Real-Time Prediction of Respiratory Motion Traces For Radiotherapy with Ensemble learning

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***Abstract*— In this paper, we introduce a hybrid method for prediction of respiratory motion to overcome the inherent delay in robotic radiosurgery while treating lung tumors. The hybrid method adopts least squares support vector machine (LS-SVM) based ensemble learning approach to exploit the relative advantages of the individual methods local circular motion (LCM) with extended Kalman filter (EKF) and autoregressive moving average (ARMA) model with fading memory Kalman filter (FMKF). The efficiency the proposed hybrid approach was assessed with the real respiratory motion traces of 31 patients while treating with CyberKnife^{TM}. Results show that the proposed hybrid method improves the prediction accuracy by approximately 10% for prediction horizons of 460 ms compared to the existing methods.**

I. Introduction

Stereotactic body radiotherapy (SBRT) aims to deliver ablative radiation dose to the targeted tumor tissues with minimal exposure to the surrounding normal tissues by tracking the real-time movement of tumor tissues [1]. To uphold the targeted tumor location details, several techniques have been developed in the recent past [1]–[3]. The commercially available robotic devices such as CyberKnife and VERO, employ the correlation technique developed in [2] to attain the real-time movement of tumor. The technique proved that the movement of external body recorded with motion capture equipment can be a good estimator for the tumor movement [1]. Nevertheless, current commercial systems require compensation for the inevitable delay of 120ms - 400ms (varies with devices [2]) between the actual movement of tumor and the movement obtained from the correlation model. The major sources of delay are inherent mechanical limitation, image acquisition and processing time. To overcome the delay, this study focuses on enhancing the real-time respiratory motion prediction technique which is predominant in tumor movement.

In recent past, several techniques have been proposed for predicting the respiratory motion [1]–[5]. Few techniques are: local circular motion (LCM) with extended Kalman filter (EKF) [4], Kernel density estimator (KDE) [3] and support vector regression (SVRpred) [5]. A comparative analysis for most of the prediction techniques can be found in [2], [4]. Of all the methods, LCM-EKF exhibited better estimation capabilities with less computational complexity [4]. Despite, the performance of LCM-EKF prone to large prediction lengths (say approx. 400ms) and subject-specific irregularities in breathing patterns. To overcome the limitations with LCM-EKF, in this paper, a hybrid method based on ensemble learning technique is proposed for estimation of motion traces. Ensemble learning is one of the successful techniques to yield synergistic algorithms for time series prediction or classification by aggregating individual methods (first-level methods) with a second-level algorithm.

The proposed hybrid method exploits the relative advantages of individual methods LCM-EKF and another classical method autoregressive moving average (ARMA) method with least-squares support vector machines (LS-SVM) as the second-level algorithm. The proposed method is experimentally assessed with the motion traces obtained from 31 patients while treating with CyberKnife. Results show that the proposed hybrid method exhibits better prediction performance compared to the existing methods.

II. Methods and Materials

A. Methods

Throughout this article, s represents the respiratory motion and $\hat{s}$ is the predicted trace. The prediction horizon is represented as k. $\hat{s}_{t+k}$ denotes the k samples ahead predicted value at t^{th} sample. For individual algorithms, the predicted values are represented with $\hat{s}^{LCM}_{t+k}$ and $\hat{s}^{ARMA}_{t+k}$.

1) LCM-EKF: LCM-EKF characterizes the respiratory motion as a local circular motion in a plane augmented with its axis and angular velocity as a part of the system state [4].

The state-space representation of LCM model is given with:

- *state equation*: $\mathbf{x}(t+1) = f(\mathbf{x}(t)) + \nu(t)$
- *measurement equation*: $\mathbf{s}(t) = H\mathbf{x}(t) + \omega(t)$

where $\mathbf{x}(t) = [x(t)\ \dot{x}(t)\ \dot{y}(t)\ \Omega(t)]$ represents position and $y(t)$ represents the auxiliary augmented axis. The state evolution function is

$$f(\mathbf{x}(t)) = \begin{pmatrix} 1 & \dfrac{\sin\Omega(t)T}{\Omega(t)} & -\dfrac{1-\cos\Omega(t)T}{\Omega(t)} & 0 \\ 0 & \cos\Omega(t)T & -\sin\Omega(t)T & 0 \\ 0 & \sin\Omega(t)T & \cos\Omega(t)T & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix}\mathbf{x}(t),$$

$H = [1\ \ 0\ \ 0\ \ 0]$, $\nu(t)$ represents process noise with covariance $\mathbf{E}[\nu(t)\nu(t)^T] = \mathrm{diag}[q_1T^3,\ q_2T,\ q_3T,\ q_4T]$

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where q_1, q_2, q_3, q_4 characterize the possible changes in $x(t)$, $\dot{x}(t)$, $\dot{y}(t), and$ $\Omega(t)$ respectively, T represents sampling period and $\omega(t)$ represents measurement noise with variance $\mathbf{E}[\omega(t)\omega(t)^T] = \sigma_\omega^2$.

Multi-step prediction for k samples ahead, with LCM is given with (1):

$$\begin{aligned}\hat{s}(t+k|t) &= \hat{x}(t|t) + \frac{\sin\hat{\Omega}(t|t)kT}{\hat{\Omega}(t|t)}\hat{\dot{x}}(t|t) \\ &- \frac{1-\cos\hat{\Omega}(t|t)kT}{\hat{\Omega}(t|t)}\hat{\dot{y}}(t|t). \qquad (1)\end{aligned}$$

A first-order EKF was employed to update the LCM parameters iteratively. For more details about LCM-EKF, see [4].

2) ARMA-FMKF: Multi-step prediction model for ARMA is only possible under the assumption the signal characteristics do not change (stationary) in a given prediction horizon. This assumption does not hold in our case since respiratory motion is non-stationary. In order to reduce the effect of prior measurements, fading memory Kalman filter (FMKF) was employed to update the state dynamics.

The state-space model of the ARMA (p, q) is:
Measurement equation: $s(t) = \mathbf{w}^T(t)\ \mathbf{\Phi}(t) + \varepsilon(t)$ and
State equation: $\mathbf{w}(t+1) = \mathbf{w}(t) + \eta(t)$
where $\mathbf{w} = [-w_1 \cdots - w_p\ \ - w_1 \cdots - w_q]^T$ represents the weights (regression coefficients), $\Phi(t) = \begin{bmatrix} s(t-1) & \cdots & s(t-p) & e(t-1) & \cdots & e(t-q)\end{bmatrix}^T$ represents delayed inputs, $\eta(t)$ represents the state noise that was modeled as a zero-mean white-noise with covariance $\mathbf{Q}$ and $\varepsilon(t)$ represents the measurement noise that was modeled with a zero-mean white-noise with covariance R [6].

The multi-step prediction model with ARMA-FMKF for h samples can be obtained as:

$$\hat{s}(t+k) = \hat{\mathbf{\Phi}}(t+k)^T\hat{\mathbf{w}}(t+k) \qquad (2)$$

where

- $\hat{\mathbf{w}}(t+k) = \hat{\mathbf{w}}(t)$ (the weights vector remains constant for t to $(t+k)$ samples)
- $\hat{\mathbf{\Phi}}(t+l) = \begin{matrix}[\hat{s}(t-l-1) \ \cdots \ \hat{s}(t-l-p) \\ e(t-1) \ \cdots \ e(t-q)]^T;\end{matrix}$

  $l = 1, 2, \cdots, h$. (the input vector $\hat{\mathbf{\Phi}}(t)$ is updated iteratively)

The FMKF update equations are given by [6], [7]:

$$\begin{aligned}\hat{\mathbf{w}}(t+1) &= \hat{\mathbf{w}}(t) + \mathbf{K}(t)(s_t - \Phi^T(t)\hat{\mathbf{w}}(t)) \\ e(t) &= s(t) - \Phi(t)^T\hat{\mathbf{w}}(t) \\ \mathbf{K}(t) &= \frac{\mathbf{P}(t-1)\Phi(t)}{\Phi^T(t)\mathbf{P}(t-1)\Phi(t) + R} \\ \mathbf{P}(t) &= \lambda((\mathbf{I} - \mathbf{K}(t)\Phi^T(t))\mathbf{P}(t-1)) + \mathbf{Q}\end{aligned}$$

where $e(t)$ is the prediction error; $\mathbf{K}(t)$ is the Kalman gain vector; $\mathbf{P}(t)$ is the error covariance matrix; λ is the forgetting factor.

3) The Proposed Hybrid Method (HM): The general framework of the proposed hybrid method is illustrated in Fig. 1.

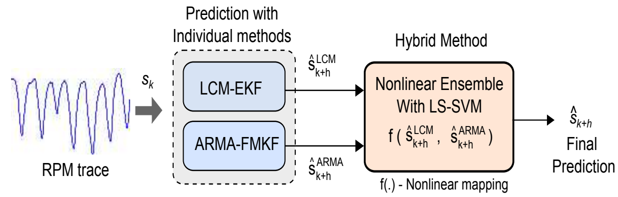

Fig. 1. Block diagram representation for the proposed hybrid method

The prediction with the hybrid method can be given by:

$$\hat{s}_{t+h} = f(\hat{s}^{LCM}_{t+k}, \hat{s}^{ARMA}_{t+k}) \qquad (3)$$

where $f(.)$ is a nonlinear function and determined offline by using LS-SVM with N training data pairs, that is, $\{s(t), y(t)\}_{t=1}^N$, where $s(t) = [\hat{s}^{LCM}_{t+k}\ \hat{s}^{ARMA}_{t+k}]$ is input vector and $y(t) = s(t+k)$ as the corresponding output variable. The regression model for LS-SVM is in the form:

$$y = \omega^T\varphi(s) + b \qquad (4)$$

where ω is the weight vector and b is the bias. We optimized the estimation of f with LS-SVM:

$$\min_{\omega,b,e} J(\omega, \xi) = \frac{1}{2}\omega^T\omega + C\sum_{t=1}^{N} e^2(k)$$

subject to the constraints $y(t) = \omega^T\varphi(s(t)) + b + e(t);\ t = 1, 2, \cdots, N$; where C is a regularization constant and $e(t)$ is the estimation error.

The final prediction model of hybrid method with LS-SVM is

$$\begin{aligned}\hat{s}_{t+k} = \ & f(\hat{s}^{LCM}_{t+k}, \hat{s}^{ARMA}_{t+k}) \\ = \ & \textstyle\sum_{i=1}^N \alpha_i K(s(i), s(t)) + b;\ t = N+1, \cdots, l. \qquad (5)\end{aligned}$$

where $K(.,.)$ represents the radial basis kernel function, α represents Lagrangian multipliers.

B. CyberKnife Respiratory motion database

The respiratory motion database employed in this paper was recorded during the radioactive therapy with CyberKnife at Georgetown university hospital from 31 patients. The database contains 304 motion traces obtained from all subjects. The traces were recorded using optical tracking system, Synchrony respiratory motion tracking system by Accuracy, Inc. $3D$ motion traces are recorded from all the three markers placed on the patient. The principal components obtained with principal component analysis (PCA) from the $3D$ motion traces of a marker are considered as the motion trace of the corresponding marker [2]. Thereby, three traces are acquired from three markers, namely m_1, m_2 and m_3. The sampling frequency was 26 Hz. For more information on the recording procedure and pre-processing of the motion traces, see [2] and [8].

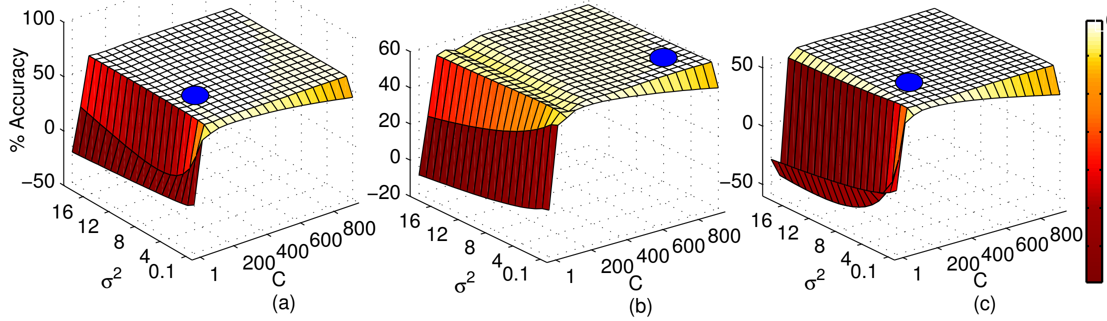

Fig. 2. Optimal parameter selection for Subject #1

C. Performance Indices

The measures employed to quantify the prediction performance are prediction accuracy and relative MSE defined with

$$\text{Accuracy} = \frac{\text{RMS}(s) - \text{RMS}(e)}{\text{RMS}(s)} \times 100 \quad (6)$$

$$\text{Relative MSE}(\hat{s}_h, s) = \frac{\text{RMS}(\hat{s}_h - s)}{\text{RMS}(\breve{s}_h - s)} \quad (7)$$

where $\text{RMS}(s) = (\sum_{k=1}^{k=m} s_k^2/m)^{0.5}$, m is the number of samples, s_k is the input signal at instant k and the error e is the mismatch between the actual and predicted signals. $\breve{s}_h$ represents the signal s delayed by h samples.

III. Results

A. Optimal Parameter Selection

For adaptive prediction methods LCM-EKF and ARMA-FMKF, appropriate initialization of parameters is necessary to obtain good performance. The parameters and initialization for LCM-EKF are well documented [4]. For ARMA-FMKF model, Akakie information criterion (AIC) [9] identified $ARMA(16, 1)$ as the optimal order for the respiration motion traces employed in this study. The regression coefficients are zero initialized. The parameters and the initialization for both the methods are provided in Table. I.

TABLE I
Methods & Parameters

Method	Model parameters and initial conditions
LCM-EKF [4]	$q_1 = 0.2$; $q_2 = 2^{-4}$; $q_3 = 2^{-3}$; $R = 0.0001$; $\mathbf{P}_0 = 0.01 \times \mathbf{I}$;
ARMA-AFKF	$p = 16$ $q = 1$; $R = 0.01$; $\mathbf{Q} = 0.01 \times \mathbf{I}$; $\mathbf{P}_0 = 0.01 \times \mathbf{I}$;

The parameters that require careful selection to attain optimal ensemble with LS-SVM are regularization constant (C), radial bias function (RBF) Kernel variance (σ^2) and number of training sample (N) [10]. We conducted extensive grid search for these parameters to identify the optimal initialization.

To identify the appropriate N for all respiratory motion traces in the database, we tested various values of N. Due to its semi-periodic characteristics with limited spectral range, we empirically identified that $N = 1000$. Larger values of N improves the prediction accuracy only marginally. Moreover, larger values of N will increase the computational complexity considerably.

To identify the appropriate initialization for C and σ^2, an extensive grid search was conducted for wide range of values ($0 < C < 1000$ and $0.1 < \sigma^2 < 20$). Results obtained for Subject #1 are shown in Fig. 2. The plots represent obtained average prediction accuracy for all traces of the subject. The region with highest prediction accuracy (white in color) is the desired region to pick the optimal initialization for the parameters. The results obtained for Subject #1, shown in Fig. 2, show a vast desirable region for m1 and m3 whereas m2 has a narrow such region. One can pick any set of values for C and σ^2 from the desired region and it will yield better prediction of traces compared to the set of values selected form the colored region. Similar analysis was conducted for the rest 30 subjects in the database. The optimal initialization is identified individually from the grid search for each maker of every subject.

B. Performance analysis for prediction horizon of 460ms

In this analysis, results of the proposed hybrid approach are compared with the results obtained by employing the LCM-EKF and the ARMA-FMKF methods. The horizon was selected considering the typical latencies involved in commercial robotic systems such as CyberKnife (approximately 230ms), and multi-leaf collimators (approximately 460ms) [11]. Comparative performance analysis for all methods is performed on the complete database for both prediction horizons.

Prediction performance obtained for all markers of a subject for a given method is similar. Thereby, to quantify the performance, $\%Accuracy$ and relative RMSE for all markers and traces for a subject are averaged. The prediction accuracies obtained with all methods for all 31 subjects are shown in Fig. 3. Results show that, the proposed hybrid method provides better prediction accuracy and has less relative RMSE compared to both LCM-EKF and ARMA-FMKF for all subjects. Further, statistical analysis was performed over all the subjects and the results obtained are shown in Fig. 4. There was a significant main effect of the predictor ($F(2, 60) = 130.60, n = 31, p < 10^{-4}$). Post-

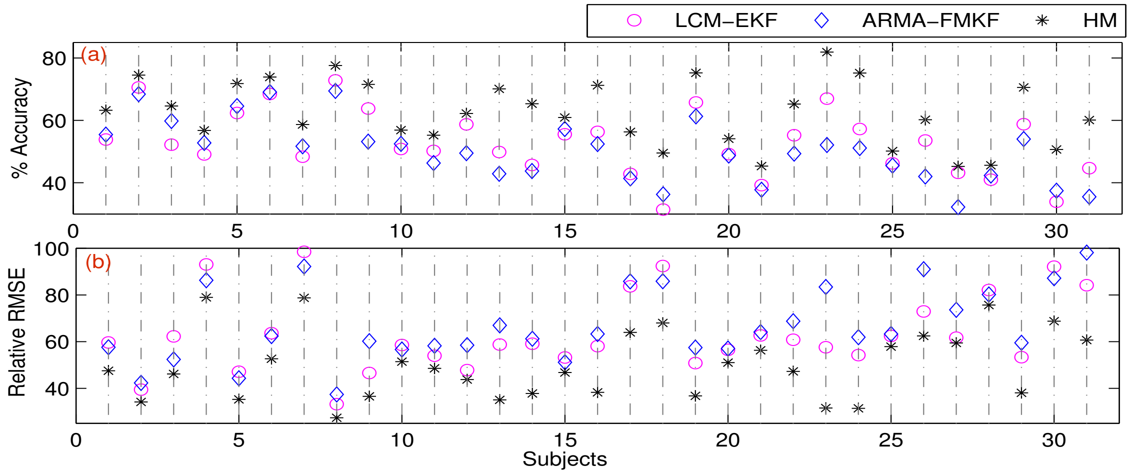

Fig. 3. Performance analysis of all methods in presence of 460ms delay for complete database (a) Prediction accuracy

hoc pair-wise t-test showed that the proposed hybrid method outperformed both LCM-EKF ($p < 10^{-4}$) and ARMA-FMKF ($p < 10^{-4}$) methods. For completeness, we report that the performance of LCM-EKF was better than that of ARMA-FMKF ($p < 10^{-4}$). From Fig. 4, it can be seen that the mean value of prediction accuracy obtained with the proposed method over all subjects achieved an improvement of approximately 10% compared to both individual methods LCM-EKF and ARMA-FMKF.

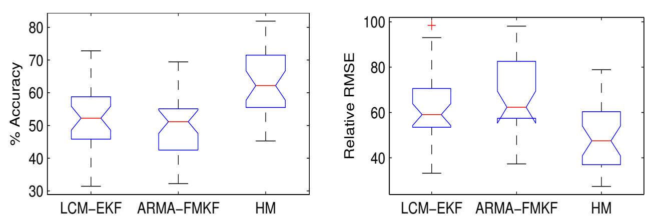

Fig. 4. Statistical analysis for prediction performance of all methods with prediction horizon as 460ms

To further analyze the performance, the improvement in prediction accuracy for all traces is tabulated in Table. II. The number of traces with prediction accuracy in the range of 60 to 70% and 70 to 80% for hybrid method are approximately three times compared to both individual methods.

TABLE II

COUNT OF TRACES REFLECTING SPREAD OF PREDICTION ACCURACIES - HORIZON: 460MS

Method	%Accuracy			
	< 50%	50 to 60%	60 to 70%	70 to 80%
LCM-EKF	103	101	52	18
ARMA-FMKF	144	100	48	12
Hybrid Method	60	64	126	54

IV. CONCLUSIONS

To enhance the prediction performance of respiratory motion traces, a hybrid method which is an ensemble of LCM-EKF and ARMA-FMKF with LS-SVM is proposed in this paper. To evaluate the performance of proposed hybrid method, analysis was conducted on the database collected form 31 subjects with CyberKnife. The analysis was performed with prediction horizons 460 ms which is well in line with the commercially available robotic radiotherapy devices. Results show that, the proposed hybrid method provides overall improvement of approximately 10% in prediction accuracy for both prediction horizons compared to LCM-EKF.

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