

Membrane-targeted Photoswitches for Cell Membrane Stimulation and Visual Restoration

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Light-responsive switches offer the possibility to use light as a clean, non-invasive, and spatiotemporally precise tool to trigger cell signalling and control a variety of biochemical functions. In this context, reversible light-sensitive ligands have proven effective in enabling selective and reversible stimulation through the photoisomerization of dyes, either freely diffusing in solution or covalently linked to ion channels, receptors, or other specific binding sites.¹

A rather different approach has been here considered, where the amphiphilic character of cationic membrane-targeted photochromic materials drives their spontaneous partitioning within the cell membrane, with specific affinity to lipid rafts. In this case, the cell signalling arises from changes in membrane properties induced by the light-driven isomerization of the photoswitch.^{2,3}

Cationic membrane-targeted aminoazobenzenes and push-pull azobenzenes have been shown to effectively stimulate neurons through distinct mechanisms, induce muscle contraction, and modulate bacterial membrane potential via optical control.⁴⁻⁶

Finally, preliminary results in fully degenerate retinas from preclinical models of Retinitis Pigmentosa show that these photoswitches are capable of restoring the physiologically complex network processing of visual information.⁷

¹ W. Szymański, J.M. Beierle, H.A.V. Kistemaker, W.A. Velema, B. Feringa, *Chem. Rev.* **2013**, *113*, 6114. ² V. Vurro, G. Bondelli, V. Sesti, F. Lodola, G.M. Paternò, G. Lanzani, C. Bertarelli, *Front. Mater.* **2021**, *7*, 631567. ³ M.L. Di Francesco, F. Lodola, E. Colombo, L. Maragliano, M. Bramini, G.M. Paternò, P. Baldelli, M. Dalla Serra, L. Lunelli, M. Marchioreto, G. Grasselli, S. Cim., L. Colella, D. Fazzi, F. Ortica, V. Vurro, C.G. Eleftheriou, D. Shmal, J.F. Maya-Vetencourt, C. Bertarelli, G. Lanzani, F. Benfenati, *Nat. Nanotechnol.* **2020**, *15*, 296. ⁴ V. Vurro, K. Shani, H.A.M. Ardo, J.F. Zimmerman, V. Sesti, K.Y. Lee, Q. Jin, C. Bertarelli, K.K. Parker, G. Lanzani, *G. APL Bioengineering* **2023**, *7*, 026108. ⁵ T.C. de Souza-Guerreiro, G. Bondelli, I. Grobas, S. Donini, V. Sesti, C. Bertarelli, G. Lanzani, M. Asally, G.M. Paternò, *Adv. Sci.* **2023**, *10*, 2205007. ⁶ V. Sesti et al., *Light: Sci.&Appl.* **2025**, *14*, 8. ⁷ G. Ziraldo, S. Cupini, V. Sesti, E. Delfino, G. Lanzani, C. Bertarelli, F. Benfenati, S. Di Marco, *Nat. Commun.* **2025**, *16*, 600.



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