A Kalman based approach with EM optimization for respiratory motion modelling in medical imaging

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Abstract—Respiratory motion degrades quantitative and qualitative analysis of medical images. Estimation and hence correction of motion commonly uses static correspondence models between an external surrogate signal and internal motion. This work presents a patient specific respiratory motion model with the ability to adapt in the presence of irregular motion via a Kalman filter with Expectation Maximisation for parameter estimation. The adaptive approach introduces generalizability allowing the model to account for a broader variety of motion. This may be required in the presence of irregular breathing and with different sensors monitoring the external surrogate signal. The motion model framework utilizing an adaptive Kalman filter approach is tested on dynamic MRI data of nine volunteers and compared to a state-of-the-art static total least squares approach. Results demonstrate the framework is capable of reducing motion to the order of $< 3\text{mm}$ and is significantly ($p < 0.001$) more effective in the presence of irregular motion, assessed using the F test for model comparison. Utilizing the total sum of squares of estimated vector field error from the calculated ground truth, we observe approximately a fifty percent reduction in root mean square error and thirty percent reduction in standard deviation utilizing the Kalman model (EKF) in comparison to a static counterpart.

Index Terms—Machine learning, Respiratory motion correction, Bayesian inference, Kalman filtering, Optimization

I. INTRODUCTION

RESPIRATORY motion is a common obfuscating issue in diagnostic imaging and image guided interventional procedures [1]. Respiratory motion causes a degradation of effective spatial resolution in Positron Emission Tomography (PET) imaging [2], ghosting and blurring artefacts in Magnetic Resonance Imaging (MRI) [3] and decreased navigation accuracy in image guided interventional procedures [4]. Numerous strategies to mitigate these effects have previously been proposed for the varying imaging situations. The most basic form fall into motion prevention for example through using breath-holds or training the patient to breathe at certain points during an image acquisition. More advanced approaches attempt to construct acquisition strategies to reduce the effect of the artefact by for example acquiring images faster and / or reordering the images to particular phases of motion. Current state of the art methods attempt to estimate the motion during image acquisition to allow for its subsequent correction and hence

removal of the aforementioned artefacts. The estimated motion, which is not observed and can be considered hidden during PET image acquisition is achieved using a motion model. The motion model is constructed during a training phase and commonly builds an association between the external surrogate of internal motion and the underlying internal motion which is often captured by an anatomical imaging modality such as CT or MRI. The motion model can therefore be defined as a process that takes some external surrogate data as input and produces an estimate of hidden internal motion as output [5]. If performed accurately subsequent correction of PET imaging data using this estimated internal motion results in amelioration of the motion induced image artefacts resulting in increased diagnostic and quantitative accuracy and confidence in interpreting PET images.

Many methods of motion modelling use or are constructed using four-dimensional computer tomography (4DCT) [6], [7] and are thus built upon an average or re-binned respiratory cycle. Any approach built upon a single respiratory cycle neglects irregular inter-cycle respiratory motion often encountered in the clinical setting [8] and thus serves as a current limitation of more advanced motion modelling techniques. Four dimensional Magnetic Resonance Imaging (MRI) [9] allows the acquisition of dynamic volumetric images with no radiation burden and lends itself well to assessing the applicability of respiratory motion models and their ability to estimate inter-cycle variability [10]. Clinically however, consideration must be given to avoid motion blurring during fast 4D-MRI acquisition sequences for respiratory motion modelling. If the MR motion model is to be used to correct PET data there is the added caveat that only a small portion of the PET-MR imaging time can be dedicated to motion modelling. With current technology however it is possible to obtain 4D-MRI of a sufficient spatial temporal resolution for this to be achievable [11]. Both patient specific [12], [13] and global [14], [15] respiratory motion models exist. Patient specific respiratory motion modelling offers the practicality of foregoing the large anatomical variations between patients which will burden a global or population based model [16].

A vast amount of literature exists on respiratory motion modelling utilizing an external surrogate signal to derive estimates of internal motion using a correspondence model as revised by [5]. Such correspondence models need to adequately represent the extent of motion present, which varies throughout the abdominal thoracic cavity and is dependent upon the anatomical location and organ composition [17]. This is commonly addressed via subspace learning methods such as principal component analysis (PCA) to construct correspondence models [18]. PCA proves advantageous by offering a

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low dimensional representation of the complex motion whilst reducing collinearities inherent in the high dimensional spaces.

A further limitation in state of the art approaches are that many respiratory motion models to date are fixed or stationary, with model parameters that are constants and inferred from the static statistical properties present during a training stage. A respiratory motion model utilizing free form deformation and PCA was first proposed when characterizing abdominal thoracic organ motion with the intended aim of identify tumor motion for Radiotherapy applications [6]. The model utilized was driven by the relative position of the diaphragm which acted as the respiratory external surrogate signal. Zhang et al.'s model has been extended [19] to utilize surface information as the external surrogate signal and a B-spline registration algorithm to determine correspondence of dynamic image volumes with respect to a reference phase. Utilizing PCA to determine a relation between dependent and independent variables (external surrogate signal and internal motion respectively) is equivalent to total least squares; i.e minimizing the orthogonal error between the data (both dependent and independent) and the model.

However, respiratory motion has demonstrated itself to be a non-stationary process with the irregularity at times resulting in no distinguishable respiratory pattern [8]. This motivates techniques to correct for irregular respiratory motion [20]; King et al. [21] have previously proposed an adaptive approach which utilizes the interpolation of multiple respiratory motion models to respond to different breathing patterns, i.e deep or fast breathing. The technique is proposed for use during image guided procedures where images of the underlying patient anatomy are available. For the application of adaptive respiratory motion estimation in clinical positron emission tomography (PET), external beam radiotherapy (EBRT), CT and MRI imaging, it is necessary to construct dynamic motion models from limited training data, e.g a single respiratory cycle, and for the model parameters to adapt to the underlying hidden internal motion and motion estimates to be made thereof.

To this avail we formulate respiratory motion estimation under a Hidden Markov Model (HMM) [22] (section II-D). We utilize a Kalman filter constructed from motion extracted from dynamic images of a single respiratory cycle and their associated observational signal. We also incorporate an EM algorithm for finding the maximum-likelihood estimates of the parameters of the HMM given a set of observations or external surrogate signals on a per cycle basis. Within this framework we hypothesize that the adaptive Kalman filter given an observation sequence of external motion can estimate irregular respiratory motion more accurately than a model with static parameters and thus provide a more generalizable method. This work focusses upon patient specific respiratory motion modelling however has scope to be extended to a global framework. The benefits of this adaptive Kalman-based approach are three-fold and distinguish this from previous work. Firstly, in situations with intermittent observations whilst the patient is in free breathing, motion model parameters can adapt to maximize the likelihood function given the observations. Intuitively, this selects the parameter

values that make the data most probable. This allows motion estimates to be made when the patient is breathing in a manner which is different to that observed during training. Secondly the framework allows one to account for changes in both model noise and observational or external surrogate signal noise. This includes heteroscedastic errors which may occur in the varying performance of respiratory monitoring devices or when it is required to utilize a different respiratory monitoring device for training and testing. For example, a correspondence model constructed during MRI may use a different external surrogate signal sensor when the model is being used in a PET investigation as in the latter there are no constraints of device MR compatibility. Thirdly by assessing the log likelihood we can parametrize the goodness of fit of the underlying model without any knowledge of the underlying organ configurations allowing us to determine confidence in the accuracy of the correction approach.

Our framework also utilizes PCA, separately, on both the external surrogate signal and parametrized internal motion thus providing a basis for projection of each into two disparate lower dimensional manifolds. A clear distinction between this adaptive approach and other prior work is that given a particular external surrogate respiratory sequence or cycle, we learn an optimal relation between the external surrogate and internal motion in their respective lower dimensional spaces allowing maximum likelihood inference of the hidden motion which facilitates adaption to changes in observed respiratory motion across time. We compare this approach with a popular method which utilizes a static total least squares / PCA type correspondence model [19]. In contrast to prior work [19] which is built on a static or fixed relationship between the external surrogate signal and internal motion.

The adaptive Kalman based approach proposed above is further developed in the remainder of this paper, which is organized as follows: Section II-A briefly introduces the concepts behind principal component analysis in the context of respiratory motion; section II-B explores the application specific details of the PCA model described in Fayad et al. [19]. Sections II-C to II-E describes the Kalman-based motion model framework including details of inference with the Kalman Filter / Smoother and learning with the EM algorithm. Section II-F describes the implementation using dynamic MRI data. In Section III we also introduce the Kullback-Liebler divergence as an assessment of irregularity of respiratory motion and discuss its application.

II. METHOD

A. Principal Component Analysis For Motion Models

Principal component analysis (PCA) is a multivariate data analysis technique allowing dimensionality reduction whilst providing a method for exploratory data analysis. PCA learns a linear model derived from a training set $\mathbf{X} = [\hat{\mathbf{x}}_1, \hat{\mathbf{x}}_2, \dots, \hat{\mathbf{x}}_k, \dots, \hat{\mathbf{x}}_K]$ of K samples or examples which are used to determine the parameters (in this case eigenvectors) of the model. In the context of respiratory motion correction $\hat{\mathbf{x}}_k$ of the internal motion training class can be considered as concatenated displacement vectors derived from dynamic

image volumes of the abdominal thoracic cavity during a single respiratory cycle consisting of K phases of respiratory motion typically acquired using MRI or CT. The displacement vectors are obtained by registering the dynamic image volumes back to a reference phase. If voxelwise registration is performed this would result in K displacement vectors for every voxel in the training cycle, in this work the reference phase is chosen as beginning of inhale. Mean subtraction of each element of the training class is a required pre-processing step of PCA, i.e $\hat{\mathbf{x}}_k = \mathbf{x}_k - \bar{\mathbf{x}}$, whereby, $\bar{\mathbf{x}} = \frac{1}{K} \sum_{k=1}^K \mathbf{x}_k$. PCA can be considered as a linear projection operator, which transforms the mean centred sample data $\mathbf{X}$ via a set of orthonormal basis vectors P_x (1) into a set of scores or weights $\mathbf{W}_x = [\mathbf{w}_1, \mathbf{w}_2, \dots, \mathbf{w}_k, \dots, \mathbf{w}_K]$, with each weight sample having reduced dimensions dependent upon the number of basis vectors retained. The Basis vectors are chosen as eigenvectors of the covariance matrix $\mathbf{X}\mathbf{X}^T$ and form columns of P_x . Projection in this manner eliminates redundancy of the projected dataset. Variance in the dataset is maximized along the principal components with sequentially reducing order dictated by the associated eigenvalue. The number of principal components required to re-represent the data should be sufficient to maintain the majority of statistical significant information. The orthonormal projection allows recovery of the data sample in its original dimensions (2);

$$\mathbf{W}_x = P_x^T \mathbf{X} \quad (1)$$

$$\mathbf{X} = P_x \mathbf{W}_x \quad (2)$$

The eigenvectors of P_x thus approximate a new subspace from a finite number of examples. An estimate of motion with respect to a reference phase can thus be made by approximating the relative weights or scores $\mathbf{W}_x$ within this new space. In a similar manner PCA can be applied to the external motion described by mean centred external surrogate signals ($\hat{\mathbf{z}}_k$) derived from spirometry [23], or marker [24] / marker-less [25] tracking of the anterior portion of the patient $\mathbf{Z} = [\hat{\mathbf{z}}_1, \hat{\mathbf{z}}_2, \dots, \hat{\mathbf{z}}_k, \dots, \hat{\mathbf{z}}_K]$. In this case each $\hat{\mathbf{z}}_k$ is a multidimensional observation made at the k^{th} phase of respiratory motion which acts as an external surrogate signal of the internal motion we would like to estimate.

B. Total Least Squares

Figure 1 gives a broad overview of the static total least squares based model for estimating internal motion, initially proposed by Zhang et al. [6]

It consists of firstly concatenating the displacement vectors and external surrogate signals for each of the K phases into an augmented data matrix $\mathbf{D}$ (3).

$$\mathbf{D} = \begin{pmatrix} \hat{\mathbf{x}}_1, \hat{\mathbf{x}}_2, \dots, \hat{\mathbf{x}}_k, \dots, \hat{\mathbf{x}}_K \\ \hat{\mathbf{z}}_1, \hat{\mathbf{z}}_2, \dots, \hat{\mathbf{z}}_k, \dots, \hat{\mathbf{z}}_K \end{pmatrix} = (\mathbf{d}_1, \mathbf{d}_2, \dots, \mathbf{d}_k, \dots, \mathbf{d}_K) \quad (3)$$

1) *PCA of large datasets*: The covariance matrix $\mathbf{D}\mathbf{D}^T$ is extremely large, and thus calculating its eigenvalues for PCA is computationally expensive. The method employed by [6] is to note that $\mathbf{D}\mathbf{V}_d$ are the eigenvectors of $\mathbf{D}\mathbf{D}^T$ where $\mathbf{V}_d$ are the eigenvectors of $\mathbf{D}^T\mathbf{D}$. This allows one to find a subspace

Fig. 1. The static motion model framework is described: 1) External surrogate respiratory signal and parametrized organ motion extracted from 4D MRI / CT training cycle(s). 2) Eigen-decomposition of the augmented data $[\mathbf{x}, \mathbf{z}]^T$ (equation 3) allows the partitioning of the associated eigenvectors $[\mathbf{V}_x, \mathbf{V}_z]^T$ for internal motion and external surrogate signal respectively (equations 6,7). 3) A test external surrogate signal $\mathbf{z}_k$ may then be used with the static model (4) to give an estimate of internal motion $\mathbf{x}_k$ at arbitrary time index k (5) (equation 8).

in the presence of extremely large datasets. As previously described in equations (1, 2), a representation of samples from the augmented training class can be decomposed into a linear combination of eigenvectors with $\mathbf{W}_d$ representing the weights in the PCA domain (4 and 5).

$$\mathbf{W}_d = \mathbf{V}_d^T \mathbf{D} \quad (4)$$

$$\mathbf{D} = \mathbf{V}_d \mathbf{W}_d. \quad (5)$$

The partitioned nature of the elements of the training class with $\mathbf{d}_k = [\hat{\mathbf{x}}_k, \hat{\mathbf{z}}_k]^T$, allows partitioning of the eigenvectors of $\mathbf{V}_d = [\mathbf{V}_x, \mathbf{V}_z]^T$ corresponding to the relative size of $\hat{\mathbf{x}}$ and $\hat{\mathbf{z}}$ respectively (6 and 7).

$$\mathbf{X} \approx \mathbf{V}_x \mathbf{W}_d \quad (6)$$

$$\mathbf{Z} \approx \mathbf{V}_z \mathbf{W}_d. \quad (7)$$

Equations 6 and 7 describe a simple principal component analysis whereby the dimensions of $\mathbf{X}$ and $\mathbf{Z}$ are reduced and may be represented in a lower dimensional domain $\mathbf{W}_d$. The eigenvectors $\mathbf{V}_x$ and $\mathbf{V}_z$ in this instance can serve as a linear model that produce uncorrelated variables with a minimal orthogonal error that explain the variance in the original dataset. Zhang's approach [6] (equation 8) diverts slightly from a traditional total least squares solution; it does however relate the independent and dependent variables via a single linear relationship $\mathbf{V}_x \mathbf{V}_z^{-1}$ utilizing PCA; hence minimizing the orthogonal error between the data (both external surrogate signal and internal motion) and the model. Firstly it is assumed that $\mathbf{V}_z^{-1}$ exists. An estimate of the deformation field at discretized time point k given an external surrogate signal, can then be obtained via equation 8, thus approximating the scores or weights of the deformation field $\mathbf{W}_x$ in the PCA domain via $\mathbf{V}_x^{-1} \hat{\mathbf{z}}_k$:

$$\hat{\mathbf{x}}_k = \mathbf{V}_x \mathbf{V}_z^{-1} \hat{\mathbf{z}}_k. \quad (8)$$

However, respiratory motion in patients who may be experiencing anxiety and difficulty in breathing can be expected to exhibit a more varied response than an assumed average single cycle, thus motivating an adaptive approach that can respond to changes in respiratory motion. Moreover, the Kalman based adaptive approach developed below to address this issue can

Fig. 2. The motion model framework described: 1) external surrogate respiratory signal and parametrized organ motion extracted from a single 4D MRI / CT training cycle. An eigenbasis for observations PCA_z and hidden motion PCA_x is found. Training data projected to lower dimensional representation. 2) Initial linear dynamical system parameter estimates found. 3) Test external surrogate respiratory signals projected into external surrogate lower dimensional domain and used to adapt model parameters using the Expectation Maximization Algorithm. 4) Inference of hidden internal motion (in domain of PCA_x) achieved with the Kalman Filter / Smoother [26]. 5) Finally an estimate of internal motion found via equation 2

also deliver a probabilistic model for the observed data to assess the accuracy of the model fit. The PCA model will also be restricted when dealing with heteroscedastic errors which may occur on the observations of the external surrogate signal found in a clinical setting.

C. Motion Model Framework

A schematic of our proposed adaptive motion model framework is described in figure 2. Firstly internal motion $\mathbf{X}$ and external surrogate signal $\mathbf{Z}$ are extracted from a dynamic MRI dataset, consisting of a single respiratory cycle. PCA is utilized on both the external surrogate signal and parametrized internal motion, resulting in the eigenbasis PCA_z and PCA_x respectively. An adaptive motion compensation framework may then be cast within a Hidden Markov Model (HMM) approach to give an optimal dynamic relationship between the weights $\mathbf{W}_x = [\mathbf{w}_{x1}, \mathbf{w}_{x2}, \dots, \mathbf{w}_{xk}, \dots, \mathbf{w}_{xK}]$ and $\mathbf{W}_z = [\mathbf{w}_{z1}, \mathbf{w}_{z2}, \dots, \mathbf{w}_{zk}, \dots, \mathbf{w}_{zK}]$ of the internal motion and external surrogate signal in their respective PCA domains. Test respiratory surrogate signals projected into their lower dimensional domain, obtained during model operation may then be used to adapt initial model parameters on an inter-cycle basis. Maximum likelihood inference of internal motion, i.e estimates of $\mathbf{w}_{xk}$ and via equation 2 $\mathbf{x}_k$ can then be achieved using the Kalman filter / smoother. What follows is an overview of the Kalman filter / smoother equations together with the EM algorithm. For ease of notation we subsequently re-label $\mathbf{W}_x$ and $\mathbf{W}_z$ to $\mathbf{X}$ and $\mathbf{Z}$ respectively with associated members $[\mathbf{z}_1, \mathbf{z}_2, \dots, \mathbf{z}_k, \dots, \mathbf{z}_K]$ and $[\mathbf{x}_1, \mathbf{x}_2, \dots, \mathbf{x}_k, \dots, \mathbf{x}_K]$.

D. Hidden Markov Model

We cast the problem of estimating internal motion from an external surrogate time varying signal as a Hidden Markov

Model (HMM) [27]. With assumed linear relations between nodes in the HMM and noise terms modelled as Gaussian the HMM is equivalent to a Linear Dynamical System (LDS) ; with the exception of discrete versus continuous state variables for the HMM and LDS respectively. The observational

Fig. 3. Schematic diagram motion estimation framework

model is a linear function which relates the low dimensional representation of the external surrogate signal $\mathbf{z}_K$, to the low dimensional representation of the motion $\mathbf{x}_K$ (figure 3) with some associated stochastic error $\mathbf{w}_k$. This represents the intrinsic model error coupled with the error of the measurement system used to capture the external surrogate signal such as a stereo camera system used to record external motion, a chest belt or spirometry system. This error term is represented as a Gaussian noise process with zero mean and variance R , i.e $\mathbf{w}_k \sim \mathcal{N}(0, \mathbf{R})$. The transition model describes the evolution of the hidden state variables which here describes the evolution or propagation of the internal motion from one phase of motion to the next. A second order m - variate vector autoregressive function, VAR(p) of order $p = 2$ is chosen which can model phenomena exhibiting regular and irregular pseudo oscillatory behaviour [28]. Uncertainty in the transition model is also given by a Gaussian noise process $\epsilon_k \sim \mathcal{N}(0, \mathbf{C})$. Model parameters are initially determined via least squares regression on a single training cycle in practice derived from a dynamic MR or CT dataset. The hidden state space is augmented to include two consecutive time indices. This allows the transition to be cast as a first order Markov process with state and noise vectors described by (9 and 10) respectively. The augmented state coefficient matrix and noise covariance matrix are thus described by (11).

$$\tilde{\mathbf{x}}_{k+1} = \begin{pmatrix} \mathbf{x}_{k+1} \\ \mathbf{x}_k \end{pmatrix} \in \mathbb{R}^{mp} \quad \tilde{\mathbf{x}}_k = \begin{pmatrix} \mathbf{x}_k \\ \mathbf{x}_{k-1} \end{pmatrix} \quad (9)$$

$$\tilde{\epsilon}_k = \begin{pmatrix} \epsilon_k \\ \mathbf{0} \end{pmatrix} \quad \tilde{\mathbf{C}} = \langle \tilde{\epsilon}_k \tilde{\epsilon}_k^T \rangle \quad (10)$$

$$\tilde{\mathbf{A}} = \begin{pmatrix} \mathbf{A}_1 & \mathbf{A}_2 \\ \mathbf{I} & \mathbf{0} \end{pmatrix} \in \mathbb{R}^{mp \times mp} \quad \tilde{\mathbf{C}} = \begin{pmatrix} \mathbf{C} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} \end{pmatrix} \quad (11)$$

The observational model now takes the form of (12), whilst the transition model is simplified to a single-order autoregressive model, i.e VAR[1] described by (14).

$$\tilde{\mathbf{B}} = [\mathbf{B} \quad \mathbf{0}] \quad (12)$$

$$\mathbf{z}_k = \tilde{\mathbf{B}}\tilde{\mathbf{x}}_k + \tilde{\mathbf{B}}_0 + \mathbf{w}_k \quad (13)$$

$$\tilde{\mathbf{x}}_{k+1} = \tilde{\mathbf{A}}\tilde{\mathbf{x}}_k + \tilde{\mathbf{e}}_k. \quad (14)$$

The state variables can now be combined with the noise variable to form single Gaussian random variables. This allows us to express the conditional densities of the state and the output (15).

$$\begin{aligned} P(\mathbf{z}_k|\tilde{\mathbf{x}}_k) &= \exp\left\{-\frac{1}{2}[\mathbf{z}_k - \tilde{\mathbf{B}}\tilde{\mathbf{x}}_k]'\mathbf{R}^{-1}[\mathbf{z}_k - \tilde{\mathbf{B}}\tilde{\mathbf{x}}_k]\right\}(2\pi)^{-m/2}|\mathbf{R}|^{-1/2} \\ P(\tilde{\mathbf{x}}_k|\tilde{\mathbf{x}}_{k-1}) &= \exp\left\{-\frac{1}{2}[\tilde{\mathbf{x}}_k - \tilde{\mathbf{A}}\tilde{\mathbf{x}}_{k-1}]'\tilde{\mathbf{C}}^{-1}[\tilde{\mathbf{x}}_k - \tilde{\mathbf{A}}\tilde{\mathbf{x}}_{k-1}]\right\}(2\pi)^{-mp/2}|\tilde{\mathbf{C}}|^{-1/2} \end{aligned} \quad (15)$$

The Markov property allows the simplification of the calculation of the joint probability. The first order Markov assumption states that $P(\tilde{\mathbf{x}}_k|\tilde{\mathbf{x}}_{k-1}) \approx P(\tilde{\mathbf{x}}_k|\tilde{\mathbf{x}}_{k-1}, \dots, \mathbf{x}_2, \mathbf{x}_1)$. Using the Markov property the joint distribution of a particular sequence, or respiratory cycle $\tilde{\mathbf{X}} = \{\tilde{\mathbf{x}}_k\}_{k=1}^K$, and $\mathbf{Z} = \{\mathbf{z}_k\}_{k=1}^K$ given current model parameters can be described by a product of the conditional distributions (16).

$$P(\tilde{\mathbf{X}}, \mathbf{Z}) = P(\tilde{\mathbf{x}}_1) \prod_{k=2}^K P(\tilde{\mathbf{x}}_k|\tilde{\mathbf{x}}_{k-1}) \prod_{k=1}^K P(\mathbf{z}_k|\tilde{\mathbf{x}}_k) \quad (16)$$

Following model construction a respiratory external surrogate signal for a particular cycle sequence can be used with the Kalman model to make inference of the hidden internal motion. This can be supported by developing an Expectation Maximization (EM) estimate of the most probable model parameters given the observational data alone; thus allowing the model to adapt and generalize to motion outside of that of the training phase.

E. Inference with the Kalman Filtering / Smoothing

With known model parameters the Kalman Filter recursively determines the posterior distribution $P(\tilde{\mathbf{x}}_k|\{\mathbf{z}\}_{k=1}^k)$ and so consists of a set of forward looking recursions. The Kalman smoother refines and minimizes the variance in the Kalman filter estimate using a set of backward recursions to determine $P(\tilde{\mathbf{x}}_k|\{\mathbf{z}\}_{k=1}^K)$. For completeness the filtering and smoothing equations are described below.

1) *Kalman Filtering*: The Kalman recursions (17) [26] for the linear dynamical system defined (9 - 14) involve estimating recursively $\tilde{\mathbf{x}}_k$, for $1 \leq k \leq K$ conditional on a measurement sequence $\{\mathbf{z}\}_{k=1}^k$. The conditional mean $E(\tilde{\mathbf{x}}_k|\{\mathbf{z}\}_{k=1}^k)$ provides the minimum mean squared error estimator of $\tilde{\mathbf{x}}_k$, denoted $\hat{\mathbf{x}}_{k|k}$ with covariance $\mathbf{V}_{k|k}$.

$$\begin{aligned} \hat{\mathbf{x}}_{k|k-1} &= \tilde{\mathbf{A}}_k \hat{\mathbf{x}}_{k-1|k-1} \\ \mathbf{V}_{k|k-1} &= \tilde{\mathbf{A}}_k \mathbf{V}_{k-1|k-1} \tilde{\mathbf{A}}_k' + \tilde{\mathbf{C}}_k \\ \mathbf{G}_k &= \mathbf{V}_{k|k-1} \tilde{\mathbf{B}}_k' (\tilde{\mathbf{B}}_k \mathbf{V}_{k|k-1} \tilde{\mathbf{B}}_k' + \mathbf{R}_k)^{-1} \\ \hat{\mathbf{x}}_{k|k} &= \hat{\mathbf{x}}_{k|k-1} + \mathbf{G}_k (\mathbf{z}_k - \tilde{\mathbf{C}}_k \hat{\mathbf{x}}_{k|k-1}) \\ \mathbf{V}_{k|k} &= \mathbf{V}_{k|k-1} - \mathbf{G}_k \mathbf{B}_k \mathbf{V}_{k|k-1} \end{aligned} \quad (17)$$

The Kalman gain $\mathbf{G}_k$ may be considered as the ratio of the covariance matrices of the prediction and the innovation. The innovation $\mathbf{e}_k$ determines the difference in our predicted observation with the actual observation. Utilizing the measurement function one obtains the innovation covariance $\mathbf{S}_k$ (18) which allows calculation of the likelihood of underlying model fit as described in II-E3.

$$\begin{aligned} \mathbf{e}_k &= \mathbf{z}_k - \tilde{\mathbf{B}}_k \tilde{\mathbf{A}}_k \hat{\mathbf{x}}_{k-1} \\ \mathbf{S}_k &= E \left[\tilde{\mathbf{B}}_k (\mathbf{z}_k - \hat{\mathbf{x}}_k + \mathbf{w}_k) \tilde{\mathbf{B}}_k' (\mathbf{z}_k - \hat{\mathbf{x}}_k + \mathbf{w}_k') \right] \\ \mathbf{S}_k &= \tilde{\mathbf{B}}_k \mathbf{V}_{k|k-1} \tilde{\mathbf{B}}_k' + \mathbf{R}_k \end{aligned} \quad (18)$$

The Kalman filter is initialized with starting conditions $\hat{\mathbf{x}}_{0|0}$ and $\mathbf{V}_{0|0}$. Note the time varying properties of the filter, with model parameters appended by k .

2) *Kalman Smoothing*: As the motion estimation problem in medical imaging is retrospective, i.e corrections are applied after all data have been acquired, then future measurements $\mathbf{z}_{k+1:K}$ can be used to correct filtered estimates $\hat{\mathbf{x}}_k$. This is achieved by Rauch-Tung-Striebel (RTS) smoothing (19). Using the estimates of the forward filtering recursions the smoothed estimates can be obtained by backward recursions for $k = K-1, K-2, \dots, 1$

$$\begin{aligned} \mathbf{J}_k &= \mathbf{V}_{k|k} \tilde{\mathbf{A}}_k' (\mathbf{V}_{k+1|k})^{-1} \\ \hat{\mathbf{x}}_{k|K} &= \hat{\mathbf{x}}_{k|k} + \mathbf{J}_k (\hat{\mathbf{x}}_{k+1|K} - \hat{\mathbf{x}}_{k+1|k}) \\ \mathbf{V}_{k|K} &= \mathbf{V}_{k|k} + \mathbf{J}_k (\mathbf{V}_{k+1|K} - \mathbf{V}_{k+1|k}) \mathbf{J}_k' \\ \mathbf{V}_{k,k-1|K} &= \mathbf{V}_{k|K} \mathbf{J}_{k-1}' \end{aligned} \quad (19)$$

The Kalman smoother is initialized with $\hat{\mathbf{x}}_{K|K}$ and $\mathbf{V}_{K|K}$ from the Kalman filter, $\mathbf{J}_k$ denotes the smoother gain.

3) *Adaptive Parameter Estimation*: The inference estimate is highly dependent upon model parameters $\Theta = \{\tilde{\mathbf{A}}, \tilde{\mathbf{B}}, \tilde{\mathbf{C}}, \mathbf{R}\}$. Continually tuning the estimator allows the model to generalize to new data which may be necessary for changes in breathing style and / or noise conditions. The maximum likelihood estimate $\hat{\Theta}$ of the parameters given a dataset composed of only observed data and unobserved or hidden data can be achieved using the Expectation Maximization (EM) algorithm. The HMM or LDS defines a joint distribution (16). This allows the likelihood function to be given by $L(\Theta) = P(\mathbf{X}, \mathbf{Z}|\Theta)$ as $\mathbf{X}$ is hidden we can maximize the marginal (log) likelihood $L(\Theta) = \log P(\mathbf{Y}|\Theta) = \int_{\mathbf{X}} P(\mathbf{X}, \mathbf{Y}|\Theta) d\mathbf{X}$. Using Jensen's inequality of the concave log function and the distribution H over the hidden variables we can obtain a lower bound for the marginal log likelihood (20).

$$\begin{aligned} L(\Theta) &= \log \int_{\mathbf{X}} P(\mathbf{X}, \mathbf{Z}|\Theta) d\mathbf{X} \\ &= \log \int_{\mathbf{X}} H(\mathbf{X}) \frac{P(\mathbf{X}, \mathbf{Z}|\Theta)}{H(\mathbf{X})} d\mathbf{X} \geq \int_{\mathbf{X}} H(\mathbf{X}) \log \frac{P(\mathbf{X}, \mathbf{Z}|\Theta)}{H(\mathbf{X})} d\mathbf{X} \\ &= F(H, \Theta) \end{aligned} \quad (20)$$

The E step consists of maximizing this lower bound $F(H, \Theta)$ with respect to $H(\mathbf{X})$. This occurs when $H(\mathbf{X}) = P(\mathbf{X}|\mathbf{Z}, \Theta)$. This is estimated using the Kalman smoother with current parameter estimates. The M step consists of maximizing the lower bound with respect to the parameters Θ . This is achieved by taking the derivative of $E_{\mathbf{X}|\mathbf{Z}}[\log P(\mathbf{X}, \mathbf{Z}|\Theta)]$ with respect

to each model parameter. The closed form maximizing solutions are summarized in (23). The EM algorithm, with t iterations is repeated until parameter convergence (21). For a more detailed discussion the reader is referred to [29].

$$\begin{aligned} \text{Estep} \quad & \Phi(\Theta|\Theta^t) = E_{X|Z}[\log P(X, Z|\Theta)] \\ \text{Mstep} \quad & \Theta^{t+1} = \arg \max_{\Theta} E_{X|Z}[\log P(X, Z|\Theta)] \end{aligned} \quad (21)$$

In practice the expected log likelihood during parameter learning can be evaluate from the predicted error or innovation sequence given the current model parameters and estimates of the state (18). The innovations are independent Gaussian random variables with covariance described by (18). The log likelihood of the observation sequence given the current model parameters is thus described by (22).

$$-\log L(\theta) = \frac{1}{2} \sum_{k=1}^K \log |\mathbf{S}_k| + \frac{1}{2} \sum_{k=1}^K \mathbf{e}_k' \mathbf{S}_k^{-1} \mathbf{e}_k \quad (22)$$

$$\begin{aligned} \tilde{\mathbf{C}}_{new} &= \frac{1}{K-1} \sum_{k=2}^K (\hat{\mathbf{x}}_{k|K} - \tilde{\mathbf{A}} \hat{\mathbf{x}}_{k-1|K}) (\hat{\mathbf{x}}_{k|K} - \tilde{\mathbf{A}} \hat{\mathbf{x}}_{k-1|K})' \\ &\quad + \tilde{\mathbf{A}} \mathbf{V}_{k-1|K} \tilde{\mathbf{A}}_k' + \mathbf{V}_{k|K} \mathbf{V}_{k|K}' - \mathbf{V}_{k|K} \mathbf{G}_k' \tilde{\mathbf{A}}_k' - \tilde{\mathbf{A}} \mathbf{G}_k \mathbf{V}_{k|K} \\ \mathbf{R}_{new} &= \frac{1}{K+1} \sum_{k=1}^K (\mathbf{z}_k - \tilde{\mathbf{B}} \hat{\mathbf{x}}_{k|K}) (\mathbf{z}_k - \tilde{\mathbf{B}} \hat{\mathbf{x}}_{k|K})' + \tilde{\mathbf{B}} \mathbf{V}_{k|K} \tilde{\mathbf{B}}' \\ \tilde{\mathbf{A}}_{new} &= (\sum_{k=2}^K \hat{\mathbf{x}}_{k|k} \hat{\mathbf{x}}_{k-1|k}') (\sum_{k=2}^K \hat{\mathbf{x}}_{k-1|k-1} \hat{\mathbf{x}}_{k-1|k-1}')^{-1} \\ \tilde{\mathbf{B}}_{new} &= (\sum_{k=1}^K \hat{\mathbf{z}}_k \hat{\mathbf{x}}_k') (\sum_{k=1}^K \hat{\mathbf{x}}_{k|k} \hat{\mathbf{x}}_{k|k}')^{-1}. \end{aligned} \quad (23)$$

F. Testing with MRI data

The total least squares and adaptive Kalman models were tested on nine volunteers using publicly available dynamic MRI data [30]. Spatial and temporal resolution of MRI data were 1.48 x 5.5 x 1.48 mm (right-left, anterior-posterior, superior-inferior) and 0.7sec respectively. Each volunteer consisted of 35 image volumes, thus encompassing 24.5 seconds of free breathing for numerous (>5) respiratory cycles. The high temporal resolution of the image volumes results in noise and gibbs ringing artefacts. These were reduced using anisotropic diffusion filtering in a similar manner to [31]. This results in smoother homogeneous image regions that contain no structural information but avoids smoothing between different tissue types, thus preserving edges.

G. Parametrization of External Surrogate Respiratory Signal

It is proposed that a depth sensor such as the Kinect is utilized to extract the patients anterior surface position however the framework allows for the incorporation of any observation of the external surrogate signal. For our purposes we simulated a pseudo-distance map analogous to the output of the Kinect. The thorax was segmented in the 4D MRI and a parallel plane is defined at 1 meter from the mean anterior surface position at the beginning of inhale of the training cycle. Distance measures at each voxel position of the plane are determined for all the remaining phases of the MRI data. As the voxel resolution in the anterior-posterior direction is 5.5mm inter-voxel distance measurements of chest positions are determined using linear interpolation at a pre-defined threshold value. Each surface depth map consists of N measurements which were organized into a state vector for each phase k of the respiratory cycle (24)

$$\mathbf{z}_k = [\mathbf{z}_{1,k}, \mathbf{z}_{2,k}, \dots, \mathbf{z}_{N,k}]. \quad (24)$$

H. Parametrization of internal motion

The internal phases were grouped into cycles dependent upon the inflection points of the extracted pseudo distance maps. Thus the temporal volumes for each phase of motion were partitioned into cycles containing an inhalation, followed by an exhalation. The first and last cycles in each dataset may be partially sampled, the second cycle is thus chosen as the training cycle. Registration to a reference phase defined as the beginning of inhale in the training cycle allowed ground truth deformation fields to be extracted. The registration process firstly uses a global affine transform maximizing a mutual information metric with a gradient descent optimizer. This initializes a multi-resolution symmetric diffeomorphic image registration maximizing the cross correlation [32]. This has the advantage of preserving topology with guaranteed symmetry of registration irrespective of choice of “fixed” and “moving” images. The vector field associated with each phase k of a respiratory cycle has $3 \times M$ components, with $M = 217 \times 45 \times 336$. Vector fields were organized into state vectors (25).

$$\mathbf{x}_k = [\mathbf{x}_{1,1,k}, \mathbf{x}_{1,2,k}, \mathbf{x}_{1,3,k}, \dots, \mathbf{x}_{M,1,k}, \mathbf{x}_{M,2,k}, \mathbf{x}_{M,3,k}] \quad (25)$$

I. Model Construction

The same training cycle was used for both total least squares and adaptive kalman models; the first fully sampled respiratory cycle in this case. As state vectors are high dimensional, construction of the covariance matrix to perform PCA is computationally expensive. The approach described in II-B1 is used. Two PCA coefficients are kept in both cases as this is deemed sufficient for accurate modelling of respiratory motion ([33]). The eigenvalues corresponding to these eigenvectors shows that the first two eigenvectors can explain approximately 90% variation in the data. Concatenating the parametrized organ motion and external surrogate signal as described in (3) allows construction of the PCA based model shown in section II-B. Similarly the initial parameters of the linear dynamical system are found as described in sections II-C and II-D. New test observational sequences are used with the EM algorithm to update model parameters in the EM-KF model (EKF) as described in section II-E3. This adaptive step is not possible in the static PCA based model and allows the adaptive Kalman filter parameters to change and thus make more accurate estimates in the presence of irregular respiratory patterns. The Kalman filtering / smoothing (sections II-E1 and II-E1) and total least squares (TLS model) method (8) allows estimates of hidden motion to be determined. These estimates can be compared to the ground truth dynamic CT vector fields to give a value of RMS voxel error and can also be compared in the PCA domain utilizing the eigenbasis constructed during the training cycle.

III. RESULTS AND DISCUSSION

As noted in Li et al. [33] for a well behaved PCA model one should not use more principal components than necessary. Figure 4 demonstrates the percentage variation captured by two principal components for each individual volunteer.

Furthermore the Catell scree test [34] recommends to retain only those principal components above the point of inflection on a plot of eigenvalues ordered by diminishing size; this analysis was performed for this dataset to determine a minimal eigenvector feature set. In this dataset, two principal components capture approximately 90% variation in the data which we assert to be caused by motion. Principal components with smaller variation represent less dominate modes of variation which may be prescribed to noise. The addition of more principal components may thus result in over fitting to the training data resulting in a model which is unable to generalize to unseen data. The percentage variation described by two

Fig. 4. Percentage Variation encapsulated by two principal components for each volunteer

principal components however doesn't encapsulate the inter-cycle variability in the dataset and more-so the difference of the test data from the training. To visualize the variability in the dynamics and internal - external motion correspondence of each volunteer a plot of the linear function of the weights of the the first principal component of the observation versus that of the internal motion is shown for each individual fully sampled cycle (figure 5). As demonstrated volunteer 1 exhibits marked inter-cycle variation with a large spread in the range of linear correspondence for each cycle. Volunteer 2 on the other hand demonstrates a small range in this variability.

As a metric for the variability portrayed in each volunteer we use the Kullback-Leibler (K-L) divergence. The K-L divergence has been proposed to asses the dis-similarity of a test case against a population based liver model [14]. In this work we use it as a distance measure between the distribution of the external surrogate signal in the training cycle in comparison to the test cycle $D_{KL}(Train||Test)$ (26).

$$D_{KL}(Train||Test) = \sum_i \ln \left(\frac{Train(i)}{Test(i)} \right) Train(i) \quad (26)$$

As can be seen (figure 6) the variability from that of the training cycle differs by varying degrees for each volunteer. Notable variability is identified in volunteers 1, 4 and 6. For evaluation of motion model performance, following the approach of Li et al. [33] we assess each patient specific model by comparing the estimated hidden deformations to

Fig. 5. Variability of inter-cycle respiratory motion

those calculated using the registration by calculation of the root mean square error (27) (RMSE) Table 1.

$$RMSE = \frac{\sum_{k=1}^K (\hat{x}_k^{calculate} - \hat{x}_k^{modelled})^2}{K} \quad (27)$$

Where the summation is over all K phases, excluding the training data.

Fig. 6. Range of K-L divergence for each volunteer, representing the variability in comparison to the training data for each volunteer

TABLE I
COMPARISON OF AVERAGE 3D MODELLING ERROR FOR ALL NINE VOLUNTEERS

Volunteer Number	Model Error (mm)	
	Total Least Squares	Kalman Model
1	4.6	2.5
2	1.2	1.3
3	1.2	1.1
4	1	0.9
5	1.5	1.5
6	1.5	1.4
7	0.8	0.8
8	0.7	0.7
9	0.7	0.7

As shown (Table 1) with the exception of volunteer 2 the Kalman model performs equally well as the total least squares model. In four volunteers, inclusive of volunteers 1, 4 and 6 the Kalman model out performs the Total least squares model. It is worthy to note the reduced variability in the observational data of volunteer 2 from the K-L divergence (figure 6). A full analysis of a comparison of the root mean square error for all cycles in all volunteers is shown in figure (7). Calculation of the total root mean square error for all volunteers, with K now being the summation over all phases in the total dataset i.e volunteers 1-9, we observe a $\approx 50\%$ reduction in root mean square error using the Kalman model. (Table II) The

TABLE II
COMPARISON OF AVERAGE 3D MODELLING ERROR FOR ALL NINE VOLUNTEERS

Volunteer Number	Model Error (mm)	
	Total Least Squares	Kalman Model
1-9	1.9	1.3

EM-Kalman model (28) can be considered an adaptive nested version of the TLS model (29). This allows a comparison of the distribution of the errors to be made and a test for

Fig. 7. A Comparison of Root Mean Square Error for All Cycles

significance as to the validity of the best suited model using the F test.

$$KF \quad \hat{\mathbf{x}}_k = \mathbf{V}_x \left[\left(\tilde{\mathbf{A}}_k - \mathbf{G}_k \mathbf{C}_k \right) \hat{\mathbf{x}}_{k|k-1} + \mathbf{G}_k \right] \mathbf{V}_z^{-1} \dot{\mathbf{z}}_k \quad (28)$$

$$TLS \quad \hat{\mathbf{x}}_k = \mathbf{V}_x \mathbf{V}_z^{-1} \dot{\mathbf{z}}_k \quad (29)$$

This type of Kalman model with per cycle EM parameter estimation has the advantage of being adaptive and is thus capable of generalizing to new observation as compared to a fixed or static approach such as the static total least squares

TABLE III
F TEST FOR MODEL COMPARISON TO REJECT NULL HYPOTHESIS OF TLS
MODEL BEST FITTING DATA

Model Choice	
Volunteer Number	F test
1	Kalman $p < 0.001$
2	TLS $p < 0.001$
3	Kalman $p < 0.001$
4	Kalman $p < 0.001$
5	TLS $p < 0.001$
6	Kalman $p < 0.001$
7	TLS $p < 0.001$
8	TLS $p < 0.001$
9	Kalman $p < 0.001$

based model. The Kalman model presents as statistically more significant in all data cases where the K-L divergence suggests test cycles are different to the training data, i.e. volunteers 1,4, 6 and 9. It is noteworthy that volunteer 6 has a high K-L divergence but doesn't demonstrate a gross reduction in error as shown in volunteer 1 when using the adaptive Kalman model in comparison to the static total least squares model (Table II). It can be observed that two cycles in volunteer 6 have more extreme deviations in variability, whereas the variability in volunteer 1 is more evenly spread across all respiratory cycles. These "outliers" in volunteer 6 over emphasize the K-L divergence which isn't reflected in the mean error. Nonetheless the Kalman model is still the superior model choice in this instance.

Concatenating each individual test cycle for all 9 volunteer allows the error of the estimated vector fields for the TLS model and KF model with EM parameter estimation (EKF model) to be succinctly presented. Figure 8 demonstrates the error of the loadings for the first principal component. Red highlights the error in the loadings for estimates made using the EKF model, whilst the black highlights the errors when using the TLS model. The first 9 cycles in figure 8 consist of a single volunteer, Volunteer 1, where the EKF model outperforms the TLS model. Figure 9 demonstrates the loadings of the first principal component for this example (Volunteer 1) highlighting the poor performance of the TLS model and demonstrating the varying nature in the respiratory pattern in comparison to the training cycle, i.e. the first fully sampled cycle.

The following 8 respiratory cycles in figure 8 are from Volunteer 2 which shows an example where the TLS model out performs the EKF model. From observing the loadings along the first principal component in this example (figure 10) we can now see how the respiratory sequence more closely matches the training cycle, thus the TLS model performs well. To visualize the effectiveness of the motion modelling; the EM Kalman filter estimated vector fields were used to register the dynamic MRI data back to the reference frame in order to perform motion correction. For this purpose Volunteer 3 was chosen arbitrarily. The maximum gradient in the MRI data at the left and right lung boundaries, de-marked in

Fig. 8. Error of weight of first internal PCA loading for the EKF (red) in comparison to the TLS model (black) for concatenated cycle numbers of MRI test data.

Fig. 9. Weight or loadings of the first internal principal component estimated by the EKF (red) and TLS model (black) versus the ground truth (blue) for Volunteer 1, demonstrating the varying nature of the respiratory cycle and the ability of the EKF to estimate motion in the presence of irregular motion.

white (figure 11) allowed their position to be tracked for the uncorrected i.e. free breathing data, and the corrected data. The root mean square distance of this motion for the left and right lung boundaries were 12mm and 6mm respectively with no motion correction. This was reduced to 2mm with motion correction. Volunteer one was also chosen to visually highlight globally the effect of the motion correction on the worse performing example in terms of model error. This example also demonstrates the most variability in their respiratory pattern. As displayed in figure 13 with no correction a large difference is observed between the reference phase and the maximum of inhale; this is reduced markedly when performing motion correction. Some residual error can be observed which is expected due to the inherent artefacts in the MRI images themselves resulting in imprecise registration during model building and model application. Also presented are the internal PCA weights for a single cycle extracted from Volunteer 3 showing the incremental increase in performance with three

Fig. 10. Weight or loadings of the first internal principal component estimated by the EKF (red) and TLS model (black) versus the ground truth (blue) for Volunteer 2, demonstrating the regular nature of the respiratory cycle and both the ability of the EKF and TLS model to estimate motion.

iterations as the likelihood function converges (figure 12).

Fig. 11. Variation in right and left lung boundary position, for the uncorrected dataset (red), versus the corrected dataset (EKF) (black) for volunteer 3.

IV. CONCLUSION

We have demonstrated the application of an adaptive Kalman model for patient specific respiratory motion estimation. Performance is comparable to a static total least squared based approach. A marginal increase in performance is observed when the variability in the observable respiratory external surrogate signal increases. This is quantified by an increase in the K-L divergence of the external surrogate signal. Although only a small difference in root mean square error is observed in this dataset the ability of the Kalman model to adapt results in it being an attractive alternative for use in the clinical setting. Future work will analyze the benefit in performance of the adaptive Kalman filter, versus the static total least squares approach when a patient changes their style of breathing.

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Fig. 12. Internal PCA loadings for a single cycle extracted from volunteer 3 demonstrating the increasing performance (red) with subsequent iterations of the EM framework. As the likelihood function converges estimates made with the Kalman filter become closer to the ground truth (blue) in comparison to the TLS model (black).

Fig. 13. For volunteer 1, from left to right: reference phase, maximum inhale phase, the difference image between maximum inhale and the reference phase, the difference image between the reference phase and the maximum inhale phase now motion corrected using the adaptive Kalman filter; finally the motion corrected maximum inhale image. This highlights the gross effectiveness of the motion correction framework in the most variable respiratory pattern demonstrated in volunteer 1.

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