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Slick Software, Slow Hardware: Balancing Biophysical Tradeoffs Drives Cellular Reprogramming

Kate E. Galloway
NIH Postdoctoral Research Fellow
University of Southern CA
Los Angeles, CA

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Abstract: Integrating synthetic circuitry into larger transcriptional networks to mediate predictable cellular behaviors remains a challenge within synthetic biology. While significant efforts have been devoted to the design of enhanced synthetic circuitry, less is understood regarding how cellular hardware may impose fundamental performance limitations on integrated circuits. Within the mammalian context, cellular reprogramming continues to generate new cell types, increasingly expanding our perspective of cellular plasticity. Despite improved genetic tools and epigenetic modulations, reprogramming remains a rare cellular event. In this talk, I will describe how I identified epigenetic roadblocks in reprogramming that arise from tradeoffs between transcription and proliferation rates. My discovery highlights how topological stress impacts the function of gene networks (e.g. native or synthetic circuits) and constrains cellular transitions. This finding opens completely new questions about how the structure of the genome stabilizes cellular identity and suggests strategies to improve the design of synthetic gene circuits.