Ultrasound triggered liposome light source for noninvasive optogenetics

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Optogenetics has revolutionized neuroscience understanding by allowing spatiotemporal control over cell-type specific neurons in neural circuits. However, visible light cannot be directly delivered to deep brain tissue, due to the severe dissipation and scattering of photons. As a result, invasive craniotomy is usually required to implant optical fibers in the brain for *in vivo* optogenetic stimulation, resulting in permanent damage and chronic gliosis in brain tissue. To achieve non-invasive optogenetics with high temporal resolution and excellent biocompatibility, we have developed focused ultrasound triggered nanoscopic light sources (Lipo@IR780/L012) for deep brain photon delivery. Synchronized and stable blue light emission was generated under FUS irradiation due to the activation of chemiluminescent L012 via nearby reactive oxygen species generated by IR780. *In vitro* tests revealed that Lipo@IR780/L012 could be triggered by FUS for light emission at different frequencies and hence activate opsin-expressing spiking HEK cells under the FUS irradiation. *In vivo* optogenetic stimulation further demonstrated that motor cortex neurons could be noninvasively and reversibly activated under the repetitive FUS stimulation after i.v. injection of lipid nanoparticles to achieve limb motions control.



Figure 1: Schematic of FUS triggered blue light emission from liposome nanoparticles.