

Line-scanning multiphoton imaging reveals rapid dynamics of calcium transients and sarcomere contraction of single primary cardiac cells

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The intracellular level of calcium ions (Ca^{2+}) plays a critical role to regulate the contraction of cardiac cells. Despite its importance, it remains challenging to probe the dynamics of local Ca^{2+} level and sarcomere contraction at the level of single contracting cardiac cells with high spatiotemporal resolution. Here we report simultaneous two-photon excited fluorescence (TPEF) and second-harmonic generation (SHG) imaging of primary cardiomyocytes, which were isolated from transgenic zebrafish that expresses Ca^{2+} -sensitive fluorescent proteins (GCaMP) in the heart [1]. We particularly apply rapid line-scanning (continuous XT mode) of TPEF and SHG along the contraction direction of electrically stimulated primary cardiac cells (red line, Figure 1a), and reveal the orchestrated dynamics of local calcium transients and sarcomere contraction achieving millisecond temporal resolution and sub-100 nm spatial precision. We show that the local Ca^{2+} transient and sarcomere contractility increased significantly after a treatment of epinephrine (Figures 1b and 1c). We anticipate that the same approach should open new routes for not only fundamental study of cardiac pathophysiology but also screening of drugs with cardiac activity and toxicity.

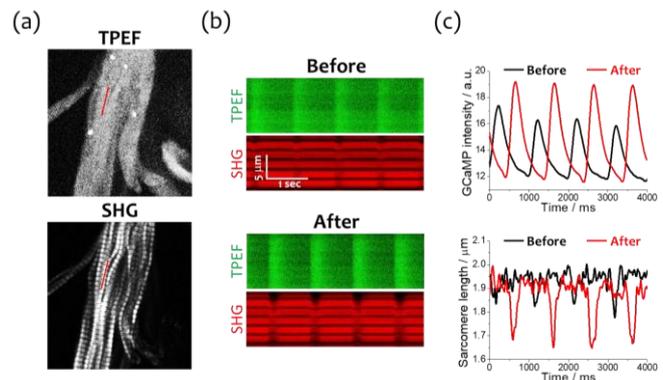


Figure 1. (a) Multiphoton (TPEF and SHG) images of a primary cardiomyocyte. (b) Line-scanning images acquired along the contraction direction of the cells (c) Time-varying calcium level (red) and sarcomere length (black) before and after stimulation with epinephrine (100 nM).

[1] R. Arnaout, T. Ferrer, J. Huisken, K. Spitzer, D. Y. R. Stainier, M. Tristani-Firouzi, N. C. Chi, “Zebrafish model for human long QT syndrome.” *Proc. Natl. Acad. Sci. U.S.A.* **104**, 11316–11321 (2007).