogReg	53%	0.547	52.8%	62.1%	0.645	62.6%	17.2%	17.9%	18.6%
Naive Bayes	52.7%	0.528	52.4%	61.9%	0.638	62%	17.5%	20.8%	18.3%
SVM	55.1%	0.55	55%	62.4%	0.613	62.7%	13.2%	11.5%	13.8%
Average	53.3%	0.533	52.9%	62.2%	0.641	62.2%	**16.8%**	**20.5%**	**17.5%**

Table 1: Performance comparison between the non-temporal and the prosed temporal forecasting approaches.

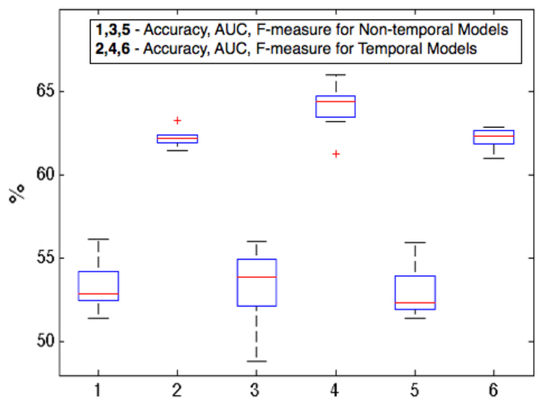


Figure 2: Boxplot for performance comparison between the non-temporal and the prosed temporal forecasting approaches.

	Accuracy	AUC	F-measure
Average Rel. Gain	16.8%	20.5%	17.5%
Average Abs. Gain	8.93%	0.106	9.25%
95% Conf. Interval	(7.88%, 9.96%)	(0.087, 0.128)	(7.91%, 10.58%)
p-value	< 0.0001	< 0.0001	< 0.0001

Table 2: Statistical significance of the performance difference between non-temporal and temporal forecasting approaches.

Discussion

It is demonstrated with experimental results and statistical analysis that the temporal forecasting model that utilizes the temporal information of ICP and related parameters significantly outperforms the non-temporal model. However, we also observe that the absolute accuracy of the temporal model is still not very satisfying. This is because, in this study, the temporal forecasting model is only proposed to demonstrate the advantage of temporal information utilization in ICP development trend forecasting, and the model is not fully optimized. To achieve a higher forecasting accuracy, the proposed temporal model can be improved in the following aspects: 1. Segmentation of data. In the current model, the time-series data is segmented into periodic windows with a fixed width. This strategy obviously lacks of flexibility. A better strategy will be to determine the width of periodic windows dynamically based on the variability of the time-series data. That is to say, when the data is relatively stable, a window with big width can be assigned; on the other hand, when the time-series data varies dramatically, windows with smaller width should be assigned to fully capture the development trends of the data. 2. Fitting of trend line. In the study, a simple linear regression algorithm is applied to fit the trend line to the time-series data. To enhance the performance of the model, more sophisticated line fitting algorithms and strategies can be explored. 3. Discretization of development trend. Based on Equation 2, the development trend of ICP is discretized into only three distinct classes: *elevate*, *stay* or *reduce*. This discretization method is fairly coarse and suffers from huge information loss. E.g. It fails to capture the difference between a 9 mmHg elevation in ICP and a 0.1 mmHg elevation. To address this, a finer and more adaptive approach can be employed. 4. Tuning of machine learning algorithms. In this study, all the machine learning algorithms were applied with the default setting. Parameter tuning is required to achieved the optimum predictive performance. E.g. for SVM, issues, including kernal selection, parameter tuning and optimization setting, all have to be carefully examined to achieve the optimum performance.

4. CONCLUSION

This study aims to demonstrate that temporal forecasting models that utilize temporal information of the historical readings of ICP and related parameters are superior, in terms of performance, compared with the non-temporal models. A systematic performance comparison framework has been developed to achieve this objective. Based on the experimental results, we observe that the temporal forecasting model outperforms the non-temporal model considerable, and, moreover, the performance difference was proven to be statistically significant.

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