Characterizing Retinal ipRGC-Responses —and the Work of CIE JTC9 (D1, D2, D3 & D6)

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“Light achieves important biological effects relevant for human health, performance and well-being that are not dependent on visual images....“ (– some early wording).

The relative contributions from different photoreceptor types vary according to which ipRGC-influenced response to light is being considered, the exposure duration, retinal irradiance, spectrum, field of view, variability and can also depend on the exposure context (subjective time, prior light history, adaptation, sleep pressure)

- The work of JTC9

* CIE Interest in...
“lighting and health”

* First CIE light & health symposium in Vienna in 2004 (D6)

*CIE Statement on Non-Visual Effects of Light
“RECOMMENDING PROPER LIGHT AT THE PROPER TIME”

Perspective: casting light on sleep deficiency.
January 2013: workshop in Manchester

- How could insights in ‘non-visual’ responses impact methods to measure light?
- Key contributors to the field
- Established consensus paper:

Measuring and using light in the melanopsin age
Trends in Neurosciences, January 2014, Vol. 37, No. 1

(also reported in: CIE TN 003:2015 “Report on the First International Workshop on Circadian and Neurophysiological Photometry, 2013.”)

CIE JTC9 (D1, D2, D3 & D6)

- CIE JTC9 - The title was even a controversy!
- The original title was: “Quantifying ocular radiation input for non-visual photoreceptor stimulation.”

- THE FINAL TITLE WAS: “CIE SYSTEM FOR METROLOGY OF OPTICAL RADIATION FOR IPRGC-INFLUENCED LIGHT RESPONSES”

- Membership:
  - Luc Schlangen (Chair)
  - Luke Price (Secretary)
  - Peter Blattner
  - Raphael Kirsch
  - Dieter Lang
  - Robert Lucas
  - Hiroki Noguchi
  - David H. Stiney
  - Manuel Spitschan
Then… What about Ganglion Cell Receptors?

ipRGCs – Berson et al, Science 295, 2002

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The importance of spatial stimuli
The Normal Human Eye

Retinal Ganglion Cells
- Absent in fovea
- In peripheral macula and peripheral retina
- Highest density at ~5° from center of fovea


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Retinal Fundus Schematic – Courtesy, Aiello
RGCs
– *Their location across the retina*

✦ Distribution of RGCs

✦ No RGCs in fovea of course
✦ And the ipRGCs?

![Graph showing distribution of rods and cones with relative intensity](image-url)
Distribution & Ageing ipRGCs

  - Superior retina had only ~½ the density of mRGCs
  - The density & distribution of the different types of human mRGCs (melanopsin RGCs) change dramatically
  - Example: the 56-year-old whole-mount human immunostained mRGCs density of different types:
    - 988 M1 (A),
    - 1874 M1d (B),
    - 802 M2 (C)
    - 1036 M3 (D) cells.

The Macula Lutea - Lutein Pigment

- In the inner and outer plexiform layers
- Thought to minimize BLH
- But ipRGCs are above this layer
many “non-visual” light responses are influenced by intrinsically-photosensitive Retinal Ganglion Cells

JTC judged that - always via the eye (not via the skin)

EXAMPLES:
• Pupillary light reflex
• Sleep-wake regulation
• Biological rhythms
• Brain activity
• Increase heart rate
• Improve alertness
• Light treatment of depression

Five retinal photoreceptors drive visual & non-visual responses

Melanopsin-based photoreceptor: intrinsically-photosensitive Retinal Ganglion Cell (ipRGC )
Classical photoreceptors: Rods & Short-, Mid- and Long-wavelength cones
Photoreceptors interact and combine to drive responses.

Combinations vary with light intensity, adaptation, sleep pressure, subjective time, response considered, ...

Further research work needed to determine which photoreceptor(s) dominate response amplitude.

Quantifying ocular radiation input for non-visual photoreceptor stimulation

Five photoreceptors, five weighting functions:

\[ E_\alpha = \int E_{\alpha} (\lambda) S_\alpha (\lambda) d\lambda \]

Five \( \alpha \)-opic irradiances, \( E_{\alpha} \):

- \( S \)-cone (\( \alpha \)-opic)
- Melanopsin (\( i \)-cone-opic)
- Rhodopsin (\( Rh \)-opic)
- \( M \)-cone (\( M \)-cone-opic)
- \( L \)-cone (\( L \)-cone-opic)

Five \( \alpha \)-opic irradiances, \( E_{\alpha} \):

\[ E_\alpha = \int E_{\alpha} (\lambda) S_\alpha (\lambda) d\lambda \]

From Luc Schlangen
### Example standard illuminants (D65 & F12)

<table>
<thead>
<tr>
<th></th>
<th>S-cone</th>
<th>Melanopsin</th>
<th>Rhodopsin</th>
<th>M-cone</th>
<th>L-cone</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>D65</strong></td>
<td><img src="image1" alt="Graph" /></td>
<td><img src="image2" alt="Graph" /></td>
<td><img src="image3" alt="Graph" /></td>
<td><img src="image4" alt="Graph" /></td>
<td><img src="image5" alt="Graph" /></td>
</tr>
<tr>
<td>(6500 K)</td>
<td>Irradiance: 4.88 mW/m²</td>
<td>0.82 mW/m² (S-cone-optic)</td>
<td>1.33 mW/m² (Melanopic)</td>
<td>1.45 mW/m² (Rhodopic)</td>
<td>1.46 mW/m² (M-cone-optic)</td>
</tr>
<tr>
<td></td>
<td>Illuminance: 1 lx</td>
<td>1 lx (F12)</td>
<td>1 lx (F12)</td>
<td>1 lx (F12)</td>
<td>1 lx (F12)</td>
</tr>
<tr>
<td><strong>F12</strong></td>
<td><img src="image6" alt="Graph" /></td>
<td><img src="image7" alt="Graph" /></td>
<td><img src="image8" alt="Graph" /></td>
<td><img src="image9" alt="Graph" /></td>
<td><img src="image10" alt="Graph" /></td>
</tr>
<tr>
<td>(3000 K)</td>
<td>Irradiance: 2.83 mW/m²</td>
<td>0.29 mW/m² (S-cone-optic)</td>
<td>0.54 mW/m² (Melanopic)</td>
<td>0.75 mW/m² (Rhodopic)</td>
<td>1.16 mW/m² (M-cone-optic)</td>
</tr>
</tbody>
</table>

From Luc Schlangen

### Considerations on “radiance”

* Ideally: the time-depended, spatial $\omega$-optic radiance distribution is measured and the spatial distribution of the photoreceivers is considered

However

* The spatial distribution of the photoreceivers on the retina is not (enough) known
* Eye / head movement will “smear out” this distribution, mainly in horizontal direction

-> Alternative concepts:

Use of vertical irradiance with limiting the vertical field of view
An ISSUE: View of JTC9 - Peak sensitivity of melopsin is at $\lambda = 480$ nm, but human pre-receptoral filtering shifts the peak to 490 nm [however, Brainard and Thappen found 470-nm peak in humans!]

\[\lambda_{\text{mel,max}} = 490 \text{ nm}\]

Another Issue:

JTC9 - Age-dependent Corrections

Typical correction for melanopic irradiance (NB depends on spectral distribution)

<table>
<thead>
<tr>
<th>$k_{\text{mel}, \tau}(\alpha)$</th>
<th>25 years</th>
<th>35 years</th>
<th>50 years</th>
<th>75 years</th>
<th>90 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.045...</td>
<td>1.055</td>
<td>1</td>
<td>0.83...0.86</td>
<td>0.57...0.65</td>
<td>0.44...0.55</td>
</tr>
</tbody>
</table>

from NRC · CARC ©
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2018-06-02
**Examples of q-opic quantities**

α-opic can be: S-cone-opic; M-cone-opic; L-cone-opic; Rhodopic; Melanopic

<table>
<thead>
<tr>
<th>Quantity</th>
<th>Formula</th>
<th>Meaning</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>α-opic radiant flux</td>
<td>$\Phi_\alpha = \int \Phi_{\alpha}(\lambda) s_\lambda(\lambda) , d\lambda$</td>
<td>weighted spectral power distribution (SPD) integrated over wavelength</td>
<td>W</td>
</tr>
<tr>
<td>α-opic irradiance</td>
<td>$E_\alpha = \int E_{\alpha}(\lambda) s_\lambda(\lambda) , d\lambda$</td>
<td>weighted SPD integrated over wavelength per area</td>
<td>W/m²</td>
</tr>
<tr>
<td>α-opic radiance</td>
<td>$L_\alpha = \int L_{\alpha}(\lambda) s_\lambda(\lambda) , d\lambda$</td>
<td>weighted spectral radiance integrated over wavelength</td>
<td>W/(m²·sr)</td>
</tr>
<tr>
<td>α-opic efficacy of luminous radiation</td>
<td>$K_{\alpha,\lambda} = \Phi_\alpha / \Phi_\lambda$</td>
<td>quotient of α-opic radiant flux, $\Phi_\alpha$, and luminous flux, $\Phi_\lambda$</td>
<td>W/ lm</td>
</tr>
<tr>
<td>equivalent daylight (D65) illuminance</td>
<td>$E_{D65}^{V,\alpha} = E_{\alpha} K_{D65}^{V,\alpha}$</td>
<td>Illuminance level of daylight D65, producing an equal α-opic irradiance as the test source</td>
<td>lx</td>
</tr>
</tbody>
</table>

**Progress of CIE JTC9**

- Mid 2016: start JTC9
- End 2017: new fast track CIE procedure for JTC9 approved
- Jan 2017: JTC9 draft International Standard CIE ED/IS 026/E:2018
- Feb 2018: passed ballot (BA/DIV)
- July 2018: publication of draft standard (CIE DIS 026) & passed NC ballot (Oct 2018) with 6 Yes-votes
- Expected Q4 2018/ Q1 2019: publication CIE standard (IS 026) + toolbox
- March 2019: IS 026 CIE tutorial Eindhoven, 2 days + extended toolbox
- June 2019: CIE 29th session: workshop + lecture?
in research, design and installation....

always specify your lighting conditions by giving:

* irradiances: give (il)luminance and all five q-opic stimuli values
* timing and duration of light exposure
* information on field of view and spatial distribution
* ....

....and this may have been true for incandescent lamps.....