Supplemental Data
Patient-Specific Modeling of Dyssynchronous Heart Failure: A Case Study

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1. Electrophysiology

For our simulations, we used the monodomain model of electrical propagation Equation (1) with zero flux boundary conditions. We use an operator splitting fully implicit collocation finite element method in which we alternate the solve of ODEs and then PDEs at each half PDE time step. The ODEs are integrated using a single iteration backwards Euler scheme, solved on a graphics processing unit (GPU). The PDE step size was set as 0.1 ms. The PDE solve is done with a direct solver, SuperLU.

$$\frac{\partial V}{\partial t} = \Delta \cdot D\Delta V_m - \frac{I_{ion}}{C_m} \tag{1}$$

The electrophysiology mesh used 5120 tri-cubic Hermite elements (51,456 degrees of freedom). Activation times were calculated at the zero crossing of the action potential at every node. Activation times at every node of the electrophysiology mesh were fitted to the nodes at of the Biomechanics mesh using tri-cubic basis functions.

2. Biomechanics

For the biomechanics (BM) simulations, we used a mesh with 128 tri-cubic Hermite elements (1672 DOF). The fitted activation time at every BM mesh node is the input to the mechanics model to initiate myofiber contraction. The material properties of the mechanics model consisted of passive and active material properties.

2.1. Boundary Conditions

Figure 1 shows the nodes where the fixed boundary conditions were applied for the biomechanics simulations. The yellow nodes on the base were constrained from moving along the long axis direction. The green and the red epicardial nodes were fixed from rotation with respect the long axis of the heart. Finally, the derivatives at the apical nodes were constrained to maintain symmetry about the long axis.

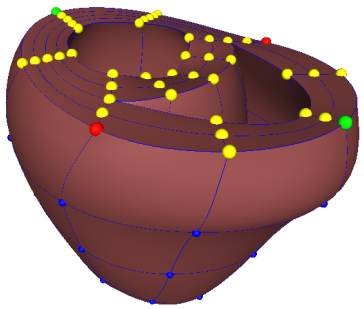

Figure 1: *Nodes that were fixed during the biomechanics simulations.*

2.2. Passive Material Model

The passive material was assumed to be transversely isotropic, slightly compressible. We employed the strain energy law shown in Equation (2).

$$W_{pas} = \frac{1}{2} C_{pas} \cdot (e^{Q} - 1) + C_{comp}(det(\mathbf{F}) ln(det(\mathbf{F}) - det(\mathbf{F}) + 1) \tag{2}$$

Were $\mathbf{F}$ is the deformation gradient tensor.

$$Q = b_f E_{ff}^2 + b_t(E_{cc}^2 + E_{rr}^2 + 2E_{cr}^2) + b_{fr}(2E_{fc}^2 + 2E_{fr}^2) \tag{3}$$

In Equation (3), E_{ff} is strain in the fiber direction, E_{rr} is the transmural radial strain transverse to the fiber, E_{cc} is cross-fiber strain perpendicular to the former two, and the remaining are associated shear strains. C_{pas}, C_{comp}, b_f, b_t and b_{fr} are material parameters. See Table 1.

Table 1: *Passive material properties of the mechanics model.*

Parameter and unit	Description	Value
C_{pas} [kPa]	Passive stress scaling constant	0.44
b_f [-]	Parameter associated with fiber strain	18.5
b_t [-]	Parameter associated with strain transmural to fiber and shear strain in radial-crossfiber plane	3.58
b_{fr} [-]	Parameter associated with shear strains in fiber-radial and fiber-crossfiber plane	1.63
C_{comp} [kPa]	Bulk modulus	350

2.3. Active Material Model

The generation of active stress in the fiber direction was calculated by the Arts model of sarcomere mechanics [Lumens et al., 2009], in which the length of the contractile element (L_{sc}) and a time-variant contractility parameter (C) were state variables. The normalized length of the series elastic element (L_{sNorm}) was calculated using Equation (4).

$$L_{sNorm} = \frac{(L_s - L_{sc})}{L_{SerEl}} \tag{4}$$

where L_s is the sarcomere length and L_{SerEl} length of the series elastic element during isometric contraction. The contractile element velocity $\frac{dL_{sc}}{dt}$ is calculated using Equation (5).

$$\frac{dL_{sc}}{dt} = \begin{cases} \frac{L_{sNorm}-1}{b_{Hill} \cdot L_{sNorm}+1} v_{max} & L_{sNorm} \leq 1 \\ \frac{L_{sNorm}-1}{b_{Hill} \cdot L_{sNorm}+1} v_{max} \cdot e^{a_{Hill}(L_{sNorm}-1)} & L_{sNorm} > 1 \end{cases} \tag{5}$$

This contractile element velocity is a modification from Lumens et al [Lumens et al., 2009], which yields a hyperbolic Hill-relation between shortening velocity and force. Contractility C is described by

$$\frac{dC}{dt} = \frac{1}{\tau_r} \cdot C_L \cdot f_{rise} + \frac{1}{\tau_d} \cdot \frac{C_{rest} - C}{1 + e^{\frac{(T-t)}{\tau_d}}} \tag{6}$$

where t is time elapsed since the electrical activation;

$$C_L = \tanh(20(L_{sc} - L_{s0})^2) \tag{7}$$

C_L regulates the contractility dependence on contractile element length.

$$f_{rise} = 0.02(8 - x)^2 x^3 e^{-x} \tag{8}$$

with $x = min(8, max(0, \frac{t}{\tau_r}))$ we regulate the rise of contractility.

$$T = \tau_{sc}(0.29 + 0.3L_{sc}) \tag{9}$$

Equation (9) regulates twitch duration as a function of the contractile element length. The active fiber stress $\sigma_{f,a}$ is calculated by

$$\sigma_{f,a} = \sigma_{act} \cdot C \cdot (L_{sc} - L_{s0}) \cdot L_{sNorm} \tag{10}$$

Active stress is also generated transverse of the myofibers, , and was about 40% of active stress generated in the myofiber direction [Lin and Yin, 1998]. Table 2 lists the values of the contractile material parameters.

Table 2: *Active material properties of the mechanics model.*

Parameter and unit	Description	Value
a_{Hill} [-]	Parameter that determines curvature of Hill relation during stretching	1.5
C_{rest} [-]	Diastolic contractility level	0.0
b_{Hill} [-]	Parameter that determines curvature of Hill relation during shortening	1.5
L_{s0} [μm]	Contractile element length at zero active stress	1.51
L_{SerEl} [μm]	Length of series elastic element during isometric contraction	0.04
v_{max} [$\frac{\mu m}{sec}$]	Unloaded sarcomere shortening velocity	5.0
τ_d [ms]	Relaxation time scaling factor	33.8
τ_r [ms]	Contraction rise time scaling factor	28.1
τ_{sc} [ms]	Twitch duration time scaling factor (prolonged relaxation)	292.5
σ_{act} [kPa]	Active stress scaling factor failing (reduced inotropy)	58.4

3. Hemodynamics

The finite element models of each of the ventricles were coupled to a three-element Windkessel model. The parameters used for LV and RV Windkessel models as well as the Windkessel models for the closed-loop circulation are shown in Table 3.

Table 3: *Circulation Model*

Systemic Circulation	
Parameter and unit	**Value**
arterial impedance [$kPa \cdot sec/lit$]	0.1
arterial compliance[ml/kPa]	5.0
peripheral resistance [$kPa \cdot sec/lit$]	80.0
venous compliance [ml/kPa]	350.0
venous resistance [$kPa \cdot sec/lit$]	6.0
Pulmonary Circulation	
Parameter and unit	**Value**
pulmonary artery impedance[$kPa \cdot sec/lit$]	0.2
pulmonary artery compliance [ml/kPa]	15.0
pulmonary resistance [$kPa \cdot sec/lit$]	20.0
venous compliance [ml/kPa]	20.0
venous resistance [$kPa \cdot sec/lit$]	6.0

4. Database

All models were constructed and solved using the Continuity software, publicly available at **www.Continuity.ucsd.edu/Continuity/Download**. All of the models used in this paper are available in the Continuity Library with **Number ID 998 and 999**, titled "Patient-Specific Modeling of Dyssynchronous Heart Failure: A Case Study".

References

Lin, D., Yin, F., 1998. A multiaxial constitutive law for mammalian left ventricular myocaridum in steady-state barium contracture or tetanus. J. Biomech. Eng.-Trans. ASME. 120, 504–517.

Lumens, J., Delhaas, T., Kirn, B., Arts, T., 2009. Three-Wall Segment (TriSeg) model describing mechanics and hemodynamics of ventricular interaction. Ann. Biomed. Eng. 37, 2234–2255.