*PySilSub*: A Python toolbox for performing the method of silent substitution with multiprimary stimulation devices.

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Abstract

Silent substitution is a technique for stimulating individual classes of photoreceptors on the retina whilst maintaining a constant level of activation in others.

Keywords: silent substitution, melanopsin, instrumentation, pupillary light reflex, software, open source

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A normal human retina contains several types of photosensetive cell (for review, see Grünert & Martin, 2020). Enabling colour vision at mesopic and photopic light levels are the short-, medium-, and long-wavelength-light-sensetive cone photoreceptors. Cone cells are packed densley into the fovea and distributed sparsely outside of this area. For scotopic (twilight) vision we have rod photoreceptors. Though not present at the fovea, rods are most numerous of the photoreceptor cells and are otherwise widely distributed in retina. Finally, discovered in human retinae only at the turn of the millenium—intrinsically photosensetive retinal ganglion cells (ipRGCs) expressing the photopigment melanopsin in their axons and soma (Provencio et al., 2000). ipRGCs do not contribute to vision in the same way as rods and cones but they do play important roles in ‘non-visual’ functions, such as circadian photoentraiment and pupil control, via direct projections to the suprachiasmatic nucleus of the hypothalamus and the olivery pretectal nucleus of the midbrain (Gamlin et al., 2007; Ruby et al., 2002).

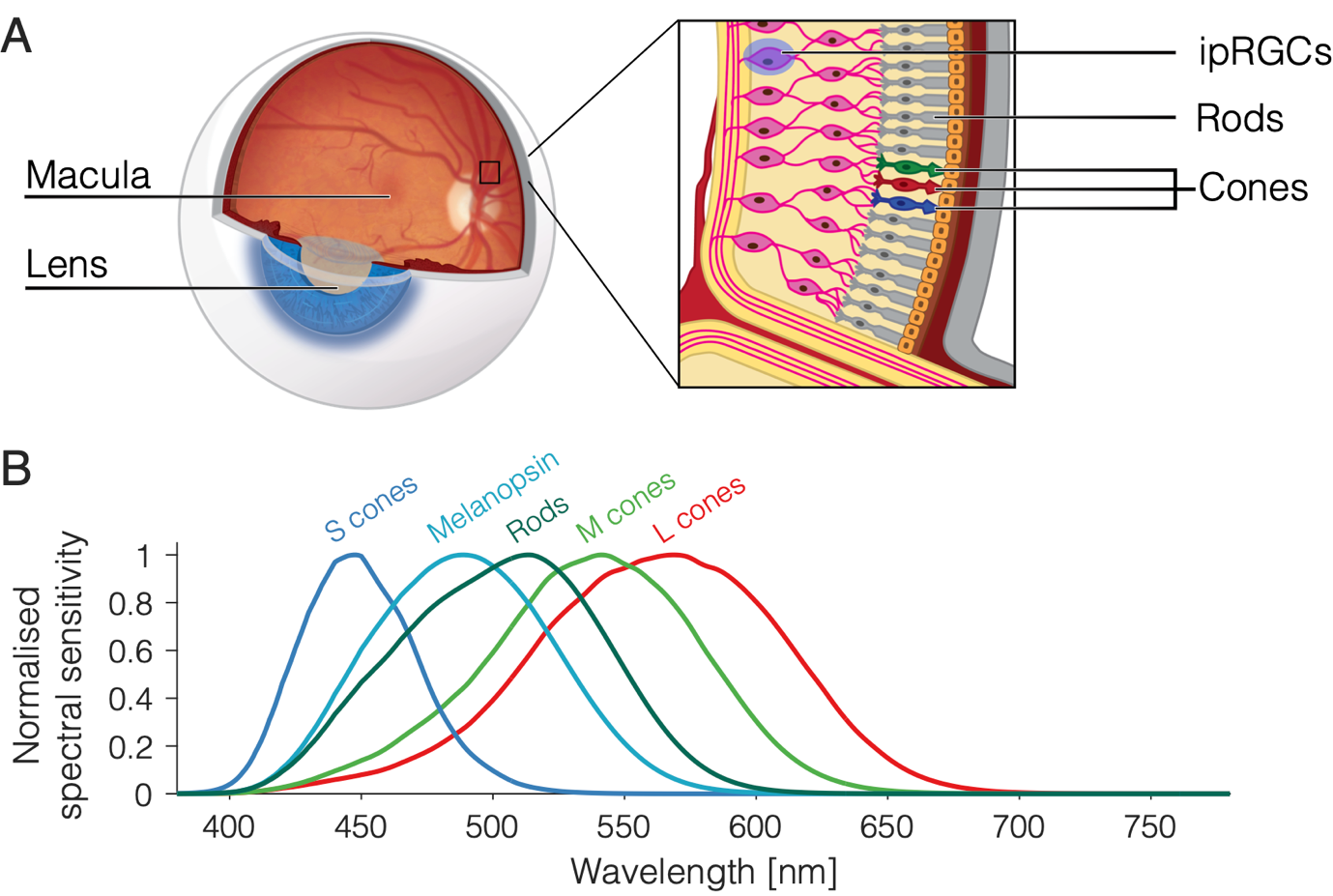


Figure . (A) Photoreceptors of the retina and (B) their spectral sensitivities.

As illustrated in Figure 1, the photoreceptors have different spectral sensetivities. The curve for each type of photoreceptor essentially describes the probability of its capturing a photon at a given wavelength. Therefore S-cones are about 10 times more likely than L-cones to capture photons at 450 nm, and the liklihood of L- and M-cones capturing at 550 nm is about the same. Because the spectral sensetivities of the photoreceptors overlap, it should be clear that most lights in the visible spectrum will stimulate all types of photoreceptor, albeit to varying degrees. However, it is possible to prepare light stimuli that selectively target a photoreceptor class via the method of silent substitution.

Silent substitution is an elegant technique that involves using pairs of lights to selectively stimulate one class of retinal photoreceptor whilst maintaining a constant level of activation in the others. This is possible owing to Rushton’s (1972) principle of univariance, which states that the output of a photoreceptor is one-dimensional and depends upon quantum catch, not upon what quanta are caught. In other words, different light spectra will have an identical effect on a photoreceptor providing they lead to the same number of photons being absorbed. The prinicple of univariance and its relevance to silent substitution is covered in greater detail by Estévez and Spekreijse (1982) along with other details regarding the early history of the method. In vision science, silent substitution has contributed to our understanding of human colour vision mechanisms (Horiguchi et al., 2013) and it has enabled researchers to examine how targeted photoreceptor stimulation affects physiological responses such as melatonin suppression (Allen et al., 2018), the electroretinogram (Maguire et al., 2017), and the pupillary light reflex (Spitschan et al., 2014). Its potential as a diagnostic tool for retinal disease has also garnered attention in recent years (Kuze et al., 2017; Wise et al., 2021).

Among the challenges to silent substitution are retinal inhomogeneities (e.g., the presence of the macular pigment at the fovea), individual differences in photoreceptor spectral sensetivities, rod intrusion, and uncertainty of the stimulation device (Spitschan & Woelders, 2018). From a practical perspective, arguably the greatest challange is in finding the settings for a multiprimary stimulation device to produce lights that selectively stimulate the photoreceptor(s) of interest. The Silent Substitution Toolbox (Spitschan et al., 2015) for MATLAB can help with this, but it requires the user to be familiar with, and possess a lisence for, MATLAB. Here we present *PySilSub*, an alternative silent substitution software written in Python. *PySilSub* offers generic support for multiprimary stimulation devices, predicitive models and solutions to silent substiotution problems with approaches based on linear algebra and numerical optimisation. In this manuscript we describe the toolbox and demonstrate use cases with three different multiprimary stimulation systems.

**Method**

**Results**

**Discussion**

**Summary**

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**Open Practices Statement**

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