

# Factors implicating the validity and interpretation of simulated microgravity studies

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May 5, 2020

## Abstract

Simulated microgravity (s- $\mu$ g) devices provide unique conditions for elucidating the effects of gravitational unloading on biological processes. However, s- $\mu$ g devices are being increasingly applied for mechanobiology studies without proper characterization of the mechanical environment generated by these systems, which confounds results and limits their interpretation. Furthermore, the cell culture methodology central to s- $\mu$ g approaches introduces new conditions that can fundamentally affect results, but these are currently not addressed. It is essential to understand the complete culture environment and how constituent conditions can individually and synergistically affect cellular responses in order to interpret results correctly, otherwise outcomes may be misattributed to the effects of microgravity alone. For the benefit of the growing space biology community, this article critically reviews a typical s- $\mu$ g cell culture environment in terms of three key conditions: fluid-mediated mechanical stimuli, oxygen tension and biochemical (cell signalling). Their implications for biological analysis are categorically discussed. A new set of controls is proposed to properly evaluate the respective effects of s- $\mu$ g culture conditions, along with a reporting matrix and potential strategies for addressing the current limitations of simulated microgravity devices as a platform for mechanobiology.

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