Sensitivity Analysis of Elastance-based Cardiovascular Models for CRT Optimization

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Context: Cardiac resynchronization therapy (CRT) is an implant-based treatment for mechanically uncoordinated hearts used in heart failure patients. Positive response notably depends on patient-specific settings for atrio and inter-ventricular stimulation delays. Some echocardiography markers have been proposed to characterize cardiac desynchronization. Among them, the left pre-ejection interval (LPEI) has been widely studied. However, cardiovascular phenomena affecting LPEI have not been quantitatively analyzed yet. In this work, we propose a sensitivity analysis of a cardiovascular model on LPEI, while simulating different CRT stimulation configurations.

Methods: A lumped-parameter model, integrating elastance-based atrial and ventricular chambers; elastance-based interventricular coupling; systemic and pulmonary circulations and a simplified model of a CRT device, is proposed, based on a previously validated model. A "Double-Hill" elastance driver function is integrated since it allows to differentiate systolic and diastolic phases. The model can reproduce, for different CRT configurations, the trans-valve flows used to estimate LPEI. Morris' sensitivity analyses are performed to analyze the contribution of each elastance's parameters to LPEI.

Results: Aortic and mitral flows respectively show a higher sensitivity to parameters associated with systolic (As) and diastolic (Ad) phases of the ventricular elastances (Figure 1). For instance, Morris' mean elementary effect on LPEI for As was 0.44s and its standard deviation was 0.14s (0.006s and 0.034s for Ad). Parameters controlling the systolic slope of atrial elastance are the most sensitive to mitral's flow A-wave and do not significantly affect LPEI. In general, the high Morris' standard deviation values underline the strong interactions between elastance parameters affecting LPEI.

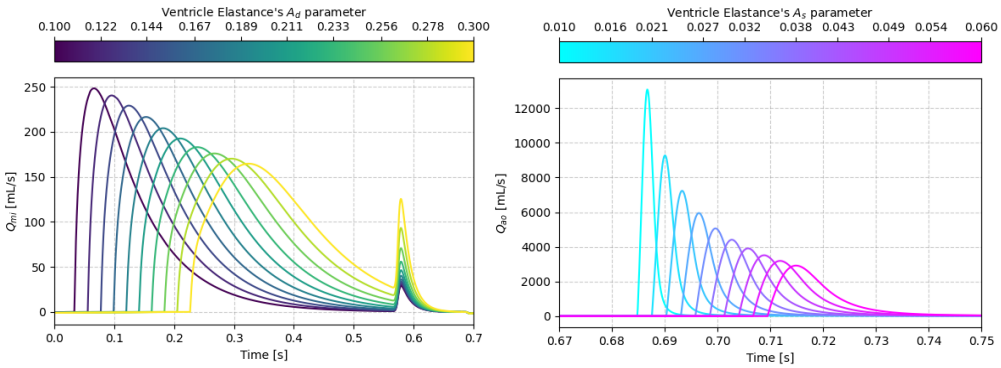

Figure 1 - Influence of ventricular elastances A_s and A_d parameters on trans-valve flows (mitral on the left-hand side and aortic on the right-hand side)

Conclusion: Simulated LPEI is modulated by various intertwined parameters, explaining the difficulty of interpreting this echocardiographic marker. A driver function differentiating systolic and diastolic dynamics is necessary to reproduce the observations during CRT optimization. Sensitive parameters identified in this work will be the target for future patient-specific optimization methods.