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Poster title: Point-and-CliC Control of Cellular Function In Deep Tissue with Intracellular Bubbles

Abstract: The ability to remotely control cellular activity in deep tissue would enable the study of cellular functions in their native contexts and novel spatially-activated therapeutic modalities. Sonogenetics, the use of ultrasound to control the activity of genetically defined cells, has emerged as a promising approach to address this need, but has typically suffered from weak robustness. Here, we report a new, robust, sonogenetics paradigm that harnesses the well-studied physical phenomenon of bubble cavitation. Using genetically encoded gas vesicles as nucleation seeds, Cavitation-linked intracellular Control (CliC) generates transient intracellular bubbles that trigger rapid calcium influx and immediate early gene (IEG) activation while preserving cell viability. Coupling this response to an IEG-sensing circuit enabled conversion of transient stimulation into modular and persistent genetic outputs. Importantly, CliC operates with mild ultrasound parameters compatible with standard diagnostic probes, enabling programmable beam steering and image-guided targeting at sub-millimeter resolution. We demonstrate spatially precise activation and genetic labeling in cultured cells, tumors, and deep brain structures in adult mice. Together, these results establish CliC as a robust, accessible, and spatially precise platform for controlling cellular function in deep tissue.