A polymer optoelectronic interface restores light sensitivity in blind rat retinas

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Interfacing organic electronics with biological substrates offers new possibilities for biotechnology by taking advantage of the beneficial properties exhibited by organic conducting polymers. These polymers have been used for cellular interfaces in several applications, including cellular scaffolds, neural probes, biosensors and actuators for drug release. Recently, an organic photovoltaic blend has been used for neuronal stimulation via a photo-excitation process. Here, we document the use of a single-component organic film of poly(3-hexylthiophene) (P3HT) to trigger neuronal firing upon illumination. Moreover, we demonstrate that this bio–organic interface restores light sensitivity in explants of rat retinas with light-induced photoreceptor degeneration. These findings suggest that all-organic devices may play an important future role in subretinal prosthetic implants.

Extracellular electrical stimulation of neurons provides the basis for many implantable prosthetic devices, that help to restore motor activity (such as electrodes for functional electrical stimulation1–3), to treat drug-resistant diseases (for example, deep brain stimulation in Parkinson’s disease4–7) and to restore sensory perception (such as in cochlear implants8 or retinal prostheses9–11). In the last decade, much effort has been dedicated to improve the interfaces between electrodes and neuronal tissues; indeed many issues related to biological affinity, biocompatibility, mechanical flexibility, ease of functionalization and cost-effectiveness have been investigated extensively. However, the use of light-enabled processes for cell stimulation has received much less attention, with the exception of the outstanding progress made in optogenetic techniques in recent years8,9. Given this scenario, the interfacing of organic electronics and biological substrates offers substantial new possibilities10–12. Organic conducting polymers have been used widely as culturing substrates13, three-dimensional scaffolds14, electrode coatings15,16, organic biosensors17,18, actuators for drug release19,20 and organic electrodes for controlling cell seeding21, growth22,23 and activity detection24. Recently, an organic photovoltaic device has also been used for neuronal photostimulation25,26. This system provides interesting improvements when compared to inorganic semiconductors2–4,27,28 and has great potential for in vivo biological applications, such as retinal prostheses.

In photovoltaic applications, the electron donor–acceptor mechanism is currently the basis of the most efficient organic solar cells. This mechanism takes advantage of the bulk heterojunction architecture to widen the interface between donor and acceptor, maximize the probability of charge pair separation and limit the charge recombination process. One of the most successful photovoltaic blends—a mixture of poly(3-hexylthiophene) and phenyl-C61-butyric-acid-methyl ester (P3HT:PCBM)—has proven to be effective in directly photostimulating neurons grown at the interface25,26. However, once in contact with the biological environment, such bio-hybrid devices may have functional mechanisms that differ from those of conventional solar cells, in which the extraction of photogenerated electrical charges is usually achieved by the aforementioned bulk heterojunction geometry. The neuronal photostimulation process is probably mediated by capacitive charging of the polymer–electrolyte interface rather than an electron transfer phenomenon. In addition, fullerenes have been demonstrated to produce reactive oxygen species upon illumination29. Based on these considerations, we hypothesized that the electron donor–acceptor interface may not be the best possible strategy for driving neuronal activity. In this Article, we demonstrate that a more simple active layer, composed only of the donor component (P3HT), can efficiently stimulate primary neurons upon illumination, and restore light sensitivity in explanted degenerate retinas.

Interface characterization

We first investigated whether illumination of a pure P3HT film is able to locally modify the electric equilibrium at the polymer–electrolyte interface and thus generate a stimulus that is able to induce membrane depolarization in neurons. To this end, we evaluated the temporal and spatial properties of the photocurrent elicited by pulsed illumination, using a patch pipette in voltage-clamp mode positioned in close proximity (<5 μm) to the P3HT layer (Fig. 1a). Pulsed illumination (20 ms, 15 mW mm−2) of the polymer area under the electrode generated large (142.6 ± 7.4 pA, n = 12, mean ± s.e.m.) and fast (43.4 ± 2.2 pA ms−1, n = 12, mean ± s.e.m.) ionic currents (Fig. 1b).

The sign of the current was consistent with the generation of an excess negative charge under the electrode, while the rest of the electrolyte (including the reference electrode) remained relatively positive. Moreover, while illuminating the P3HT surface with a train of repetitive pulses (20 ms, 15 mW mm−2) at a frequency of 2 Hz (Fig. 1c), the generated photocurrent decayed very slowly (last response: 72.83 ± 0.86% of the first response). This suggests the possibility of applying a train of pulses for repetitive neuronal stimulation.

To understand the gradient distribution of the photogenerated current, we examined the intensity profile of the photocurrent by...
Figure 1 | Characterization of the photostimulus generated by the polymeric interface. a, Schematic representation of the stimulation and recording paradigm. A patch-clamp amplifier is used to detect photocurrents generated by light stimulation through a patch pipette positioned in close proximity (<5 µm) to the P3HT surface. b, Photocurrent detected in voltage-clamp mode with light illumination (20 ms, 15 mW mm⁻²; green bar). The trace represents an average of five consecutive sweeps. c, Photocurrents generated with repetitive light pulses (20 ms, 15 mW mm⁻²; green bars) at a repetition rate of 2 Hz. A substantial preservation of the photocurrent is observed during the light pulse train. d, Distribution of photocurrent along the P3HT surface and at increasing distances from the polymer surface. The green circle represents the light spot (100 µm, 20 ms, 15 mW mm⁻²), and the white and red dots represent the points at which the patch pipette was sequentially positioned. The black dot represents the starting position. e, Mean (±s.e.m.) photocurrent along the P3HT surface, normalized to the amplitude of the first response, is shown as a function of distance from the spot centre ($n = 6$). f, Left: photocurrent detected in voltage-clamp mode upon light illumination at increasing distances from the polymer surface. Right: mean (±s.e.m.) photocurrent intensity, normalized with respect to the amplitude of the first response, as a function of distance from the polymer surface ($n = 6$).
progressively increasing the distance of the pipette from the illuminated spot in both horizontal and vertical planes (Fig. 1d). Outside the light spot, the intensity of the photocurrent was dramatically reduced (42% reduction at 25 μm from the spot edge) and had an exponential profile (Fig. 1e). We also observed an exponential decrease in the photogenerated current with increasing distance from the polymer–electrolyte interface (Fig. 1f). These observations confirm that charge accumulation in response to illumination occurs at the polymer–electrolyte interface and is localized to the illuminated area.

**Photostimulation of primary neurons**

We then asked whether, upon illumination, the P3HT photovoltaic layer was able to excite primary neurons cultured on the polymer surface by the generation of local stimuli in the electrolyte. Rat hippocampal neurons were grown on P3HT-coated glass:indium tin oxide (ITO) substrates and analysed at 18–21 days in vitro with viability assays and patch-clamp recordings (Fig. 2a). The biocompatibility of the P3HT:PCBM blend has previously been demonstrated in cultured hippocampal neurons. As an additional control, we performed a cell viability assay (Supplementary Fig. S1a) of neurons cultured on either P3HT-coated glass:ITO or control glass:ITO substrates at 21 days in vitro. No significant differences were found in either cell viability (Supplementary Fig. S1b, Student’s t-test, \( P = 0.818, n = 6 \)) or mortality (Supplementary Fig. S1c, Student’s t-test, \( P = 0.639, n = 6 \)) under these culture conditions, indicating that the P3HT layer did not alter neuronal viability over a long period of time. As further proof of cell viability, comparison of the resting membrane potential of neurons cultured on either P3HT-coated glass:ITO or control glass:ITO substrates did not reveal any significant difference (Supplementary Fig. S1d, Student’s t-test, \( P = 0.128 \)).

When neuronal activity was assessed by patch-clamp analysis in current-clamp configuration, we found that a light pulse (20 ms, 15 mW mm\(^{-2}\)) was able to depolarize neurons and induce them to fire action potentials (Fig. 2b, left panel, black trace) with short peak latencies and a negligible latency jitter (Fig. 2b, right panel). Outside the illuminated area. Right: mean (+ s.e.m., Student’s t-test; latency jitter: P3HT 0.98 ± 0.12 ms, P3HT:PCBM 1.48 ± 0.25 ms, \( P = 0.361 \), mean ± s.e.m., Student’s t-test). In contrast, light stimulation was virtually ineffective for neurons grown onto control glass:ITO coverslips (Fig. 2b, left panel, grey trace). Moreover, we were able to effectively trigger spike trains at up to 20 Hz of pulsed illumination, with high reproducibility, in the 1–10 Hz range (Fig. 2c); only at 20 Hz were a limited number of failures observed (inset of Fig. 2c). The percentage of successful spikes in the train, computed over all recorded neurons as a function of the stimulation frequency, confirmed the tight coupling between light stimulation and firing frequencies (Fig. 2d). The optimal pulse duration was chosen by testing various pulse widths under stimulation from a train of 20 pulses delivered at 1 Hz (Supplementary Fig. S2a). Using a 20 ms pulse, the number of successful spikes from a train of 20 pulses was \( \approx 100\% (96.67 ± 1.67\%, \text{mean ± s.e.m.; Supplementary Fig. S2b}) \). Under this condition, the depolarizing current amplitude was \( −75.51 ± 4.61\, \text{pA (mean ± s.e.m., } n = 5 \) (measured by patch-clamp analysis in voltage-clamp configuration at a holding potential of \( −60\, \text{mV} \)).

To evaluate the efficiency of the single-donor-component active layer in depolarizing neurons, we compared the extent of neuronal depolarization with that obtained with the P3HT:PCBM blend active layer by performing current-clamp experiments in the presence of tetrodotoxin (TTX, 1 μM), a blocker of voltage-dependent Na\(^+\) channels that inhibits action potential generation (Supplementary Fig. S3a). The amplitudes of depolarization elicited by light pulses of various durations (20–100 ms) were similar, regardless of the presence of PCBM in the active layer (Supplementary Fig. S3b). Moreover, no detectable differences in the resting potentials were observed in neurons cultured on either glass:ITO, P3HT-coated glass:ITO or P3HT:PCBM-coated glass:ITO substrates in the presence of TTX (Supplementary Fig. S3c).

**Photostimulation of retinal explants**

The high spatial and temporal resolution demonstrated by the P3HT active layer in stimulating cultured neurons, together with the properties of the polymer interface (biocompatibility, no external bias or heat generation), suggests a potential application in the...
field of retinal prostheses. We therefore investigated the ability of the polymer layer to restore light sensitivity in retinas explanted from albino rats with a light-induced degeneration of the photoreceptor layer (Fig. 3a,b). Acutely dissected retinas were placed on either P3HT-coated glass:ITO or glass:ITO alone in a subretinal configuration (that is, external layers in contact with the polymer). As an additional control, retinas from littermates housed under dim light conditions were also analysed. Multi-unit activity (MUA) recordings, performed with an extracellular electrode in the retinal ganglion cell (RGC) layer and representing the output response of the retina to light, showed that a light stimulus (10 ms, 4 mW mm\(^{-2}\); 16-fold lower than the safe limit for pulsed illumination that can be delivered to the retina in ophthalmic application, see Methods) failed to induce spiking activity in degenerate retinas on glass:ITO, but this stimulus elicited intense activity in control retinas. Strikingly, light-induced spiking activity resumed in degenerate retinas placed on P3HT-coated glass:ITO, to levels indistinguishable from those recorded in control retinas (Fig. 4a,b). This response appeared with a delay of ~70–100 ms after the onset of the light pulse and was specifically blocked by TTX (Supplementary Fig. S4). The response latency and the persistence of the local field potential (LFP) associated with synaptic activity indicated that the firing of RGCs in degenerate retinas was mediated by activation of the external cell layers interfaced with the polymer. To evaluate the efficiency of the retinal interface, dose–response analyses of both spiking activity (Fig. 4c) and LFP amplitude (Supplementary Fig. S5) versus light intensity were performed in degenerate retinas over P3HT-coated glass:ITO or glass:ITO alone. Remarkably, spiking activity was observed in degenerate retinas over the polymer, with a response threshold (10% of maximal amplitude) below 0.3 \muW\(\text{mm}^{-2}\), a linear increase in the 1–100 \muW\(\text{mm}^{-2}\) range, and a response saturation (90% of maximal amplitude) at 100 \muW\(\text{mm}^{-2}\) (still below the safe limit of radiant power that can be delivered chronically to the retina in ophthalmic applications, see Methods). In contrast, spiking activity in degenerate retinas recorded over glass:ITO displayed low levels of spiking activity only at very high light intensities (threshold, 80 \muW\(\text{mm}^{-2}\); Fig. 4c). A fourfold increase in the amplitude of the light response at saturation and a significant left shift of the dose–response curves were obtained in retinas placed over the P3HT-coated interface. Consistent results (threshold for the response below 0.2 \muW\(\text{mm}^{-2}\); linear response in the 1–100 \muW\(\text{mm}^{-2}\) range; response saturation at 100 \muW\(\text{mm}^{-2}\)) were also observed in the dose–response analysis of LFP amplitudes (Supplementary Fig. S5).

**Discussion**

We have documented that a single-component organic polymer film is sufficient to build efficient opto-neuronal interfaces. We investigated this novel polymer–electrolyte system by measuring the photocurrent locally generated at the interface, characterizing the effect of the biological environment on the properties of the polymer film and identifying the mechanisms leading to efficient neuronal photo-excitation. The use of the single P3HT component seems particularly favourable for reducing material toxicity during light exposure, as fullerene photo-excitation has been reported to result in singlet oxygen formation from the triplet state\(^{29}\).

We have demonstrated that, although poorly efficient as a solar cell, once the P3HT film is in contact with an electrolytic solution, it becomes capable of depolarizing neurons upon illumination, with high reproducibility, in a manner similar to that previously observed with bulk heterojunctions (P3HT:PCBM blend)\(^{20}\). These findings indicate that the two configurations are equivalent for the purpose of interfacing organic polymers with biological tissues. This is consistent with an effective charge dissociation occurring mainly at the interface with ITO, with minor contributions from carriers generated in the bulk (where the presence of PCBM is crucial for efficient dissociation). We also found that contact with the electrolyte was associated with an increase in p-doping of the P3HT polymer, a process probably mediated by molecular oxygen, which causes oxidation of the polymer and the generation of free holes (Supplementary Results and Fig. S6). Analysis of the photocurrent resulting from interface polarization was compatible with an accumulation of negative charges at the illuminated polymer surface; these attract positive ions from the electrolytic solution and from the liquid shell wetting the external face of the neuronal membrane. Thus, stripping the excess extracellular positive charge is probably the mechanism that triggers membrane depolarization and, eventually, neuronal firing.

The ability of the organic interface to photostimulate neurons prompted us to investigate its efficacy in restoring light sensitivity to blind retinas. Sight restoration in blind people is one of the new frontiers for prosthetic devices that enable the electrical stimulation of neurons. In particular, diseases that affect the retinal pigment epithelium and photoreceptors but preserve the inner retinal layers, such as Retinitis pigmentosa, Stargardt’s disease or age-related macular degeneration, are preferential targets for implantation of visual prostheses. Several approaches for the treatment of patients with degenerative diseases of the outer retina have previously been described\(^{30}\), including the regeneration of lost photoreceptors by transplantation\(^{31,32}\), gene therapy\(^{33}\) or the use of artificial/engineered photoreceptors. The last category includes the implant of retinal prosthetic devices or the expression of microbial opsins\(^{34,35}\). Optogenetic probes are an emerging, widely used tool in neuroscience, but their application in humans remains limited by the viral expression of the probes. In contrast, silicon-based retinal prosthetic devices implanted in either an epiretinal or subretinal\(^{47}\) configuration have entered the level of clinical experimentation and have yielded partial sight restoration. However, no retinal prosthesis reported to date is totally autonomous in

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**Figure 3** The photoreceptor layer is replaced in the degenerate retina by the organic polymer. a, Schematic illustrations of the retinal structure (left) and the stimulation/recording interface for degenerate retinas (right). b, Confocal images of latero-dorsal control (left) and degenerate (right) retinal sections labelled with the nuclear stain bisbenzimide (gcl, ganglion cell layer; inl, inner nuclear layer; onl, outer nuclear layer). Scale bar, 50 \mu\text{m}.
functioning: existing silicon-based electronic devices remain limited by the electrode spatial resolution and the requirement for connections for data processing and/or a power supply. Recently, an elegant solution based on silicon photodiodes driven by near-infrared illumination was proposed to eliminate the need for cables\(^5\). However, this solution still requires the use of a goggle-embedded imaging-capturing camera\(^36\), which can potentially cause image fading during head/eye movements. Finally, it has recently been reported that the intraocular injection of a photo-switchable probe transiently restores light sensitivity in mouse models of Retinitis pigmentosa without any exogenous gene delivery\(^37\).

The possibility of photostimulating neurons via an organic interface prompted us to test the efficacy of this method in retinas (explanted from albino rats) with reproducibly induced photoreceptor degeneration due to light damage\(^38,39\). However, we were concerned with the possibility that the interface coupling with a retinal explant would be less effective and potentially associated with higher impedance values than that with primary neurons growing in strict adhesion with the polymer surface. Despite these concerns, the mono-component interface in the subretinal configuration was extremely efficient in eliciting LFPs in the retinal networks and action potential firing of the RGCs to levels indistinguishable from normal retinas (Fig. 4b). This finding indicates that the interface is able to take over the role of photoreceptors in activating the processing of the inner retina and to rescue light sensitivity.

Natural rod photoreceptors have an inherent amplification system for increasing light sensitivity. This is composed of stacks of disks rich in the light-sensitive molecule rhodopsin. Light sensitivity is therefore an incredible challenge for the generation of retinal prostheses. Many proposed approaches are not sensitive enough to irradiance levels in the daylight range and require external light projectors, the design of which should take into account the maximum permissible exposures for ocular safety allowed for ophthalmic applications\(^40\). Interestingly, our organic photovoltaic device proved to have a remarkable light sensitivity, with a response threshold of 0.3 µW mm\(^{-2}\), 30-fold lower than the ocular safety limit for continuous exposure to visible light (106.93 µW mm\(^{-2}\)), and a response saturation at 100 µW mm\(^{-2}\), still below the limit. Moreover, the response threshold closely matched the range necessary for the identification of objects.

Figure 4 | The P3HT layer restores responses in blind retinas. a. Top row: MUAs recorded with light stimulation (10 ms, 4 mW mm\(^{-2}\)) of a control retina over a glass:ITO substrate (left), a degenerate retina over a glass:ITO substrate (middle) and a degenerate retina over a P3HT-coated glass:ITO substrate (right). Bottom row: normalized post-stimulus time histograms (PSTHs; bin, 25 ms) computed based on all sweeps recorded in single retinas (10 ms, 4 mW mm\(^{-2}\)) for the three experimental conditions. Green bars/arrows represent the light stimulus. b. Comparison of mean (+ s.e.m.) PSTHs (bin, 25 ms) obtained from control retinas on glass:ITO (black bars, n = 5), degenerate retinas on glass:ITO (open bars, n = 10) and degenerate retinas on P3HT-coated glass:ITO (red bars, n = 10) in response to light illumination (10 ms, 4 mW mm\(^{-2}\); green arrow). Significantly different bins are indicated (Student’s t-test, ***P < 0.001). c. Dose-response analysis of the mean (+ s.e.m.) firing rate versus light intensity performed in degenerate retinas over P3HT-coated glass:ITO (red dots, n = 6) or glass:ITO alone (open dots, n = 6). Mean firing rates were calculated in a window of 250 ms after the light pulse. Dashed line: computed maximum permissible radiant power for chronic exposure (see Methods). Dose-response curves were fitted using a sigmoidal dose–response model. Solid grey lines represent the response threshold (10% of the maximal response), and dotted grey lines represent the average half-maximum effective dose (ED\(_{50}\)) calculated from the fitting procedure (12.11 and 120.78 µW mm\(^{-2}\), respectively). Right: representative PSTHs (bin, 25 ms; means ± s.e.m.) obtained in the presence (red) or absence (grey) of P3HT. The green arrow represents the light stimulus.
of retinal irradiance during common daily outdoor activity\textsuperscript{41,42}, thus suggesting a possible future implementation without any external light projectors. Another interesting feature of our interface is related to the linear dynamic range of operation, which spans 2 log units of retinal irradiation (1–100 μW mm\textsuperscript{−2}). This linear operating range allows modulation of the retinal output (ganglion cell spiking activity) depending on the light dose reaching the polymer-retina interface. As a result, the peak spiking activity of ganglion cells could be tuned between 1 and 30 Hz (Fig. 4c, right panel). The possibility of directly modulating the retinal spiking output depending on the light dose is an extremely important requirement in developing artificial prostheses aimed at restoring the physiological function of the retina.

Notwithstanding these promising results, some improvements in the light sensitivity and gain of the linear range are still needed to match the physiological functioning of the retina. The documented linear dynamic range of the organic device (1−100 μW mm\textsuperscript{−2}) only partially covers the range of daylight retinal irradiance (0.1–10 μW mm\textsuperscript{−2}), and we would therefore require an increase in light sensitivity or in stimulation efficiency. Moreover, the linear gain in output spiking (1 to 30 Hz in 2 log units of retinal irradiation) is lower than the typical gain of spiking activity in RGCs under physiological conditions. Several possible strategies can be envisaged to improve organic bio-interface performance, including (i) fine-tuning the active-layer film thickness and using a higher-mobility semiconducting polymer to enhance the number of absorbed photons and thus the number of charge carriers, (ii) using a multilayer architecture for the device to broaden the spectral sensitivity, and (iii) improving the wettability of the polymer surface by appropriate chemical engineering and/or realization of a three-dimensional microstructured polymer scaffold to lower the impedance of the electrical contact. The combination of the mentioned and other possible strategies will help in developing a new generation of fully organic prosthetic devices for subretinal implants.

The organic photovoltaic interface has many potential advantages over previously proposed devices for \textit{in vivo} applications, including biocompatibility, freedom from the need for an external bias or power supply, negligible heat generation, absorption in the green–orange region of the visible spectrum (closely resembling the bias or power supply, negligible heat generation, absorption in the artificial prostheses aimed at restoring the physiological function of the retina.

As previously described\textsuperscript{38}, Sprague–Dawley albino rats were reared in cages containing two animals, fed \textit{ad libitum}, and kept under a 12 h:12 h light–dark cycle (light intensity between 5 and 10 lx) from birth. To induce photoreceptor degeneration, two-month-old animals were exposed to bright (1,000 lx) light generated by a white fluorescent source for 72 h, following overnight dark adaptation. Animals were then returned to the 12 h:12 h light–dark cycle. Untreated animals were maintained on a 12 h:12 h light–dark cycle (light intensity between 5 and 10 lx). Four to six weeks after light damage, animals were dark-adapted for at least 2 h and anaesthetised with isofluorane. The dissection procedure was performed in the dark in a dimly lit room to avoid photic stimulation. Eyes were enucleated and transferred to a Petri dish containing carboxygenated Ames medium (Sigma-Aldrich). The cornea, iris, lens and vitreous were subsequently removed, and the retina was detached from the sclera. The dorsal part of each retina was transferred to the microscope stage, where they were continuously perfused with carboxygenated Ames medium heated to 35 °C. All animal manipulations and procedures were performed in accordance with the guidelines established by the European Community Council (Directive 2012/63/EU of 29 September 2010) and were approved by the Italian Ministry of Health.

**Photostimulation.** Light stimulation was performed on a setup consisting of a Nikon inverted microscope (Nikon Instruments). Photostimulation was carried out using a wide-band, high-power-light-emitting diode (peak at 532 nm, OPTOLED, Cairn Research). A circular illumination spot (diameter, ∼100 μm) around the neuron was obtained by passing light through a pin hole and focusing the light with a ×16/0.8 NA water immersion objective (Nikon Instruments).

**Electrophysiology.** Whole-cell patch-clamp recordings of cultured neurons were performed at room temperature using patch pipettes (4–6 MΩ), under G1 patch seals with an Axopatch 200B (Axon Instruments). The extracellular solution contained NaCl (135 mM), KC\textsubscript{L} (5.4 mM), Mg\textsubscript{Cl}\textsubscript{2} (1 mM), Ca\textsubscript{Cl}\textsubscript{2} (1.8 mM), HEPES (5 mM) and glucose (10 mM), and was adjusted to pH 7.4 with NaOH. The intracellular solution contained K-glutamate (126 mM), KCl (4 mM), MgSO\textsubscript{4} (1 mM), Ca\textsubscript{Cl}\textsubscript{2} (0.02 mM), BAPTA (0.1 mM), glucose (15 mM), HEPES (5 mM), ATP (3 mM) and GTP (0.1 mM), and was adjusted to pH 7.3 with KOH. Responses were amplified, low-pass-filtered at 10 kHz, digitized at 50 kHz, stored, and analysed with pCLAMP 10 (Axon Instruments).

MUA recordings of acute retinal explants were performed with glass pipettes (2–3 MΩ) filled with Ames medium, amplified and bandpass-filtered at 0.1–300 Hz using a DAM80 amplifier (World Precision Instruments), digitized at 20 kHz, stored, and analysed with pCLAMP 10. Data for spike detection were bandpass-filtered at 100–300 Hz, and LFP data were bandpass-filtered at 0.1–300 Hz.

**Optical safety considerations.** According to ocular safety standards for commercial implants\textsuperscript{43}, we calculated the maximum permissible radiant power (MPR) that could enter the pupil chronically or in a single short exposure. For single-pulse exposures (between 50 μs and 70 ms) at 532 nm, the peak limit was described by the equation MPR = 6.93×10\textsuperscript{−2} C\textsubscript{M} C\textsubscript{T}\textsuperscript{0.27} = 146.17 mW, where C\textsubscript{M} = 0.01 s, C\textsubscript{T} = 1 in the range of 400–700 nm and C\textsubscript{M} is a function of the visual spectrum.
angle $a$. For retinal spot sizes greater than 1.7 mm, $a = a_{\text{max}} = 100$ mrad and $C_0 = 6.67 \times 10^{-6} \text{C}_\text{L} \text{P}^{-1} = 84.69 \mu \text{V}$, with $C_0 = 1$, $P = 5.44$ and $C_0 = 66.7$ W. For photochemical damage, $MPD = 5.56 \times 10^{-10} \text{C}_\text{L} \text{P}^{-1} = 242.70 \mu \text{W}$, where $C_0 = 100$ (at 532 nm and $a$ is the visual angle (for long exposures, $a$ was set to $a_{\text{max}} = 100$ mrad). Thus, for chronic exposures, $MPD = 242.70 \mu \text{W}$. In Maxwellian illumination, which is often used in ophthalmic instruments, the maximum permissible retinal radiant exposure, $MPH$, is given by the power entering the pupil, $\Phi$, divided by the retinal exposed area. For $a = a_{\text{max}} = 100$ mrad, the diameter of the illuminated retina is assumed to be 1.7 mm. Thus, for single-pulse exposure $MPH = 64.40 \text{mW mm}^{-2}$, and for chronic exposure $MPH = 106.93 \text{mW mm}^{-2}$.

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Author contributions
D.G. prepared cell cultures, degenerate animals and retinal explants, planned experiments, performed photostimulation experiments and cell viability assays, analysed data and wrote the manuscript. M.R.A. planned the experiments, discussed the results and wrote the manuscript. R.M. prepared degenerate animals, performed retinal sections and acquired confocal images. E.L. prepared polymer samples. S.R., E.L. and N.M. performed polymer-film electro-optical characterization and analysed data. M.M. and G.P. discussed results. S.B. discussed electrophysiological experiments with retinal explants. G.L. and F.B. planned experiments, interpreted and discussed the data, wrote the manuscript and supervised the research. All authors discussed the results and revised the manuscript.

Additional information
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Competing financial interests
The authors declare no competing financial interests.