

**Title:**

A GENERAL EQUILIBRIUM MODEL TO STUDY INTRACELLULAR CALCIUM HOMEOSTASIS. NEW INSIGHTS ON VENTRICULAR FUNCTION

---

**Authors:** Enrique Alvarez-Lacalle<sup>1</sup>; David Conesa<sup>1</sup>; Blas Echebarria<sup>1</sup>; Inmaculada R Cantalapiedra<sup>1</sup>; Angelina Peñaranda<sup>1</sup>; Yohannes Shiferaw<sup>2</sup>;

---

**Institutions:** <sup>1</sup>Universitat Politècnica de Catalunya (UPC-BarcelonaTech), Department of Physics, Barcelona, Barcelona, Spain; <sup>2</sup>California State University Northridge (CSUN), Department of Physics, Northridge- Los Angeles, California, United States;

---

**Body:**

*Calcium homeostasis is reached when calcium concentrations in a cell along consecutive beats return to the same values on average. The amount of calcium entering the cell via LCC channels, must be the same amount that leaves the cell, mainly due to Sodium-Calcium exchanger. Also, the amount of calcium leaving the SR via the RyR2 must be the same as the calcium entering the SR mainly via SERCA. Since large calcium loads lead to large contractions and vice versa cell functionality is thus directly related with the homeostatic balance.*

*We present a general framework to understand and analyze the homeostatic process in order to make predictions about calcium levels when key properties of the different proteins involved in calcium handling or external pacing are changed. We demonstrate how non-linear interactions render linear intuition worse than useless, misleading. More specifically, we show why some species may increase the level of calcium upon decreasing the pacing rate, or how increasing the conductivity of the LCC can lead directly to depletion of calcium in the cell. We find ourselves in a similar situation as macroeconomists. A system with highly complex interactions where we would like to know whether a global averaged parameter such as GDP in macroeconomics, calcium level in our case, would decrease or increase when facing a particular shock. We actually demonstrate that the proper way to think about the nonlinearities in ventricular cell is the same used in the IS-LM Keynesian macroeconomic model. In both, a minimum model of simultaneous double equilibration captures the essential nonlinearities and interactions providing impressive insights on cell function. We show that the independent variables of this model are pre-systolic SR calcium load and pre-systolic total calcium in the cell. Once this framework is understood, further predictions are possible without falling into false linear projections.*