

BIOINFORMATICS SEMINAR

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UNDERSTANDING CELL SIGNAL PERCEPTION VIA HIGH-THROUGHPUT OPTOGENETICS

Despite decades of cell signaling studies, we have a limited understanding of the cell signaling code: how do intracellular signals encode a cell's dynamic environment, and how do these signals drive essential cell functions like proliferation and differentiation? Light activatable—or, optogenetic—tools now provide a powerful toolset to examine these questions through direct, dynamic control of signaling proteins within living cells. In this talk, I will first describe new instrumentation that empowers optogenetics by allowing high-throughput manipulation of optogenetic probes in microwell plates. These devices—the optoPlates—permit a systematic understanding of a cell's input/output response and enable rapid, robust, and reproducible optogenetic experiments. I will briefly detail two examples of how high throughput optogenetics can uncover fundamental principles of cell signal perception and its break down in disease. In the first example, we used optogenetic profiling to discover that certain BRAF-mutant cancer cells process Ras-Erk input signal dynamics in a pathological manner. In the second example, we used multi-color optogenetics to study signal integration between Ras and PI3K signaling, and we uncovered new synergies between these two well-studied pathways. We anticipate that our high-throughput approaches will find broad utility and will help realize the potential of optogenetics for the quantitative dissection of cell biology.

BIOGRAPHY

Lukasz Bugaj is an Assistant Professor of Bioengineering at the University of Pennsylvania. He earned his PhD with David Schaffer at UC Berkeley/UCSF, and he was an Arnold O. Beckman Postdoctoral Fellow in the lab of Wendell Lim at UCSF. Through his training, Lukasz pioneered optogenetic methods to probe signaling pathways in cells, focusing on signaling through the Wnt/ β -catenin and Ras-Erk pathways. At Penn, the Bugaj Lab leverages these approaches to understand how key signaling features — like dynamics, amplitude, and context — can drive important cell fate decisions like stem cell differentiation, and how a cell's perception of these features can be pathologically altered in disease. We ask these questions both in cell and tissue models of stem cell regulation, as well as in patient-derived cancer cell models. Understanding the operational principles of cell signaling will have important therapeutic applications, for example to more effectively interfere with aberrant signaling in cancer treatment, or to predictably control the behavior of engineered cell therapies.



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