1056-92-1833 **Ian M. Besse*** (ibesse@math.uiowa.edu), 2014 S.E. 12th Ave., #104, Portland, OR 97214, and **Colleen C. Mitchell**, **Erwin F. Shibata** and **Thomas Hund**. *Modeling Stochastic Cardiac Caveolae: a potential source of arrhythmogenic persistent sodium current in cardiomyocytes.*

Contraction of a cardiac myocyte is initiated by a transient depolarization of the cell membrane called an action potential. The electric currents which generate an action potential result from the rapid movement of ions across the membrane through pores called ion channels. Recent studies of membrane microdomains, called caveolae, reveal that caveolae are reservoirs of "recruitable" sodium ion channels. As such, caveolar channels constitute a substantial and previously unrecognized source of sodium current in cardiac cells. Additionally, links have been established between mutations in caveolin-3, the primary structural protein for caveolae, and a particular type of Long QT Syndrome (LQTS), a condition which collectively refers to any of several distinct arrhythmogenic channelopathies affecting cardiac myocyte repolarization. In this research we model caveolar sodium current contributions to the cardiac action potential and show that stochasticity in caveolae, in the absence of any channelopathy, is sufficient to produce delays in myocyte repolarization, the hallmark of LQTS. Our results suggest that alterations to caveolar opening dynamics due to caveolin-3 mutation, rather than alterations to ion channel kinetics, underlie this caveolin-related type of LQTS. (Received September 22, 2009)