Model-Based Strategies for Biomedical Image Analysis: LV Strain Analysis from 4DE

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I. Introduction
   - Recovering Quantitative Information From Biomedical Images: an ill-posed problem
   - Models as a substrate for recovery
   - Underlying example in this talk: recovery of cardiac strain from echocardiography
   - Current computational idea running through our work: sparse representations

II. Geometrical Models for Segmenting Structure
   - deformable boundary models
   - sparse coding/dictionary learning of appearance for boundary finding

III. Physical Models for Recovery of Soft Tissue Deformation
   - measurement of left ventricular (cardiac) strain from 4D images
   - sparse coding/dictionary learning for finding dense displacement vector fields

IV. Conclusions/Remaining Challenges
Image Analysis Systems Incorporate Quantitative Models and Use Mathematical Decision Making

Model

Mathematical decision maker

Feature detector

Image-derived quantitative information

3D/4D Image
What types of models are useful for quantitative image analysis?

- Size/shape/appearance of anatomical structure
- Size/shape of abnormal structure (e.g. tumors)
- Coherent functional information (e.g. time series)
- Motion/Deformation characteristics/ physiological information

Where do useful models come from?

- Typically geometry, functional relations or physics
- In biomedical world: guided by anatomy, physiology (or biology)
Nonischemic Occluded Vascular Bed

Infarct

15 Minutes 40 Minutes

3 Hours 6 Hours LAD

LV RV

LAD

Nonischemic Occluded Vascular Bed (area at risk) Infarct
Example 4DE Image Dataset

Philips iE33 system w/ X7-2 probe

Center freq = 4.4 MHz
Aperture = 9.25mm x 9.25mm
Transmit focal depth = programmable
FOV = 90 degrees x 90 degrees

Volume frame rates = ~ 40Hz
4DE Image Acquisition

- B-mode

Endo- and Epi-cardial Surface Segmentation (Dictionary Learning-based)

- Local Curvature & confidence

- Regularized Shape tracking (G-RPM)

GPU Correlator (using phase & magnitude)

- Viterbi Filter

Integration

Key application: 4D Stress Echo

Geometry/appearance

Shape-based displacements

\( U_{\text{shape}} \)

Speckle-based displacements

\( U_{\text{speck}} \)

Dense biomechanics

\( U_{\text{dense}} \)
II. Geometrical Models:
Object Segmentation
Multiframe Model for Cardiac Segmentation

- \( I_{1:N} = \{I_1, I_2, \ldots, I_N\} \) is a given cardiac sequence
- \( s_t \) is the segmentation at frame \( t \)
- Chan-Vese Level Sets – point sampled

\[
\hat{s}_t = \arg \max_{s_t} P(s_t \mid I_{1:t}) = \arg \max_{s_t} P(I_t \mid s_t, I_{1:t-1}) P(s_t \mid I_{1:t-1})
\]

\[
= \arg \max_{s_t} P(I_t \mid s_t) \underbrace{P(s_t \mid \hat{s}_{1:t-1})}_{\text{data adherence}} \underbrace{P(s_t \mid \hat{s}_{1:t-1})}_{\text{dynamical shape prior}}
\]

Nakagami pdf model for 3DE, Gaussian for MRI
Use Nakagami distribution (Shankar 2000): compromise between Rayleigh (fully-developed speckle), pre-Rayleigh (weak) and post-Rayleigh (periodically-distributed speckles)

- LV Blood Pool
- LV Myocardium
- Background

\[
P_1(I) = \frac{2\mu_1^{\mu_1}}{\Gamma(\mu_1)\omega_1^{\mu_1}} I^{2\mu_1-1} \exp\left(-\frac{\mu_1}{\omega_1} I^2\right)
\]

\[
P_2(I) = \frac{2\mu_2^{\mu_2}}{\Gamma(\mu_2)\omega_2^{\mu_2}} I^{2\mu_2-1} \exp\left(-\frac{\mu_2}{\omega_2} I^2\right)
\]

\[
P_3(I) = \sum_{k=1}^{M} \alpha_k P_k(I; \mu_{3,k}, \omega_{3,k})
\]

\[
\log P(I | s) = \sum_{l=1}^{3} \int_{\Omega_l} \log P_l(I) \, dx
\]
Incorporating Multiframe/Multisubject Information for Segmentation (Zhu, et al., MICCAI 2008)

Training Phase (use tensor decomposition)
\[ S = Z \times_1 V_{\text{subject}} \times_2 V_{\text{motion}} \times_3 V_{\text{landmark}} \]

Prediction Phase

Step 1: projection
\[ \hat{V}_{\text{subject}} = B \times_1 \hat{S}_{1:t-1} \]
\[ B \propto (Z^{-1} \times V_{\text{motion}}^{-1} \times V_{\text{landmark}}^{-1}) \]

Step 2: prediction
\[ S^*_t = Z \times_1 \hat{V}_{\text{subject}} \times_2 V_t \times_3 V_{\text{landmark}} \]

Predicted segmentation at frame \( t \) based on frames 1:t-1 selecting info out of training space

Dynamical Shape Prior
\[ P(S_t | \hat{S}_{1:t-1}) \propto \exp \left\{ -\frac{\alpha}{2} \int \|S_t - S^*_t\|^2 \right\} \]
Qualitative Results

Solid Red: Automatic ENDO, Solid Green: Automatic EPI
Dotted Yellow: Manual ENDO, Dotted Blue: Manual EPI

3DRT typically w/ 20-22 frames over full cycle
Quantitative Evaluation
(3 Algorithms compared vs. Manual Tracing)

N=15 open chest canine studies
RT3D images (20-22 frames) acquired w/ Philips iE33 system

| A = auto (algorithm) segmentation | B = manual segmentation ("gold standard") |

Mean absolute distance (MAD)
\[
\text{MAD}(A, B) = \frac{1}{2} \left\{ \frac{1}{N} \sum_{i=1}^{N} d(a_i, B) + \frac{1}{M} \sum_{j=1}^{M} d(b_j, A) \right\}
\]

Hausdorff distance (HD)
\[
\text{HD}(A, B) = \frac{1}{2} \left\{ \max_i d(a_i, B) + \max_j d(b_j, A) \right\}
\]

Percentage of true positives
\[
\text{PTP} = \frac{\text{Volume}(\Omega_A \cap \Omega_B)}{\text{Volume}(\Omega_A)}
\]
Quantitative Evaluation (cont.)

3 Algorithms tested vs. Manual Tracing:
- **SSDM** = Subject Specific Dynamic Model (Our approach)
- **GDM** = General Dynamic Model (prediction from previous 2 frames)
- **SM** = Static Model (PDM-like)

Mean absolute distance (MAD)  
Hausdorff distance (HD)  
Percentage of true positives

<table>
<thead>
<tr>
<th></th>
<th>MAD (mm)</th>
<th>HD (mm)</th>
<th>PTP (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ENDO</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>automatic-manual (SSDM)</td>
<td>1.41 ± 0.40</td>
<td>2.53 ± 0.75</td>
<td>95.9 ± 1.24</td>
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<tr>
<td>automatic-manual (GDM)</td>
<td>1.52 ± 0.46</td>
<td>3.25 ± 0.98</td>
<td>94.8 ± 1.56</td>
</tr>
<tr>
<td>automatic-manual (SM)</td>
<td>2.33 ± 0.67</td>
<td>4.31 ± 1.26</td>
<td>93.1 ± 1.51</td>
</tr>
<tr>
<td><strong>EPI</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>automatic-manual (SSDM)</td>
<td>1.74 ± 0.39</td>
<td>2.79 ± 0.97</td>
<td>94.5 ± 1.74</td>
</tr>
<tr>
<td>automatic-manual (GDM)</td>
<td>1.77 ± 0.41</td>
<td>2.91 ± 0.95</td>
<td>93.6 ± 1.78</td>
</tr>
<tr>
<td>automatic-manual (SM)</td>
<td>1.81 ± 0.65</td>
<td>3.18 ± 1.23</td>
<td>92.3 ± 1.91</td>
</tr>
</tbody>
</table>

Mean and SD over all points X all frames X all subjects
A database-free contour tracking framework

- A dynamical appearance model
- Individual data coherence; spatiotemporal constraint
- Multiscale sparse representation; dictionary learning
- First work applying sparse modeling to this problem
- Level sets; maximum a posteriori (MAP) estimation
LV Segmentation via Online Dictionary Learning

**Sparse Representation**

\[ u \in \Omega \rightarrow \text{appearance vector} \rightarrow y \in \mathbb{R}^n \]

\[ D \in \mathbb{R}^{n \times K}, K > n \]

\[ x \in \mathbb{R}^K \]

Multiscale appearance dictionary

**Online Dictionary Learning**

Pairs of dictionaries are learned at each scale using AdaBoost where multiple weak learners are found by varying one column at a time per scale…..and then multiple scales are combined.

Dynamical dictionary update interlaced with sequential segmentation.
Examples of learned dictionaries

Blood Pool

Myocardium

Coarse scale

Fine scale
Two problems in sparse modeling

- **Sparse coding**

  \[
  \min_{x} \| y - Dx \|_2^2 \quad \text{s.t.} \quad \|x\|_0 \leq T_0
  \]

  *Greedy algorithms*: matching pursuit (MP), orthogonal matching pursuit (OMP), etc.
  *Convex optimization*: least angle regression (LARS), coordinate descent, iterative shrinkage-thresholding algorithm (ISTA), etc.

- **Dictionary learning** (uses sparse coding at each step of Adaboost framework via k-SVD)

  \[
  \min_{D,X} \| Y - DX \|_2^2 \quad \text{s.t.} \quad \forall i, \|x_i\|_0 \leq T_0
  \]

  K-SVD, method of optimal directions (MOD), online dictionary learning (ODL), etc.
Sparse representation of local appearance

Dynamical appearance model

appearance vector
\[ y \in \mathbb{R}^n \]

dictionary
\[ D \in \mathbb{R}^{n \times K}, K > n \]

sparse representation
\[ x \in \mathbb{R}^K \]

appearance classes
\[ \Omega^1_t, \Omega^2_t \]

dictionaries
\[ D_1, D_2 \]

sparse coding
\[
\min_x \| y - Dx \|_2^2 \text{ s.t. } \| x \|_0 \leq T_0
\]
\[ y_i \text{ from class } i \]

reconstruction residues
\[ R(y_1, D_2) > R(y_1, D_1) \]
\[ R(y_2, D_1) > R(y_2, D_2) \]

Residues computed in test data
LV Segmentation via Online Dictionary Learning

**MAP Estimation**

**Goal:** estimate the segmentation $s_t$ of frame $I_t$, given $I_{1:t-1}$ and $s_{1:t-1}$.

$$
\hat{\Phi}_t = \arg \max_{\Phi_t} p(\hat{\Phi}_{1:t-1}, I_{1:t-1}, I_t | \Phi_t) p(\Phi_t)
\approx \arg \max_{\Phi_t} p(\Phi^*_t, R_t, I_t | \Phi_t) p(\Phi_t)
\approx \arg \max_{\Phi_t} p(\Phi^*_t | \Phi_t) p(R_t | \Phi_t) p(I_t | \Phi_t) p(\Phi_t).
$$

**Experimental Results**

Typical segmentations by our method (red, purple) and manual tracings (green).
Experimental Results (Contd.)

<table>
<thead>
<tr>
<th></th>
<th>expressed as mean±std</th>
<th>DICE (%)</th>
<th>PTP (%)</th>
<th>MAD (mm)</th>
<th>HD (mm)</th>
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<tbody>
<tr>
<td><strong>Endocardial</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rayleigh [12]</td>
<td>74.9 ± 18.8</td>
<td>83.1 ± 16.3</td>
<td></td>
<td>2.01 ± 1.22</td>
<td>9.17 ± 3.37</td>
</tr>
<tr>
<td>DAM</td>
<td>93.6 ± 2.49</td>
<td>94.9 ± 2.34</td>
<td>0.57 ± 0.14</td>
<td>2.95 ± 0.62</td>
<td></td>
</tr>
<tr>
<td>SSDM [5]</td>
<td>—</td>
<td>95.9 ± 1.24</td>
<td>1.41 ± 0.40</td>
<td>2.53 ± 0.75</td>
<td></td>
</tr>
<tr>
<td><strong>Epicardial</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Rayleigh [12]</td>
<td>74.1 ± 17.4</td>
<td>82.5 ± 12.0</td>
<td></td>
<td>2.80 ± 1.55</td>
<td>16.9 ± 9.30</td>
</tr>
<tr>
<td>DAM</td>
<td>97.1 ± 0.93</td>
<td>97.6 ± 0.86</td>
<td>0.60 ± 0.19</td>
<td>3.03 ± 0.76</td>
<td></td>
</tr>
<tr>
<td>SSDM [5]</td>
<td>—</td>
<td>94.5 ± 1.74</td>
<td>1.74 ± 0.39</td>
<td>2.79 ± 0.97</td>
<td></td>
</tr>
</tbody>
</table>

DAM is just as good as SSDM w/o prior database

Figure 7. Comparisons of segmentation results by the Rayleigh model (top) and our DAM (bottom). Green: Manual. Red: Automatic endocardial. Purple: Automatic epicardial.
III. Physical Models:

Cardiac Motion/Deformation Analysis
4DE Image Acquisition

B-mode

RF

Endo- and Epi-cardial Surface Segmentation (Dictionary Learning-based)

Local Curvature & confidence

Regularized Shape tracking (G-RPM)

GPU Correlator (using phase & magnitude)

Viterbi Filter

Integration (meshed or meshless)

Geometry/appearance

Shape-based displacements $U_{\text{shape}}$

Speckle-based displacements $U_{\text{speck}}$

Dense biomechanics $U_{\text{dense}}$
e.g., note Bending Energies:
\[ \epsilon_{be}(u, v) = \kappa_1^2(u, v) + \kappa_2^2(u, v) \]
(White = less bending away from flat plane, Green = more bending)
RF-based Speckle Tracking from 4DE (M. O’Donnell, et al.)

**RF (complex) Images**

**B-mode axial, elevation plane for t=16/40**

**Corr. Coeff**

t=16 to t=17

ρ(x,t,t+1)

**Axial, elevational, lateral displacements t=16 to t=17**

uspeckle(x, t, t+1)

cspeckle(x, t, t+1)

**Dense Displacement Field Estimation U_{dense}**

**FPGA**

**Real-time trashogram**

**Correlation Function Filtering**

**Display (Real-time trashogram)**

**Sub-pixel Displacement and Confidence Estimation**

**n-D Correlator**

**I/O**

**RAM**
Effect of Increasing Model Stiffness

\[
C^{-1} = \begin{bmatrix}
\frac{1}{E_p} & -\nu_{pp} & -\nu_{fp} & 0 & 0 & 0 \\
-\nu_{pp} & \frac{1}{E_p} & \frac{1}{E_f} & 0 & 0 & 0 \\
-\nu_{fp} & \frac{1}{E_p} & \frac{1}{E_f} & 0 & 0 & 0 \\
0 & 0 & 0 & \frac{2(1+\nu_{pp})}{E_p} & 0 & 0 \\
0 & 0 & 0 & 0 & \frac{1}{G_f} & 0 \\
0 & 0 & 0 & 0 & 0 & \frac{1}{G_f}
\end{bmatrix}
\]

\(E_f = \) fiber stiffness  \\
\(E_p = \) cross fiber stiffness (\(E_f \sim 4E_p\))  \\
\(\nu_{fp}, \nu_{pp} = \) corresponding Poisson’s ratios (\(\sim .4\))  \\
\(G_f \sim \frac{E_f}{2(1+\nu_{fp})}\) (shear modulus across fibers)

\(F_r = 5000\) Pascal  \\
\(F_c = 1000\) Pascal

\(E = 20000\) Pascal  \\
\(E = 40000\)  \\
\(E = 70000\)
Solution via Finite Element Method

Now write the logarithmic version of the a-posteriori solution:

\[
\hat{u} = \arg \max_u \left( \log p(u^m | u) + \log p(u) \right)
\]

Data Term  Model Term

\[
\hat{U} = \max_U \sum_{\text{all elements}} \left[ (U-U^m)^t A(U-U^m) + U^t K U \right]
\]

Differentiating wrt U yields:

\[
A(U-U^m) = K U
\]

which can be solved for U
Strain from MRI (Shape-Tracking: Sinusas, et al, AJP, 2003)

Normal Canine Heart 1 Hour Post- LAD Occlusion

Infarct region strains for N=6 dogs

![Graph showing strain comparison between normal and infarct regions](image-url)
Sparse to Dense Displacements: Options

- **Free Form Deformation (FFD):**
  - must place control points on regular lattice
  - difficult to model complex geometries

- **Extended Free Form Deformation (EFFD):**
  - allows for complex geometry
  - complicated meshing procedure
  - segmentation necessary

- **Finite Element Method (FEM):**
  - sensitive to data distribution
  - computationally intensive
  - complicated formulation

- **Boundary Element Method (BEM):**
  - requires mapping of interior points to boundaries
  - difficult to implement for non-homogenous material

- **Radial Basis Functions (RBF):**
  - no meshing required
  - easy to model complex geometry
  - can either interpolate or approximate
Integration of Speckle (Green) and Shape (Red) Displacements (Compas, et al., *IEEE TMI*, Feb, 2014)

- FEM Methods require meshing (difficult w/ certain geometries) & are computationally costly
- Recently moved toward combining the complementary shape and speckle-tracked information using mesh-free techniques: radial basis functions (RBFs)
- Model Deformation field as a linear combination of basis functions

\[ \hat{u} = \arg \max_u P(u/I_{rf}, I_{bm}) \]
\[ U(x) = \sum_{k=1}^N \lambda_k \phi(||x - x_k||) \]
Sector-based Strain Comparison: Integrated 4DE vs MR tagging (N=8 dogs)
Radial Basis Function (RBF) interpolation Of Displacement Vector Fields: Sparsity Formulation

- Approximation of a function value at any point $x$ is given by sum of values of $N$ radial basis functions evaluated at any $x = <x, y, z>$:

$$f(x) = \sum_{k=1}^{N} w_k \phi_{\sigma_k}(||x - c_k||)$$

- Writing each radial basis function component as $h_k$, and consolidating them together as a matrix $H$, we can write the dense displacement estimates $U$ as (in 2D):

$$U = <Hw_x, Hw_y>$$

- Solving for $U$ is equivalent to solving for $w_x$ and $w_y$.

- We can solve for $w_x$ and $w_y$ in the following way by using their $l_1$ norms as penalties:

$$\hat{w}_x, \hat{w}_y = \arg\min_{w_x, w_y} \sum_{i \in A_{sh}} ||U(i) - U_{sh}(i)||_2^2 + \sum_{i \in A_{sp}} ||U(i) - U_{sp}(i)||_2^2 + \lambda||w_x||_1 + \lambda||w_y||_1$$

(A_{sh} and A_{sp} index the speckle tracked and shape tracked displacement values)

RBFs as a dictionary and sparsity

Radial basis functions of varying widths and positions.

Each column vector is $x, y$ (and $z$) position and a width.

Fig: Figure displaying how radial basis functions of different widths and different positions are considered and implicitly chosen using the sparsity constraints. The yellow, green and pink colors encode the basis function variety.
Sparse coding with RBFs

- Because in practice minimizing $l_1$ norm leads to a sparse solution (Chen et al., 2001), in context of our problem, it means the weights corresponding to several basis functions will be zero.
- This implies that only certain number of basis functions we consider for interpolation are relevant.

Fig: (left) Visualization of the RBF of different widths over sparse data. (Right) Only the significant RBFs, interpolating the dense field
Learning with RBFs

- The choice of the ‘dictionary’ of basis functions to carry out the interpolation is possibly an important determinant in the efficacy and the quality of the interpolation results.
- This is something we look to explore and hopefully exploit.
- Choosing a set of RBFs of different width profiles, would lead to a different dictionary. Based on the distribution of the data and the displacement values, we hope to learn the appropriate one.
- AT THE MOMENT: just find the sparsest coded combination of multiscale RBFs to fit data.....

- IN THE FUTURE: learn more efficient displacement dictionaries from collections of frames and/or training sets and apply to a test set (i.e. a multiframe, spatiotemporal displacement dictionary)

Fig: (left) Visualization of the RBF of different widths over dense data. (Right) RBFs of half the width on left used result in different orientations (scaling not exact)
Fig: (left) B-mode image. (right) Region consisting of the myocardium displayed.

Fig: (Left) Sparse shape (yellow) and speckle (green) displacements. (Right) Dense displacement field.
Biomechanical information

- We are also looking to explore how we can possibly include biomechanical constraints into our estimation scheme that models how the myocardium deforms in reality.

- One such method is including the divergence free constraint to the displacement field. This is supposed to model the incompressibility property of the myocardium.

- We are looking into either using the divergence free RBFs (Lowitzsch 2002) or implicitly including the constraint into our objective function while minimizing it.
Towards 4D Stress Echocardiography

<table>
<thead>
<tr>
<th></th>
<th>Mean ± Stdev</th>
<th>Radial Strain %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remote</td>
<td>18.3±6.7</td>
<td></td>
</tr>
<tr>
<td>Peri-infarct</td>
<td>10.9±7.3</td>
<td>p&lt;.001 vs. rem</td>
</tr>
<tr>
<td>Infarct</td>
<td>6.0±6.7</td>
<td>p&lt;.001 vs. peri</td>
</tr>
</tbody>
</table>

Time 1

Time 2

Difference

Volumetric segments
IV. Remaining Challenges

• Need to consider/model abnormal structure (e.g. infarcted regions---some of this happening w/ sparse coding)

• Move toward more complete temporal motion models.

• Consider formulating core algorithmic principles (e.g. statistical shape theory; sparsity)

• Develop robust validation/evaluation strategies including development of common (training and testing) databases
Colleagues/Collaborators

**Segmentation**:  
- Larry Staib  
- Xiaolan Zeng  
- Hemant Tagare  
- Jing Yang  
- Xiaojie Huang

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- Ping Yan  
- Yun Zhu  
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• Check out Bioimage Suite (www.bioimagesuite.org):

(developer: X. Papademetris)