**Appendix II:**

The Eulerian vectors in a DENSE displacement field at any time frame ($t\_{f}=t\_{1},…,t\_{F}$) reference the corresponding tissue position at time $t\_{0}$. With this information, the Eulerian displacement vector origin ($P\_{0}$) can be computed for each frame as $P\_{0}=\left[\begin{matrix}i-E\_{x\_{f}}\\j-E\_{y\_{f}}\end{matrix}\right]$, where *i* and *j* are image grid points, and $E\_{x\_{f}}$ and $E\_{y\_{f}}$ are the corresponding Eulerian displacements for frame, *f*, in the *x*- and *y*-directions, respectively. In case of 3D DENSE, a third row will be added corresponding to the *z*-direction.

Using the RSTLS formulation of Eq. 4, as discussed in appendix I, the Lagrangian displacement $L\_{f}=\left[\begin{matrix}L\_{x\_{f}}\\L\_{y\_{f}}\end{matrix}\right]$ is computed by:

$$L\_{f}=(\hat{A}^{T}\hat{A})^{-1}\left(\hat{A}^{T}\hat{E}\_{f}\right), \hat{A}= \left[\begin{array}{c}A\\λ B\\μ\end{array}\right], \hat{y}\_{f}= \left[\begin{array}{c}E\_{f}\\0\\μ L\_{f-1}\end{array}\right]$$

To implement above equation, we modified methods described by D’Errico [23].

$\hat{A}$ **computation:**

To compute the Lagrangian displacement of a point on the grid at time t0, the first step is to define the interpolation method. For 2D DENSE we used bilinear interpolation and for 3D DENSE we used trilinear interpolation.

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| Figure A.1. Bilinear interpolation using 4 neighbors. |

As DENSE provides the origin of each Eulerian displacement measurement, *P*0(*x*,*y*) (Figure A.1), the interpolation equation is computed as:

$$E\_{P0}\left(x,y\right)=\left(1-t\_{x}\right)\left(1-t\_{y}\right)L\_{1}+t\_{x}\left(1-t\_{y}\right)L\_{2}+t\_{x}t\_{y}L\_{3}+\left(1-t\_{x}\right)t\_{y}L\_{4}$$

where *EP0* is the Eulerian displacement for the origin point *P*0(*x*,*y*), and *L1*,…,*L4* are the unknown Lagrangian displacements of the four nearest neighbor grid points defined as

$L\_{1}=L(i\_{1},j\_{1})$, $L\_{2}=L(i\_{2},j\_{1})$, $L\_{3}=L(i\_{2},j\_{2})$, $L\_{4}=L(i\_{1},j\_{2})$.

Also, $t\_{x}=\frac{x-i\_{1}}{i\_{2}-i\_{1}} and t\_{y}=\frac{y-j\_{1}}{j\_{2}-j\_{1}}$ where *P*0 is enclosed by $i\_{1}$ and $i\_{2}$ in the *x*-direction ($i\_{1}<x<i\_{2}$) and $j\_{1}$ and $j\_{2}$ in the *y*-direction ($j\_{1}<y<j\_{2}$).

$E\_{P0}\left(x,y\right)$ can be written in matrix form as:

$$E\_{P0}\left(x,y\right)=A\_{1×ngrid}L\_{ngrid×1}, $$

$$where the elements a\_{i,j} of A= \left\{\begin{array}{c}\left(1-t\_{x}\right)\left(1-t\_{y}\right) i=i\_{1}, j=j\_{1}\\t\_{x} \left(1-t\_{y}\right) i=i\_{2}, j=j\_{1}\\t\_{x} t\_{y} i=i\_{2}, j=j\_{2}\\\left(1-t\_{x}\right)t\_{y} i=i\_{1}, j=j\_{2}\\0 otherwise\end{array}\right., and L=\left[\begin{array}{c}L\_{1,1}\\\vdots \\L\_{i,1}\\L\_{1,2}\\\vdots \\L\_{i,2}\\\vdots \\L\_{1,j}\\\vdots \\L\_{i,j}\end{array}\right] $$

Then, we can create the interpolation matrix $A\_{n×ngrid}$ for all myocardial tissue points, where $n$ is the total number of myocardial tissue points and $ngrid$ describes the number of points in a rectangle encompassing the myocardium. The rectangle has dimensions of $n\_{i}×n\_{j} $, therefore,$ ngrid= n\_{i}×n\_{j}$. Each row in the A matrix corresponds to one origin point and each column represents the grid nodes. A is a sparse matrix with 4 non-zero values (4 neighbors) in each row.

The next step is to build the **B** matrix which is a spatial regularizer using the second derivative for all grid points. Here, B is not a Laplacian regularizer ($∆L=\frac{∂^{2}L}{∂i^{2}}+\frac{∂^{2}L}{∂j^{2}}$), instead it is the uncoupled second derivative ($\left[\begin{array}{c}\frac{∂^{2}L}{∂i^{2}}\\\frac{∂^{2}L}{∂j^{2}}\end{array}\right]$) that can be calculated using three grid points for each direction. Figure A.2 shows the numerical second derivative equation for grid point (2) using three unevenly spaced points in the *i*-direction.

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| Figure A.2. A simple configuration demonstrating the use of unevenly spaced points used to calculate the second derivative of point (2) in the *i*- and *j-*directions for matrix **B**. Red and blue colors show the grid neighbors used in the *i-* and *j-*directions, respectively. |

Referring to Figure A.2,

$$\frac{∂^{2}L}{∂i^{2}}=\frac{2[di\_{2}L\_{1}-\left(di\_{1}+di\_{2}\right)L\_{2}+di\_{1}L\_{3}]}{di\_{1}di\_{2}(di\_{1}+di\_{2})}$$

$$\frac{∂^{2}L}{∂j^{2}}=\frac{2[dj\_{2}L\_{1}-\left(dj\_{1}+dj\_{2}\right)L\_{2}+dj\_{1}L\_{3}]}{dj\_{1}dj\_{2}(dj\_{1}+dj\_{2})}$$

where $di\_{2}=i\_{3}-i\_{2}, di\_{1}=i\_{2}-i\_{1}, dj\_{2}=j\_{3}-j\_{2}, dj\_{1}=j\_{2}-j\_{1}$, and $L\_{1}, L\_{2}, L\_{3} $ are the unknown Lagrangian displacements of 3 nodes.

The sparse B matrix is created for all $ngrid=ni×nj$ grid points in both the *i* and *j* directions and then concatenated as $B=\left[\begin{array}{c}\frac{∂^{2}L}{∂i^{2}}\\\frac{∂^{2}L}{∂j^{2}}\end{array}\right]\_{(2×ngrid)×ngrid}$.

Finally, for $\hat{A}$, the matrices $A\_{n×ngrid}$, $B\_{(2×ngrid)×ngrid}$ and $I\_{ngrid×ngrid}$ are concatenated and weighted such that $\hat{A}= \left[\begin{array}{c}A\\λ αB\\μ I\end{array}\right]$. The values of the spatial and temporal weighting factors λ and μ, respectively, are determined empirically. The λ value controls the spatial smoothness of the estimated surface, and μ controls the temporal smoothness. The last scaling factor is $α$, which is given by $α=\sqrt{\frac{number of rows in matrix A}{number of non-zero rows in matrix B }}$. As this parameter is determined by the A and B matrices, to simplify the equations (1-3) we refer to $αB$ as the $B$ matrix. More information about $α$ can be found in [23,24].

$\hat{E}\_{f}$ **computation:**

$\hat{E}\_{f}= \left[\begin{array}{c}E\_{f}\\0\\μ L\_{f-1}\end{array}\right]$, where $E\_{f}\_{n×1}$ is the vectorized Eulerian displacement for myocardial tissue points (*n*) in frame $f, f=1,…,F$. $ L\_{f-1}$ is the calculated Lagrangian displacement of frame *f-1* computed using the RSTLS method. For the initialization, we assume there is no displacement at time $t\_{0}$, such that $L\_{0}=0.$

**λ and μ weighting factors**

For RSTLS solutions for DENSE myocardial Lagrangian displacements, λ must have a positive value. We empirically determined that, for cine DENSE imaging of the human heart, λ should be in the range [3, 10]. We have found that circumferential and longitudinal strain values are relatively insensitive to this parameter and $λ=8$ provides reliable values for these strains. In contrast, radial strain is highly sensitive to the specific value of λ, where lower λ values reduce spatiotemporal smoothness of radial strain but provide more accurate (higher) radial strain values. For radial strain we recommend using λ=3. The temporal weighting factor is μ. If the DENSE images have a very high SNR (i.e., phase SNR > 20), μ could be set to zero. For the general case, our recommendation is $μ\in \left[0.05 , 0.3\right]$. All figures and results in this manuscript computed by $λ=8, and μ=0.2$.