# Mechano-Electrical Coupling Explains Worsening of Cardiac Function in the Asynchronous Heart

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In experimental studies it was found that cardiac function deteriorates over time in the asynchronous heart. The role of mechano-electrical coupling (MEC) in this process is unclear. In a multi-scale model we tested the hypothesis that deterioration of cardiac function in the asynchronous heart can be explained by remodeling of ionic membrane currents and calcium handling.

The model described hemodynamic interaction between the left and right ventricle as well as mechanical interaction of three wall segments, i.e., left and right ventricular free wall, and ventricular septum (LVfw, RVfw, and Septum, respectively). Electromechanical behavior of each wall segment was represented by a cardiac fiber composed of $150$ segments that were mechanically and electrically coupled in series. Ionic membrane currents and calcium handling were described for each fiber segment. Isometric contractile force was related to intracellular calcium concentration and sarcomere length. Physiological pressure-volume loops were obtained by simulating the pulmonary and systemic circulations, including atria, valves, arteries, and veins. MEC was incorporated by local adaptation of L-type $Ca^{2+}$ current to obtain a homogeneous distribution of work load throughout the ventricles. Normal activation was simulated by simultaneous electrical activation of the septum and the LVfw. Asynchronous activation was simulated by delaying activation of the LVfw with $80$ ms.

With normal activation, MEC improved cardiac function and led to prolonged action potential duration (APD) in early-activated regions and reduced APD in later-activated regions. APD distribution was consistent with experimental observations in the normal heart and explains T-wave concordance of the ECG. In contrast with normal activation, cardiac function deteriorated with asynchronous activation due to MEC as indicated by a decrease in $dP/dt_{max}$ and ejection fraction and an increase in end diastolic volume and diastolic pressure. We conclude that deterioration of cardiac function in the asynchronous heart can be explained by MEC.