be feedback processes so that the activity of one cell may affect the activity of the others in the vicinity [6]. Donor history, including factors such as infections and stress, is likely to be an important consideration when determining the fraction of time that exposures to RF fields lead to changes in neutrophil activity. The gradient of the electric fields can lead to small drift currents that can increase the rate at which C-AMP molecules strike the surface of the neutrophils [7] and thus can affect neutrophils' behavior. In short, our study indicates that the effects of RF exposure on neutrophil chemotaxis should be considered for further exploration in larger and more controlled studies.

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Complexity Analysis of Arterial Pressure During Periods of Abrupt Hemodynamic Changes

Roberto Hornero*, Mateo Aboy, Carlos Gómez, Daniel S. Hagg, and Charles R. Phillips

***Abstract*—In this communication, we estimated the Lempel–Ziv complexity (LZC) on over 40 h of arterial blood pressure (ABP) recordings corresponding to 18 mechanically ventilated animal subjects. In this study, all subjects underwent a period of abrupt hemodynamic changes after an induced injury involving severe blood loss leading to hemorrhagic shock, followed by fluid resuscitation using either lactated ringers or 0.9% normal saline. The LZC metric experienced a statistically significant increase ($p < 0.01$) immediately following the induced injury and a statistically significant reduction following the administration of fluid therapy ($p < 0.01$). These results indicate that LZC of ABP may be useful as a dynamic metric to assess fluid responsiveness.**

***Index Terms*—Arterial blood pressure (ABP), fluid responsiveness, hemodynamic changes, Lempel–Ziv complexity (LZC).**

I. INTRODUCTION

In this study, we analyzed the arterial blood pressure (ABP) signals during periods of abrupt hemodynamic changes using Lempel–Ziv complexity (LZC). This complexity metric was proposed by Lempel and Ziv [1] to evaluate the randomness of finite sequences. It is a nonparametric and simple-to-calculate measure of complexity for 1-D signals that does not require long data segments to be computed [2]. LZC has been widely applied in biomedical signal analysis. It has been used to study the electroencephalogram (EEG) signal of epileptic seizure [3] and the brain information transmission [4]. LZC was also applied to EEG signals in order to quantify the relationship between brain activity patterns and depth of anesthesia [5]. Moreover, EEG and magnetoencephalogram recordings from Alzheimer's disease patients have been analyzed with this measure [6], [7]. LZC has also been used to detect ventricular tachycardia and fibrillation [2], to characterize complexity of DNA sequences [8], and to quantify the complexity in uterine electromyography [9].

In [10], we studied the LZC and its interpretability in terms of classical signal processing concepts such as frequency, number of harmonics, frequency variability of signal harmonics, and signal bandwidth. Our results indicated that LZC was particularly useful as a scalar metric to estimate the bandwidth of random processes.

In this study, we estimated the LZC on over 40 h of ABP recordings corresponding to 18 mechanically ventilated animal subjects. All subjects underwent a period of abrupt hemodynamics changes after an induced injury involving severe blood loss, followed by fluid resuscitation.

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*R. Hornero is with the Grupo de Ingeniería Biomédica (GIB) E.T.S. Ingenieros de Telecomunicación University of Valladolid Camino del Cementerio s/no, 47011 Valladolid, Spain (e-mail: robhor@tel.uva.es).

C. Gómez is with the Grupo de Ingeniería Biomédica (GIB) E.T.S. Ingenieros de Telecomunicación University of Valladolid Camino del Cementerio s/no, 47011 Valladolid, Spain.

M. Aboy is with the Electronics Engineering Technology Department at Oregon Institute of Technology, Portland, OR 97006 USA.

D. S. Hagg and C. R. Phillips are with the Pulmonary and Critical Care Medicine Division, Oregon Health and Science University, Portland, OR 97201, USA.

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TABLE I
WEIGHT (WT), BLOOD LOSS DURING INJURY (EBL_INJ), BLOOD LOSS DURING RESUSCITATION (EBL_RES), CHANGE IN PPV, CARDIAC OUTPUT (CO), AND GLOBAL END-DIASTOLIC VOLUME (GEDV) VALUES, AT BASELINE (BASELINE), DURING INJURY AFTER THE BLEEDING STOPPED (BLEED STOP) AND AFTER POSTRESUSCITATION (POST RESUS)

SUBJECT ID.	WT (KG)	EBL_INJ (ML)	EBL_RES (ML)	CHANGE PPV INJ (%)	BASELINE CO (L/MIN)	BLEED STOP CO (L/MIN)	POST RESUS CO (L/MIN)	BASELINE GEDV (ML)	BLEED STOP GEDV (ML)	POST RESUS GEDV (ML)
Subj. 1	34.4	537.2	66.4	57.5	2.7	2.2	4.9	494	401	548
Subj. 2	39.0	494.9	37.6	36.7	2.7	1.7	3.6	421	327	443
Subj. 3	37.5	595.9	247.6	42.1	2.0	1.7	5.6	473	339	505
Subj. 4	38.0	883.2	324.9	43.8	3.7	2.7	5.8	539	392	521
Subj. 5	32.8	563.5	625.8	45.8	3.3	2.2	6.7	449	363	557
Subj. 6	35.0	543.2	135.8	27.6	3.2	2.5	5.3	461	442	513
Subj. 7	36.2	555.0	136.2	55.2	--	2.1	6.1	--	358	481
Subj. 8	37.3	642.6	484.5	67.4	3.3	2.2	4.6	463	375	423
Subj. 9	39.8	869.5	116.6	59.8	3.1	2.2	5.0	551	424	578
Subj. 10	36.2	763.6	302.3	30.4	2.6	2.2	5.1	590	488	612
Subj. 11	34.8	776.2	513.1	49.8	2.1	1.6	3.9	528	392	539
Subj. 12	33.4	844.6	86.3	49.8	2.8	2.0	2.9	485	461	430
Subj. 13	32.7	513.5	315.5	36.5	2.7	2.1	4.9	518	385	564
Subj. 14	34.2	1124.3	485.7	49.5	4.4	1.4	6.6	557	342	617
Subj. 15	30.5	896.3	216.2	49.2	2.3	1.3	4.6	470	259	430
Subj. 16	32.6	416.4	324.3	45.8	2.8	2.4	4.0	490	394	443
Subj. 17	32.8	850.9	292.0	51.1	2.8	1.8	7.0	475	276	511
Subj. 18	26.2	583.0	332.6	73.7	2.2	2.0	5.6	382	299	446
Mean ± SD	34.6 ± 3.3	691.9 ± 189.3	280.2 ± 168.4	48.4 ± 11.8	2.9 ± 0.6	2.0 ± 0.4	5.1 ± 1.1	490 ± 52	373 ± 60	508 ± 63

Prediction of fluid responsiveness in mechanically ventilated patients is a clinically significant problem. Several studies have investigated the predictive factors of fluid responsiveness in intensive care unit (ICU) patients. These studies concluded that dynamic parameters should be used preferentially to static parameters [11]. In contrast to standard static preload indices, stroke volume variation (SVV) and pulse pressure variation (PPV) showed good performance in predicting fluid responsiveness in patients with several critical conditions [12]–[14]. These dynamic parameters quantify changes in arterial pulse pressure as a measure of the sensitivity of the heart to changes in filling volume induced by changes in intrathoracic pressures with mechanical ventilation. These cyclic changes cause transient changes in stroke volume and thus PPV in preload dependent, but not in preload-independent states. Consequently, in this study, we investigated the LZC of ABP in mechanically ventilated subjects, because our previous results [10] involving the interpretation of LZC indicate that this complexity metric can capture the variability in ABP due to positive pressure ventilation.

II. LEMPEL–ZIV COMPLEXITY

LZC is a nonparametric measure for finite sequences related to the number of distinct substrings and the rate of their occurrence along the sequence, with larger values corresponding to more complexity in the data [1]. LZC analysis is based on a coarse-graining of the measurements, so the ABP signal must be transformed into a finite symbol string. In this study, we used the simplest way: a binary sequence conversion (zeros and ones). By comparison with the mean value T_d, the original data are converted into a 0-1 sequence. The binary string obtained is scanned from left to right and a complexity counter $c(n)$ is increased by one unit every time a new subsequence of consecutive characters is encountered in the scanning process. The complete computational algorithm of $c(n)$ is described in [5].

III. SUBJECTS AND DATA

The database used in this study included 18 ABP signals sampled at 50 Hz obtained from 18 mechanically ventilated crossbred Yorkshire swine (over 40 h of ABP recordings). These recordings were acquired at the Animal Laboratory of the Oregon Health and Science University (Portland, OR). The subjects underwent Grade V liver injury after splenectomy, while receiving mechanical ventilated, and general anesthesia with isoflurane. All subjects in the database underwent a period of abrupt hemodynamic changes after an induced Grave V liver injury involving severe blood loss resulting in hemorrhagic shock, followed by fluid resuscitation with either 0.9% normal saline or lactated ringers solutions. For each subject, Table I details weight, blood loss during injury, blood loss during resuscitation, and change in PPV. Cardiac output and global end-diastolic volume values at baseline, during injury after the bleeding stopped and after postresuscitation were also showed. The study protocol was reviewed and approved by the Institutional Review Board at Oregon Health and Science University.

Before LZC estimation, the ABP signals were bandpass filtered to eliminate the low-frequency components (baseline trend) and remove the mean pressure [direct current (dc) component]. We used a bandpass finite-impulse response (FIR) filter with cutoff frequencies of 0.1 and 10 Hz. This guaranteed that our LZC estimations obtained from the ABP signal were based exclusively on the ABP morphology, because both the mean ABP and the baseline trend were eliminated with the filter. The 10-Hz FIR low-pass filter was used to eliminate high-frequency noise due to artifact. Each filtered ABP signal was windowed into segments of 10 s in duration. LZC was estimated for each segment.

Statistical analysis was aimed at determining the statistical significance of the mean LZC changes in ABP signals before injury, immediately following injury, and after fluid resuscitation for each of the 18 subjects. Mean LZC values were obtained for 10-min windows immediately before injury, during hemorrhagic shock (after injury), and after fluid resuscitation.

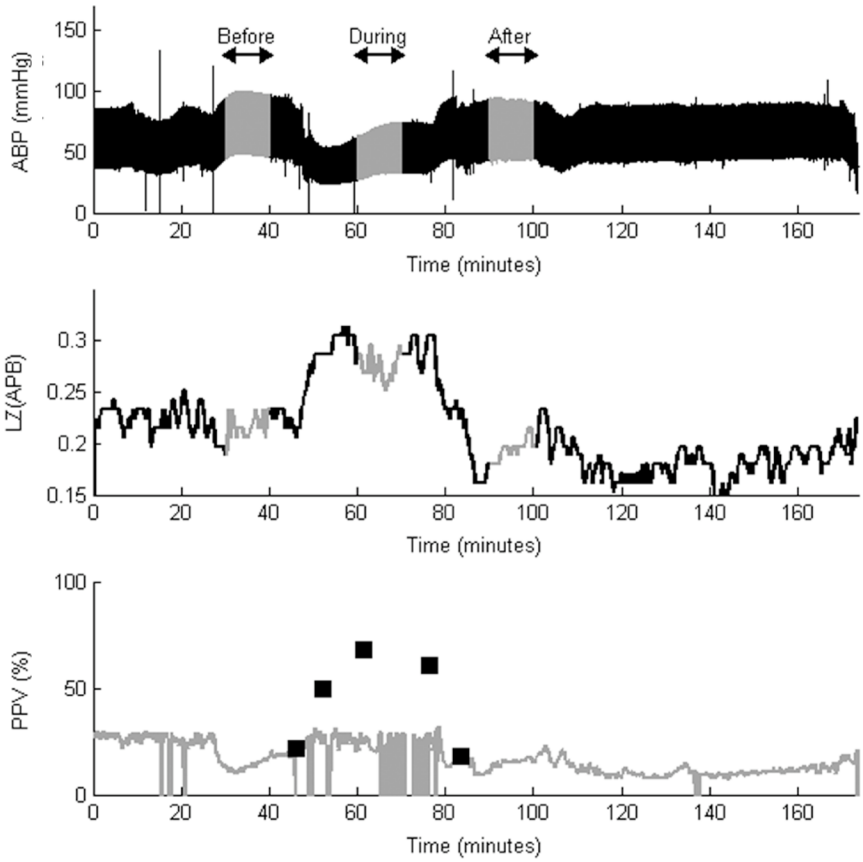

Fig. 1. Representative example of an ABP signal during this experiment. LZC was evaluated on the ABP signal before injury ("before"), during hemorrhagic shock after injury ("during"), and after fluid resuscitation ("after"), using a moving window of 10 s. Bottom plot shows the estimated PPV using a commercial monitoring system (PICCO®). Five "gold standard" PPV manual annotations calculated by trained experts during periods of abrupt ABP changes are shown as black squares.

IV. Results

LZC was evaluated on the high-pass filtered ABP signal using a moving window of 10 s to guarantee that the LZC estimate was based exclusively on the ABP pulse morphology and not on the mean ABP. Mean LZC values of ABP segments were obtained from the 18 subjects before injury, during hemorrhagic shock after injury, and after fluid resuscitation. The mean LZC was higher in the region immediately following the Grade V liver injury [0.2905 ± 0.0407; mean $\pm$ standard deviation (SD)] than during the stable region preceding injury (0.1905 ± 0.0150) and the recovering period after fluid resuscitation (0.1821 ± 0.0227). Both the mean increase in LZC from the state of normal ABP (stable region) to the severed blood loss region, and the reduction in LZC following fluid resuscitation were determined to be statistically significant using the multiple comparisons Sheffé's procedure ($p < 0.01$). There were no statistically significant differences in LZC between stable region and recovering region following fluid resuscitation [$p = 0.67 > 0.01$, not significant (NS)]. Moreover, receiver operating characteristic (ROC) curves were used to assess the ability of our method to identify baseline, hemorrhagic shock, and recovery periods. Mean LZC values, obtained for the 10-min windows immediately before injury, during hemorrhagic shock, and after fluid resuscitation, were used in this statistical analysis. A ROC curve was applied to our complexity results in order to evaluate the ability of LZC in discriminating severed blood loss region from the recovering period. Specificity and sensitivity values of 100% were achieved with a 0.23 optimum threshold, indicating that all mean LZC values from the region during hemorrhagic shock after injury are higher than those obtained after fluid resuscitation. Another ROC analysis was used to determine the optimum threshold between baseline and hemorrhagic shock regions. We obtained an accuracy of 100% at a 0.23 cutoff point (100% sensitivity, 100% specificity).

The top plot of Fig. 1 shows an example of the ABP signals analyzed in this study. In this figure, we indicate examples of the 10-min ABP segments used for analysis. The bottom plot shows PPV estimated with a commercial monitoring system (PiCCO® Pulsion Medical Systems, Munich, Germany). The PiCCO® physiological monitor has been used extensively in research studies for hemodynamic monitoring [12], [15]. Additionally, we plot the gold-standard PPV manually annotated by trained experts at five time instances during the period of abrupt hemodynamic changes. These expert manual annotations (black squares in the figure) provide a "gold standard" for algorithm comparison and validation. Fig. 1 shows that PPV assessed by the PiCCO® system performed well in regions of normal hemodynamic changes. However, the algorithm failed to accurately estimate the PPV during the periods between the injury and fluid resuscitation, and consequently it failed to predict fluid responsiveness during the periods of severe blood loss. Table II details LZC values, PPV PiCCO®, and PPV manual annotations calculated by trained experts, before injury, during hemorrhagic shock after injury, and after fluid resuscitation.

Pearson's linear correlation coefficient has been used to compare the performance of PiCCO® system and our method. Pearson's coefficient between PPV annotations by trained experts and mean LZC values (0.667) is higher than the coefficient obtained between PPV manual annotations and PiCCO® system results (-0.425), indicating that our method based on LZC works better than PiCCO® system in the determination of PPV during regions of abrupt hemodynamic changes.

TABLE II
LZC VALUES (LZC), PPV PICCO AND PPV MANUAL ANNOTATIONS CALCULATED BY TRAINED EXPERTS AT BASELINE (BASELINE), DURING INJURY AFTER THE BLEEDING STOPPED (BLEED STOP), AND AFTER POSTRESUSCITATION (POST RESUS)

SUBJECT ID.	BASELINE *LZC*	BLEED STOP *LZC*	POST RESUS *LZC*	BASELINE PPV PICCO (%)	BLEED STOP PPV PICCO (%)	POST RESUS PPV PICCO (%)	BASELINE PPV (%)	BLEED STOP PPV (%)	POST RESUS PPV (%)
Subj. 1	0.1772	0.2890	0.1847	19	26	7	15.7	56.0	5.9
Subj. 2	0.2176	0.2340	0.1892	22	17	11	16.3	43.1	13.2
Subj. 3	0.1769	0.2484	0.1464	15	27	5	13.0	53.0	3.4
Subj. 4	0.1775	0.3135	0.1686	19	0	0	10.3	70.9	14.4
Subj. 5	0.1993	0.3111	0.1961	20	0	0	19.1	71.2	10.4
Subj. 6	0.1853	0.2555	0.1972	17	30	12	16.7	63.2	12.9
Subj. 7	0.1715	0.2806	0.2218	17	30	18	15.3	47.9	19.5
Subj. 8	0.1739	0.2454	0.1635	14	32	10	14.9	41.9	9.0
Subj. 9	0.1847	0.3371	0.1931	19	29	13	25.2	60.4	14.7
Subj. 10	0.1856	0.2498	0.1551	9	27	9	21.7	60.6	10.8
Subj. 11	0.1966	0.3007	0.1775	13	15	7	11.2	70.9	6.6
Subj. 12	0.1931	0.2977	0.2295	18	0	19	20.7	71.9	22.1
Subj. 13	0.2155	0.2738	0.1961	0	24	19	21.7	68.1	17.8
Subj. 14	0.2229	0.2770	0.1491	13	0	6	16.9	80.1	6.6
Subj. 15	0.1865	0.3565	0.1853	13	28	10	11.1	67.1	6.4
Subj. 16	0.1913	0.2516	0.1671	15	0	10	14.5	58.6	13.5
Subj. 17	0.1847	0.3703	0.1686	25	16	5	13.7	86.6	3.2
Subj. 18	0.1886	0.3374	0.1898	15	36	7	19.2	73.3	6.0
Mean ± SD	0.1905 ± 0.0150	0.2905 ± 0.0407	0.1821 ± 0.0227	15.7 ± 5.6	18.4 ± 13.5	9.2 ± 5.8	16.5 ± 4.1	63.6 ± 12.1	10.9 ± 5.5

These results suggest that while the PiCCO® system is a useful tool to estimate PPV and predict fluid responsiveness in situations where normal hemodynamic changes are expected, it may not provide accurate PPV values in certain situations involving abrupt hemodynamic changes. These results also demonstrate that despite its simple definition, PPV is a difficult parameter to estimate automatically. On the other hand, LZC can be calculated directly using a simple well-defined computational algorithm and our results indicate that it may be useful as a dynamic parameter to assess fluid responsiveness.

V. DISCUSSION

We analyzed ABP signals during periods of abrupt hemodynamic changes caused by severe blood loss from Grade V liver injury in 18 anesthetized mechanically ventilated animal subjects. We estimated the LZC from these ABP signals before injury, immediately following injury (during hemorrhagic shock), and after fluid resuscitation. Our results showed that LZC of ABP increased as subjects progressed from a stable state of normal hemodynamics to severe blood loss ($p < 0.01$). Moreover, we found a statistical significant decrease in LZC following fluid resuscitation ($p < 0.01$). As shown in the top plot of Fig. 1, the results of our study also showed that spontaneous elevation in mean blood pressure following cessation of hemorrhage occurred following the injury.

LZC is related to the number of distinct substrings and the rate of their recurrence along the given sequence, with larger values corresponding to more complexity in the data. Based on our simulation studies involving LZC, the LZC can be interpreted as a metric that quantifies the bandwidth of the signal harmonics [10]. Thus, increases in LZC after an induced injury involving blood loss and hemorrhagic shock correspond to an increase in the stochastic variability of ABP signals. LZC is higher in amplitude modulated quasi-periodic signals such as ABP during regions of severe pulse pressure changes due to respiration. LZC can capture directly the additive, amplitude modulation, and frequency modulation respiratory effects on ABP. Respiratory changes in ABP have been shown to have clinical use for hemodynamic monitoring to predict fluid responsiveness in mechanically ventilated patients in a variety of critical conditions [12]–[14].

Our preliminary results indicate that LZC may be used as a dynamic parameter to predict fluid responsiveness and to perform hemodynamic monitoring. LZC may be related or be complementary to other established dynamic parameters such as PPV or SVV. A potential advantage of LZC over PPV and SVV is that can be calculated directly from the ABP signal using a simple well-defined computational algorithm. On the other hand, automatic estimation of PPV and SVV requires the use of sophisticated algorithms [16].

Some limitations of our research work merit consideration. First, our study was conducted analyzing data already collected (i.e., retrospective data). Moreover, fluid responsiveness has not been investigated. Thus, future research includes designing and conducting a prospective study to determine the positive and negative predictive value of LZC as a dynamic parameter to estimate fluid responsiveness, and to study the relationship between PPV, SVV, and LZC. If the predictive power of LZC is comparable to that of PPV or if PPV can be estimated from LZC analysis of ABP in mechanically ventilated subjects, then LZC would be an ideal dynamic parameter for bedside hemodynamic monitoring, because it can be easily calculated.

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DCT-Based Complexity Regularization for EM Tomographic Reconstruction

Max Mignotte*, Jean Meunier, and Jean-Paul Soucy

***Abstract*—This paper introduces a simple algorithm for tomographic reconstruction based on the use of a complexity regularization term. The regularization is formulated in the discrete cosine transform (DCT) domain by promoting a low-noise reconstruction having a high sparsity in the frequency domain. The resulting algorithm simply alternates between a maximum-likelihood (ML) expectation-maximization (EM) update and a decreasing sparsity constraint in the DCT domain. Applications to SPECT reconstruction and comparisons with a classical estimator using the best available regularization terms are given in order to illustrate the potential of our reconstruction technique.**

***Index Terms*—Discrete cosine transform (DCT), expectation-maximization (EM), reconstruction, SPECT tomography.**

I. Introduction

A major challenge for Bayesian image reconstruction algorithms is the design of efficient image prior models summarizing the intrinsic properties of the object being evaluated. This allows to restrict the types of reconstructions (*a priori*) defined as acceptable solutions.

Except for wavelet-based regularization methods, little attention has been given to the use of complexity-based regularization in Bayesian tomographic reconstruction. Wavelet-based methods exploit the sparsity of the wavelet coefficients by using either prefiltering of the acquired raw-data [1], postfiltering of the reconstructed images [2], [3], or a regularization strategy during the optimization process, using a maximum *a posteriori* (MAP) formulation [4]–[6].

In such a framework, the simple discrete cosine transform (DCT) could also be used to constrain the problem of reconstruction from projections. As opposed to the widely used wavelet transform, this transform can be used locally, by using a strategy of local filtering on (overlapping) individual blocks. Therefore, this local filtering approach also allows to take into account, indirectly, the nonstationarity property of the object being reconstructed.

What we propose in this paper is a simple and efficient, DCT-based reconstruction method which alternates between a maximum-likelihood (ML) EM update and DCT-based filtering, using an easily implemented decreasing thresholding rule. The potential of this reconstruction technique will be illustrated through a series of examples reconstructed both with this approach and a more classic estimator using the best available regularization terms.

II. Bayesian Tomographic Reconstruction

Reconstructing an emission tomography study can be considered in a statistical framework where we consider a pair of random fields (Y, X),

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*M. Mignotte is with the Département d'Informatique et de Recherche Opérationnelle (DIRO), Université de Montréal, C.P. 6128, Succ. Centre-ville, Montréal H3C 3J7, QC, Canada (e-mail: mignotte@iro.umontreal.ca).

Meunier is with the Département d'Informatique et de Recherche Opérationnelle (DIRO), Université de Montréal, Montréal H3C 3J7, QC, Canada .

J.-P. Soucy is with the Research Center of the University of Montréal Medical Center, Montréal H2L 4M1, QC, Canada (e-mail: jean-paul.soucy.chum@ssss.gouv.qc.ca).

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