# Revealing Cellular Signaling Dynamics with Light-Activated Molecules: From Receptor Ligands to Second Messenger

J. Erl[1]; C. Haag[1]; B. König[1]; J. Wegener[1,2]

[1] Faculty of Chemistry and Pharmacy, University of Regensburg, 93053 Regensburg (Germany)
[2] Fraunhofer Research Institution for Microsystems and Solid State Technology EMFT, Division Cell-Based Sensor Technology, 93053 Regensburg (Germany)
julia.erl@chemie.uni-regensburg.de

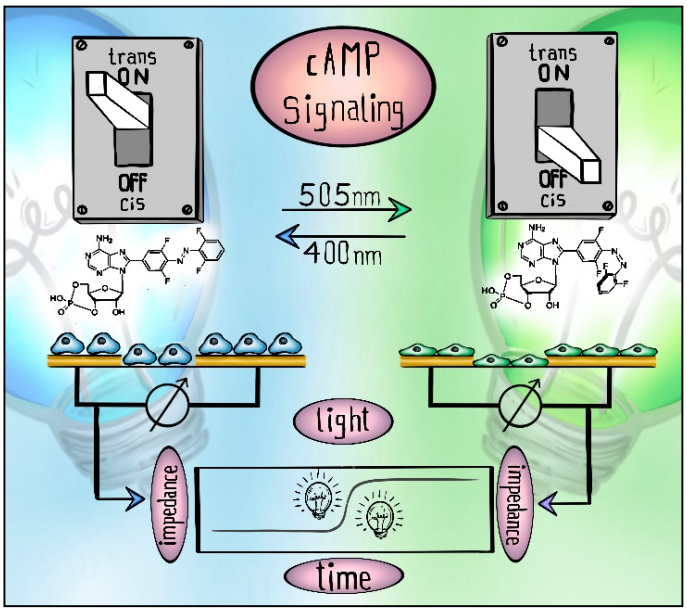


**Figure 1**. Schematic illustration of the measurement principle. Cells cultured on gold-film electrodes are stimulated with photochromic molecules, such as cAMP derivatives. Light-induced conformational changes in these molecules modulate cellular signaling, leading to alterations in cell shape that are detected as changes in the impedance signal.

Decoding the spatiotemporal dynamics of G protein–coupled receptor (GPCR) signaling remains a major challenge in cell biology. Classical pharmacological approaches often fail to capture the reversible and dynamic nature of these pathways. To overcome this, we employed photoresponsive molecules as optical triggers in combination with impedance-based readouts. At the receptor level, photoswitchable ligands for the neuropeptide Y4 receptor enabled precise, light-controlled GPCR activation. [1]

A novel two-electrode ECIS configuration further allowed localized stimulation within a single well and simultaneous monitoring of cellular responses. Downstream in the same pathway, photochromic derivatives of cyclic adenosine monophosphate (cAMP) were synthesized to directly modulate a key second messenger and assess its role in shaping signaling output. [2].

These optically controllable molecules, combined with real-time impedance measurements, provide unprecedented temporal and spatial resolution for dissecting GPCR-mediated signal transduction.

**References:**

[1] J. Erl, U. Wirth, S. Azzam, C. Höring, M. Skiba, R. Singh, K. Hochmuth, M. Keller, J. Wegener, B. König, *Angew. Chem. Int. Ed.* 62 (2023) e202215547.

[2] C. Haag, J. Erl, K. Helbig, J. Wegener, B. Koenig, *ChemRxiv*, (2024); 10.26434/chemrxiv-2024-cq5rz