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Phototransduction and signal pathways of the visual and circadian systems

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- Mark Rea, PhD
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Light isn't just for vision anymore

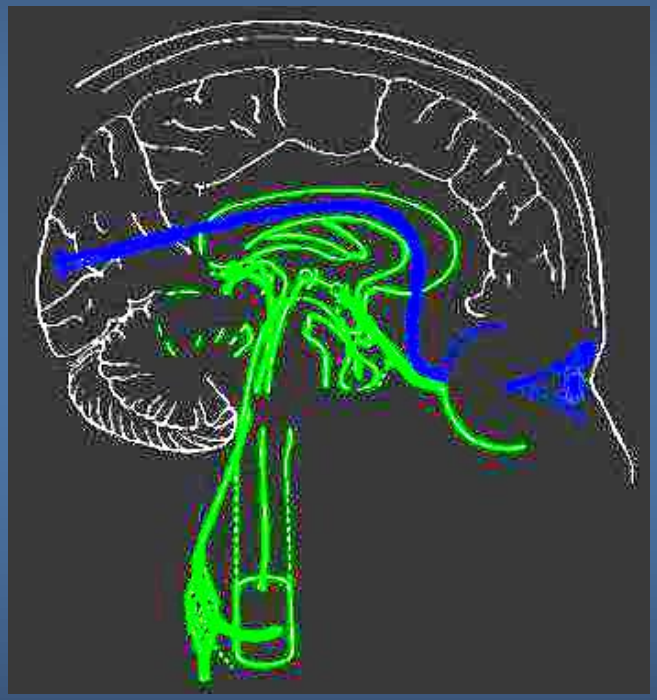
- Light reaching the retina has two effects on human behavior:
  - Visual effects – ability to perform visual tasks
  - Nonvisual effects – synchronize our circadian system to a 24-hour day
- Light is not the same for vision as it is for the circadian system

Circadian system

- All plants and animals exhibit patterns of behavioral changes over an approximately 24-hour cycle that repeat over successive days—these are circadian rhythms

  circa = about; dies = day

- Circadian rhythms are influenced by exogenous and endogenous rhythms
  - Light/dark patterns are the strongest entrainment stimulus for the circadian system

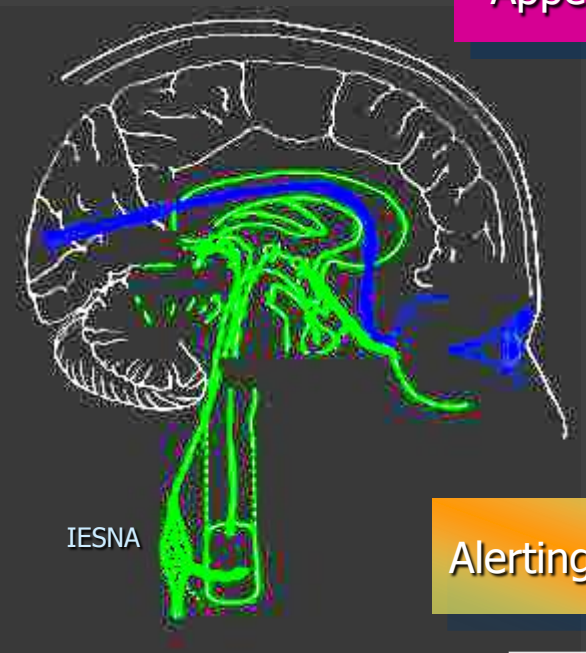


Adapted from IESNA Handbook

Circadian system

- Biological (circadian) rhythms can be measured in several ways
  - Melatonin concentration
  - Core body temperature (CBT)
  - Sleep/wake cycle
  - Brain activities (EEG)
  - Subjective alertness

New paradigm for light



IESNA

Intensity
Spectrum
Distribution
Timing
Duration

Appearance
Visual System
Visual Performance

Performance, Well-being, Satisfaction, and Comfort

Culture, Experience, Expectations

Alerting Effects
Circadian System
Phase Shift

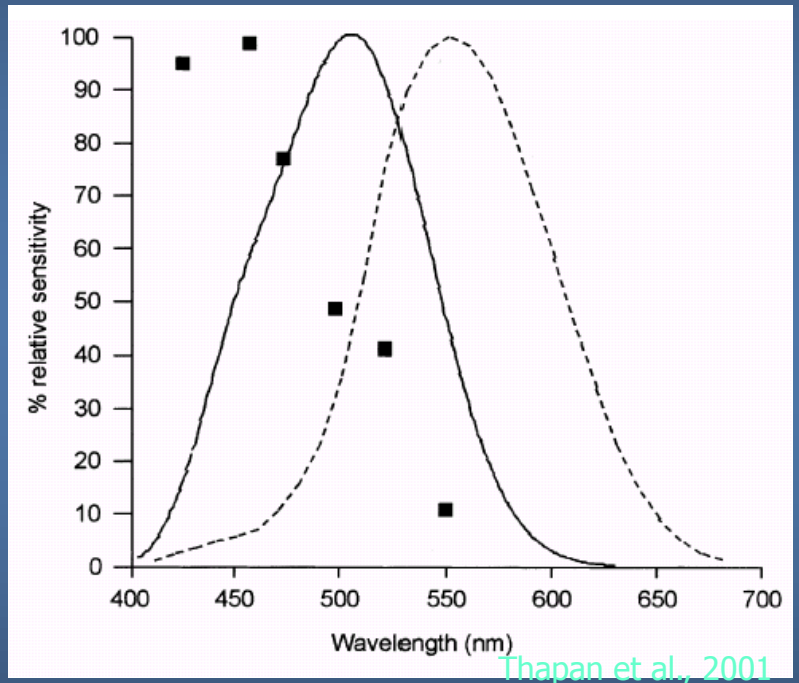
Intensity
Spectrum
Distribution
Timing
Duration

Circadian photoreceptors

- Foster et al., 1991, 1998; Provencio and Foster, 1995; Freedman et al., 1999; Lucas et al., 2001
  - Mice with severe degeneration of classical photoreceptors were still able to reset the clock in normal response to light
- Provencio et al., 2000
  - Discovered melanopsin, a vertebrate opsin that is directly photosensitive and was found in the mammalian retina (peak at 483 nm)

Circadian photoreceptors

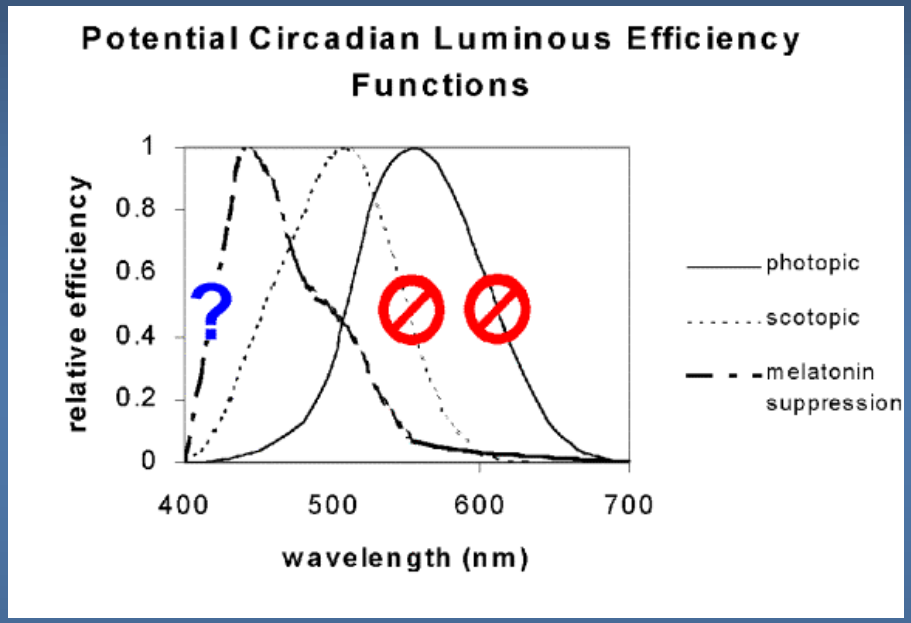
- Brainard et al., 2001 and Thapan et al., 2001
  - Used various wavelengths of monochromatic light to investigate the spectral sensitivity of the circadian system (melatonin suppression by light)
  - Both concluded that a novel photoreceptor (opsin with a peak sensitivity at 460 nm) was responsible for circadian phototransduction



Thapan et al., 2001

Circadian photoreceptors

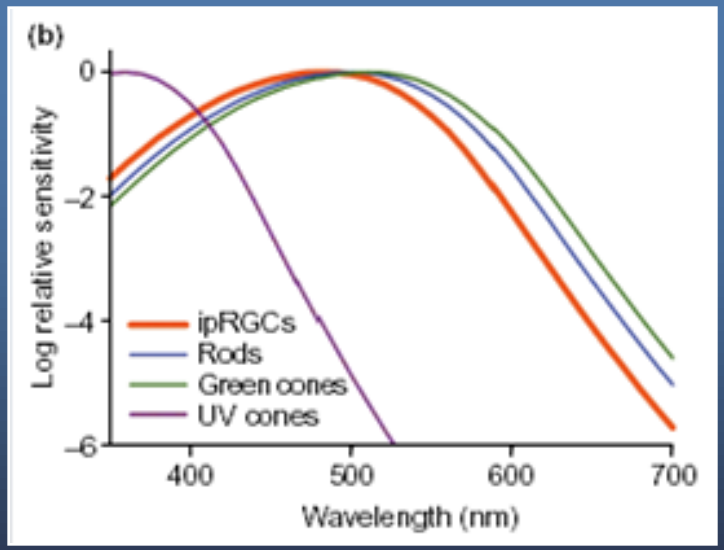
- Agreement
  - Short wavelength sensitivity
- But…
  - Peak at 450 nm, not 460 nm or 480 nm
  - Empirical function is too wide for a single opsin
- We hypothesized…
  - A combination of classical and novel photoreceptors seems likely

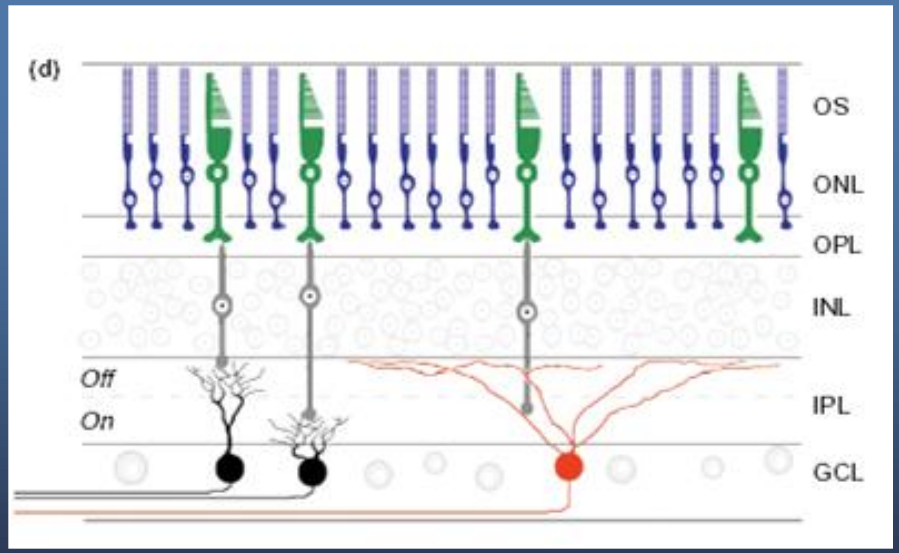


Rea, Bullough, Figueiro, 2001 and 2002

Circadian photoreceptors

- Berson et al., 2002
  - Discovered retinal ganglion cells innervating the SCN that contain melanopsin and are directly photosensitive





Images from Berson, 2003

Circadian photoreceptors

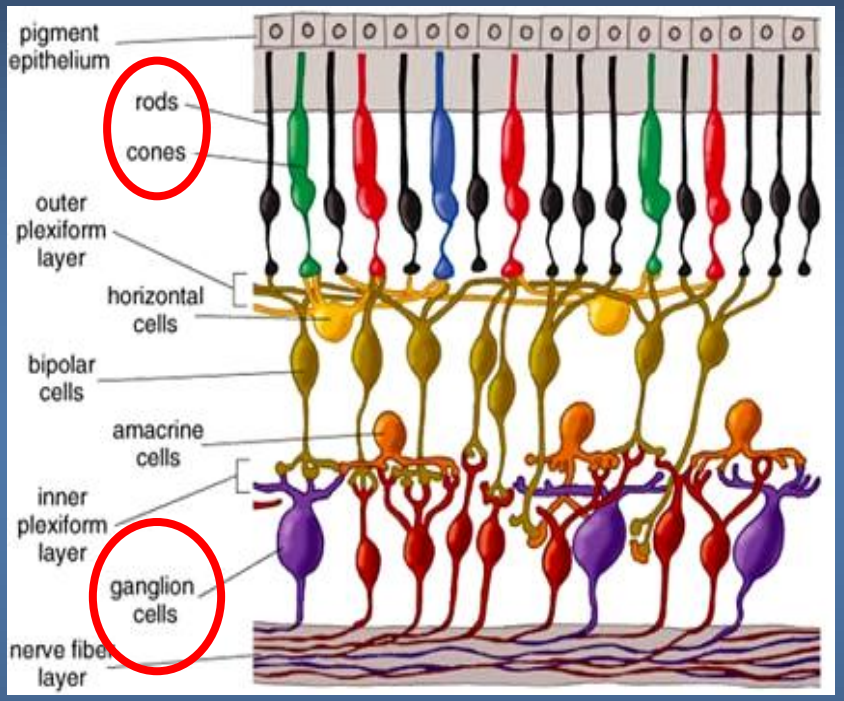
- Gooley et al., 2002
  - Melanopsin-containing RGCs project to SCN and OPN
- Ruby et al., 2002
  - Melanopsin-deficient mice showed magnitude of phase shifting 40% lower
- Panda et al., 2002
  - Melanopsin-deficient mice showed magnitude of phase shifting 45% lower
- Lucas et al., 2003
  - Melanopsin-deficient mice showed incomplete pupil light reflex at high light levels
- Hattar et al., 2003
  - "Knockout" mice lacking melanopsin still show, though reduced, circadian phase shifting responses
  - Triple "knockout" mice have no circadian response

Circadian photoreceptors

- Bullough et al., 2005
  - Demonstrated additivity in mouse phototransduction
  - Modeled the relative contributions of S-, M-cones and ipRGCs in wild type mice
- Dkhissi-Benyahya et al., 2007
  - Demonstrated a specific role of medium wavelength opsins (M-cones) in circadian photoentrainment
  - Developed a model explaining wavelength-dependent photoentrainment by melanopsin and M-cones

Circadian phototransduction

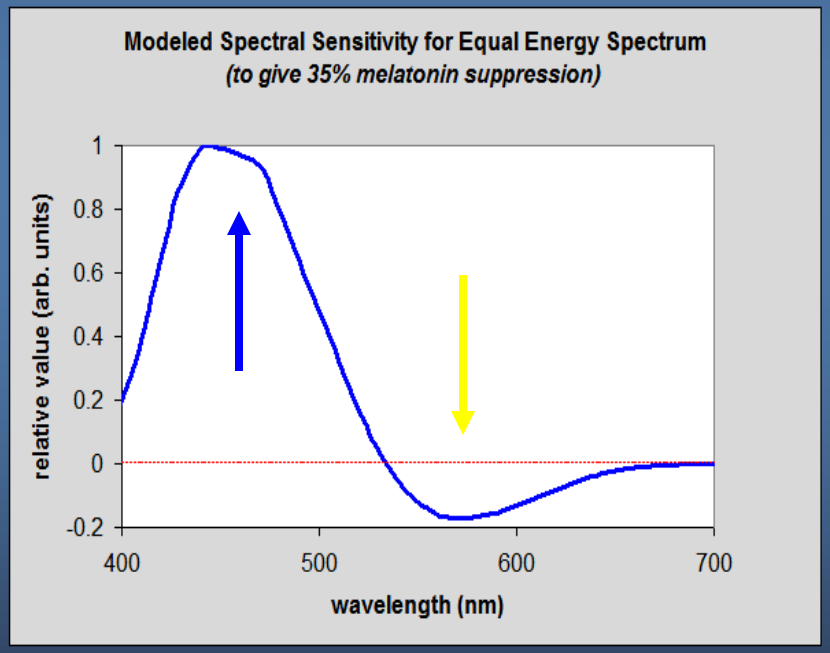
- Melanopsin-containing retinal ganglion cells (ipRGCs) and classical photoreceptors are all involved in circadian phototransduction …but how?

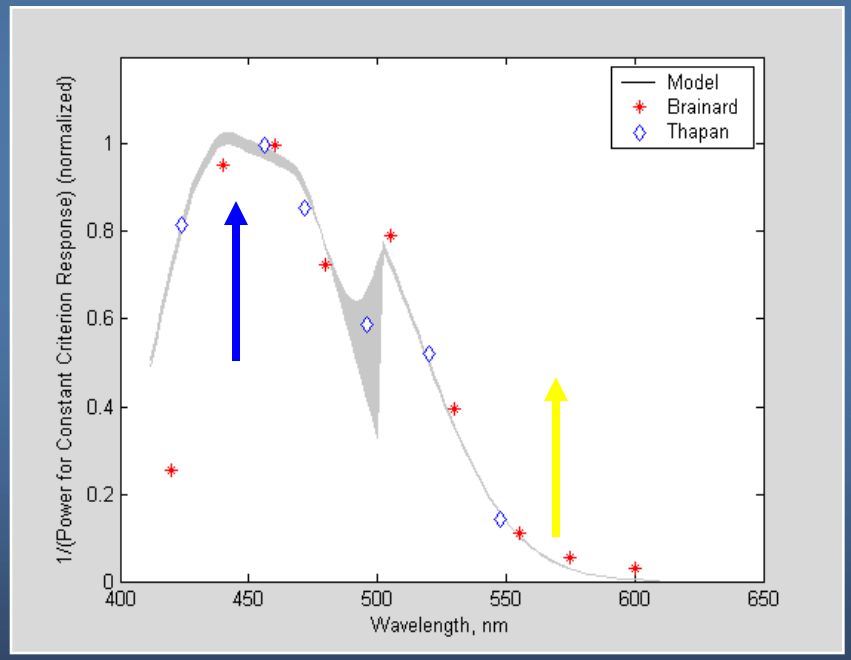


Kolb et al., 2003

A proposed model

- LRC developed and published a model for human circadian phototransduction





Rea et al., 2005; Figueiro et al., 2004

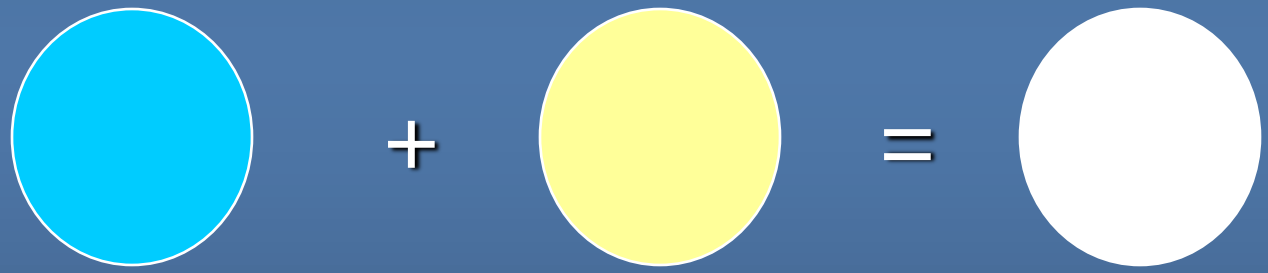
Potential spectral response functions for
(equal energy) white light and for monochromatic light

Brightness perception

- Luminance channel
  - Luminance follows the Abney's law of additivity (1L + 1L = 2L)
- Luminance ≠ brightness
- Brightness is a non-linear combination of the luminance channel and the color channels
  - Brightness is non-additive (1B + 1B ≠ 2B!)
    - Dresler (1953); Alman (1977); Ware and Cowan (1983)

Key question

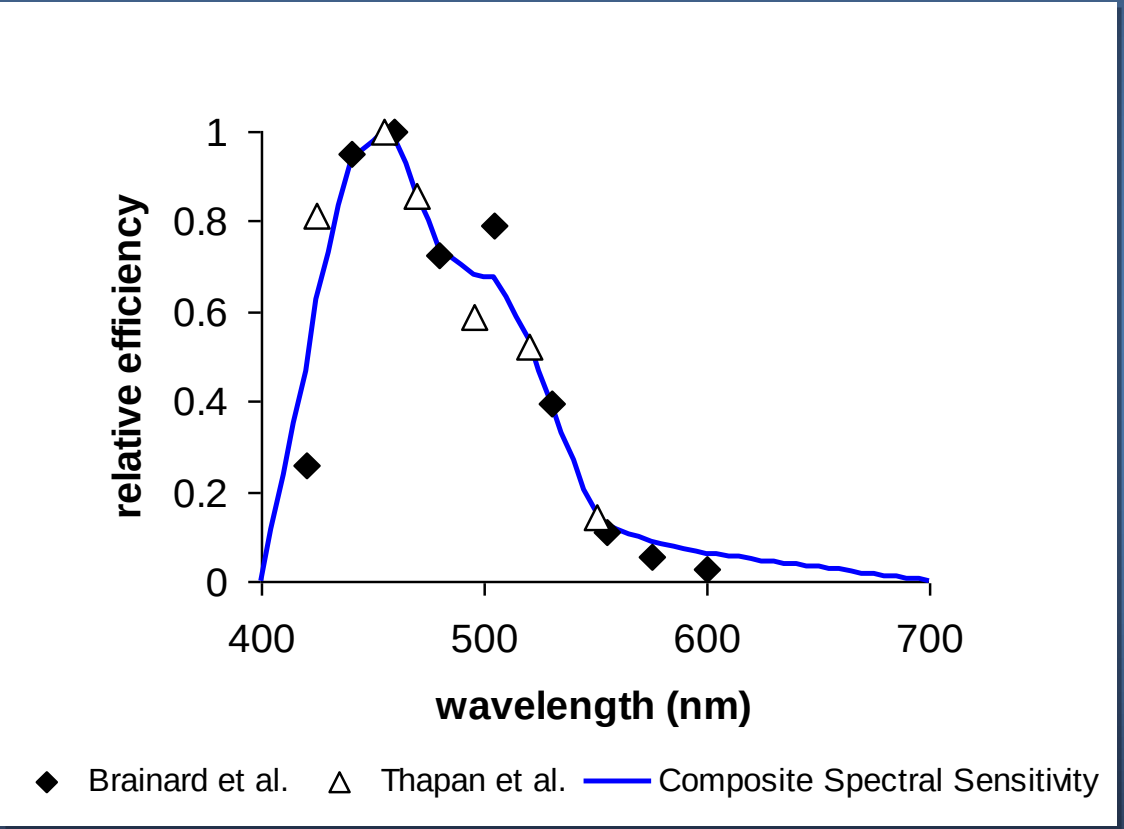
- Is circadian phototransduction like luminance (additive) or like brightness (subadditive)?



1L+1L = 2L or 1B+1B > 2B

Spectral opponency, 1st experiment

Development of an additive empirical spectral efficiency function

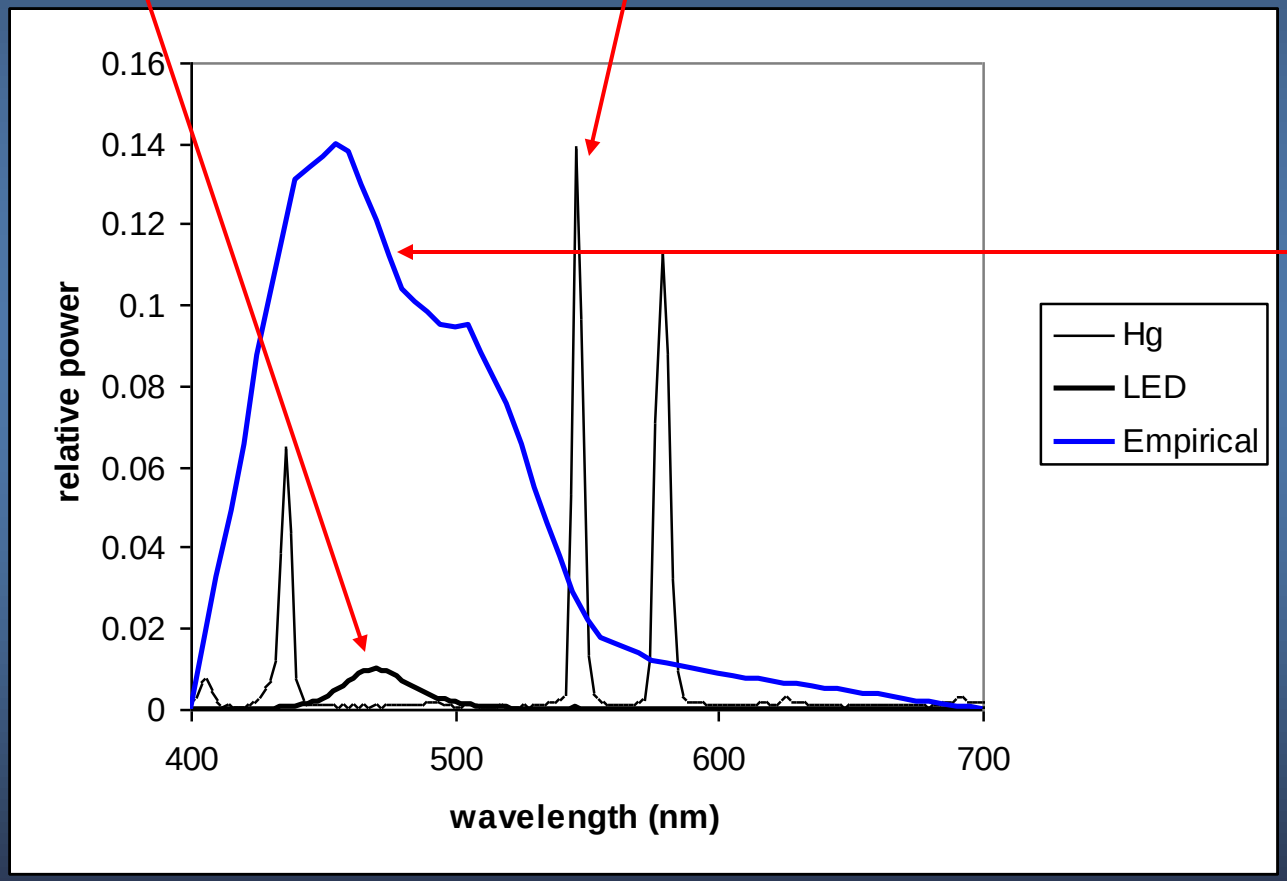


(Brainard et al., 2001; Thapan et al., 2001)

Spectral opponency, 1st experiment

LED, 743 "circadian" lux

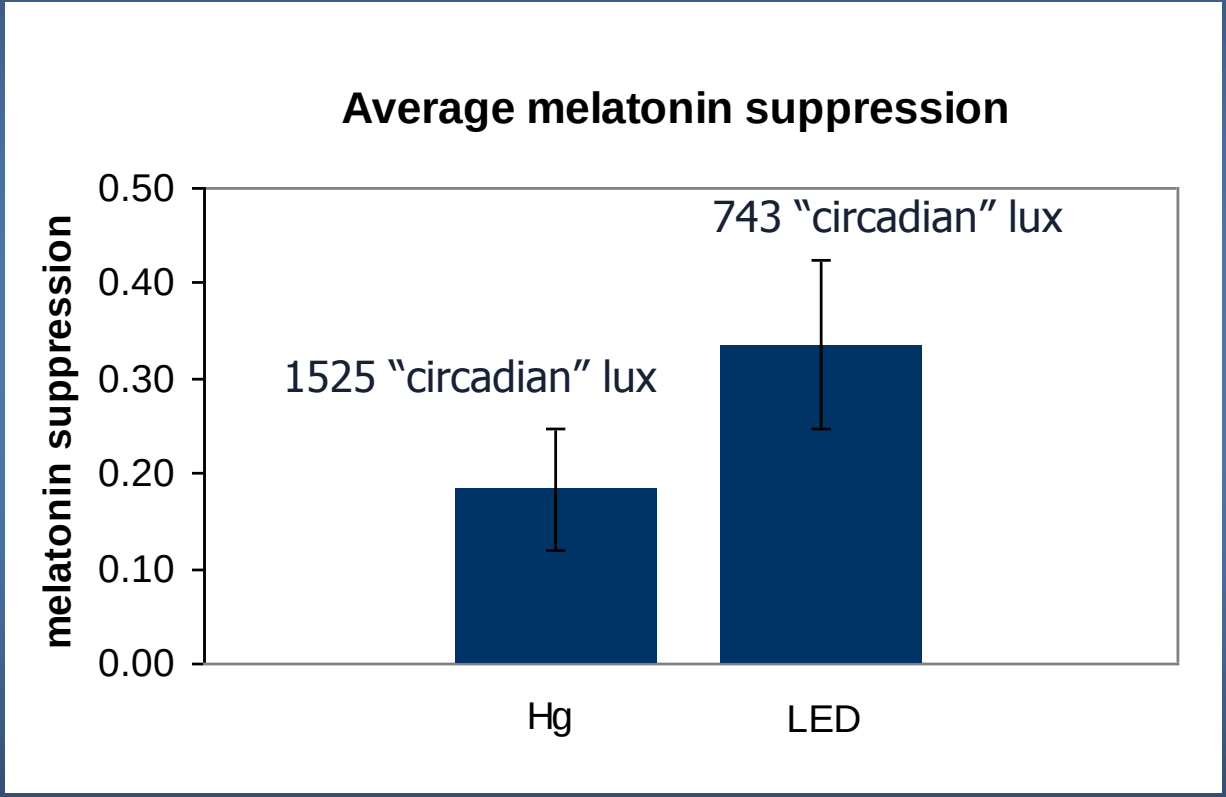
Hg, 1525 "circadian" lux



Empirical Function

Absolute SPDs and Empirical Spectral Efficiency Function

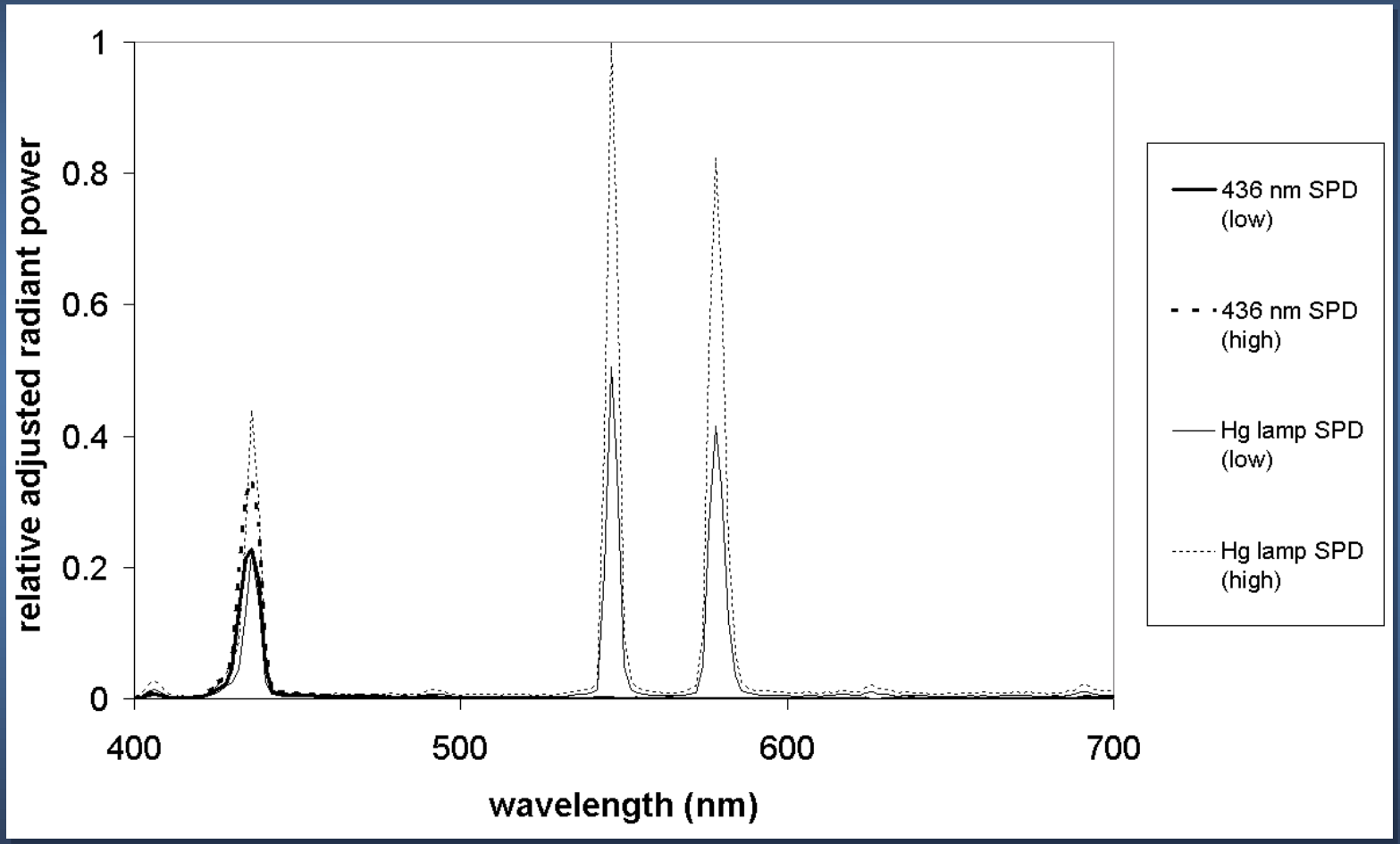
Spectral opponency, 1st experiment



Figueiro et al., 2004

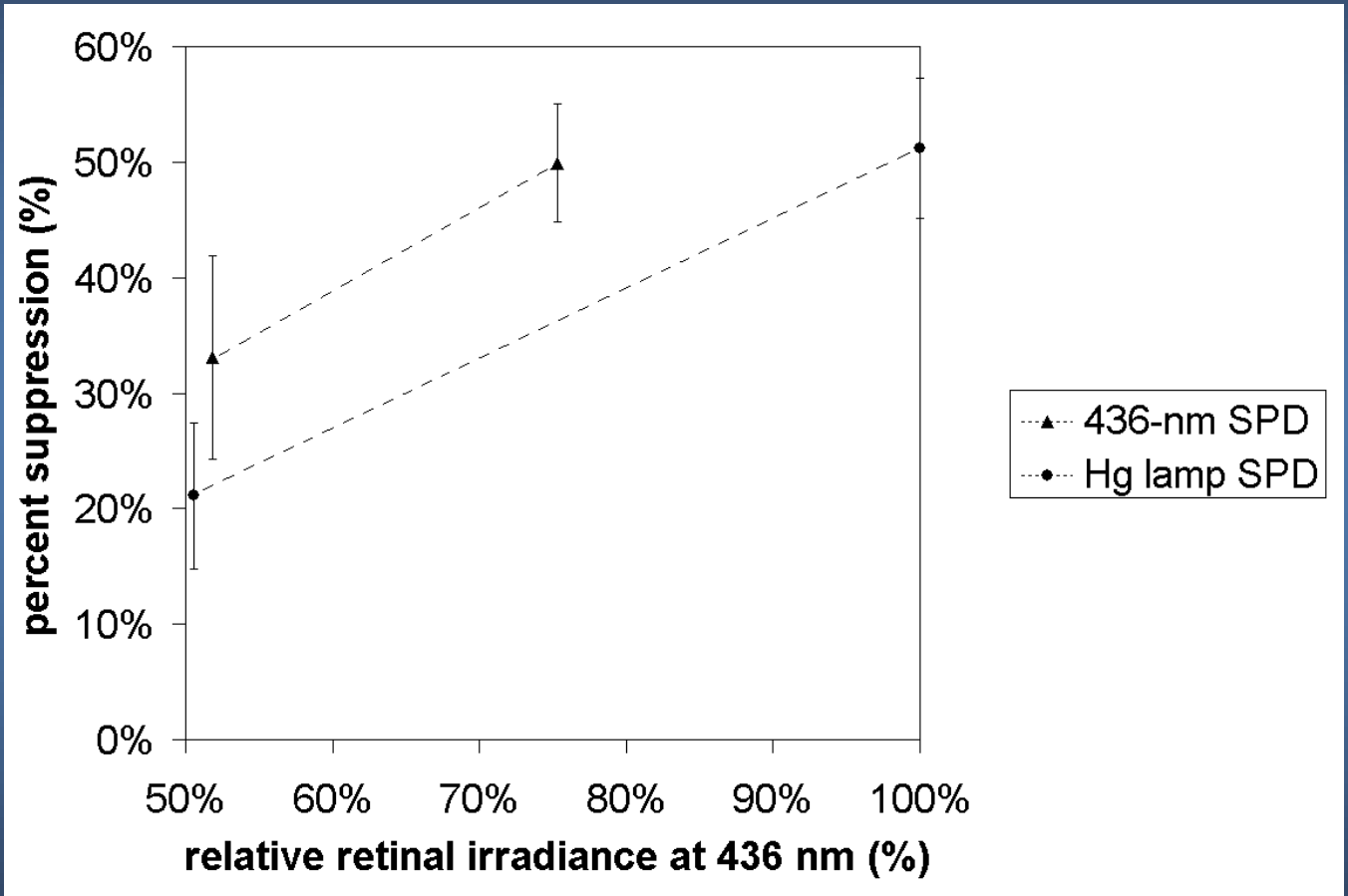
Mean + s.e.m.

Spectral opponency, 2nd experiment



Figueiro et al., 2005

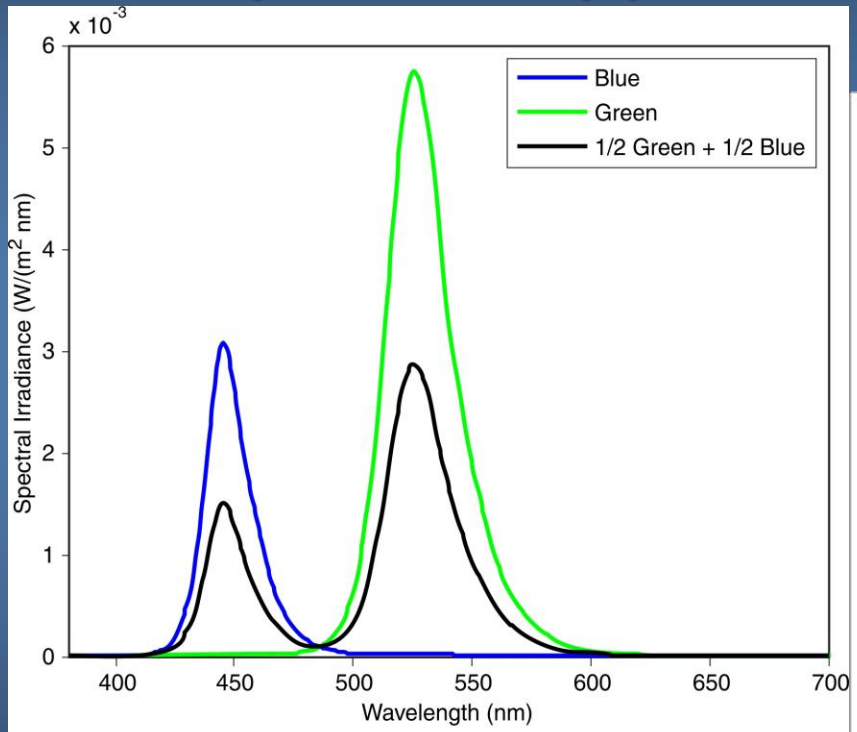
Spectral opponency, 2nd experiment



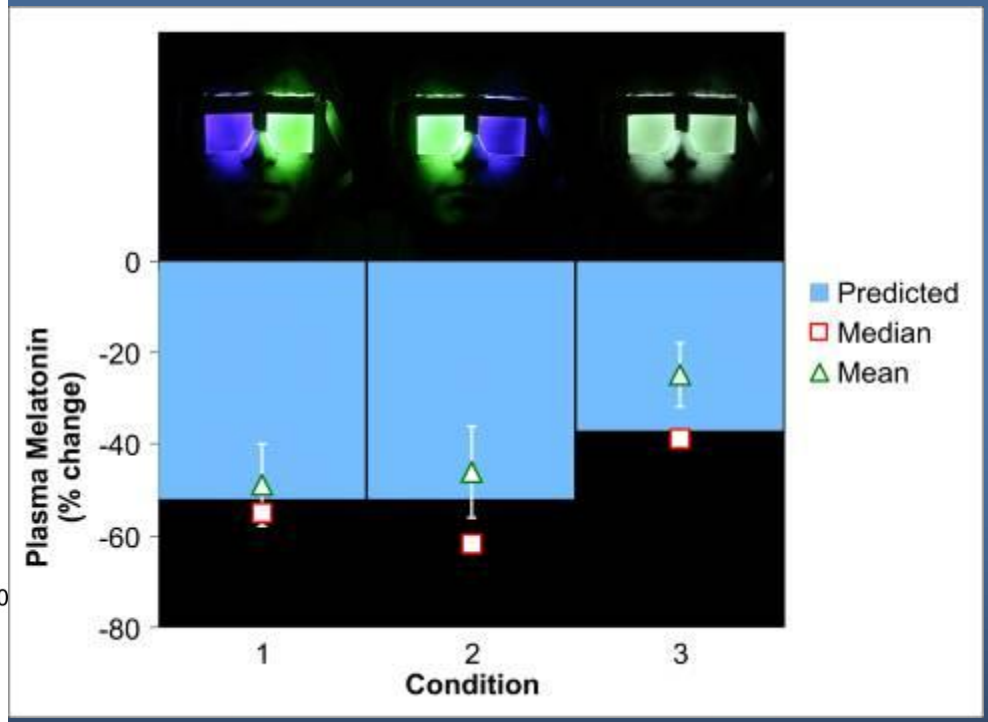
Figueiro et al., 2005

Spectral opponency, 3rd experiment

- Is spectral opponency formed in the retina?



Monocular Stimulus	Illuminance (lux)	Irradiance (W/m²)
Blue	3.0	0.077
Green	113.2	0.211
1/2 Blue + 1/2 Green	57.7	0.142



Figueiro et al., in press

Sponsor: James D. Watson Investigator Award - NYSTAR

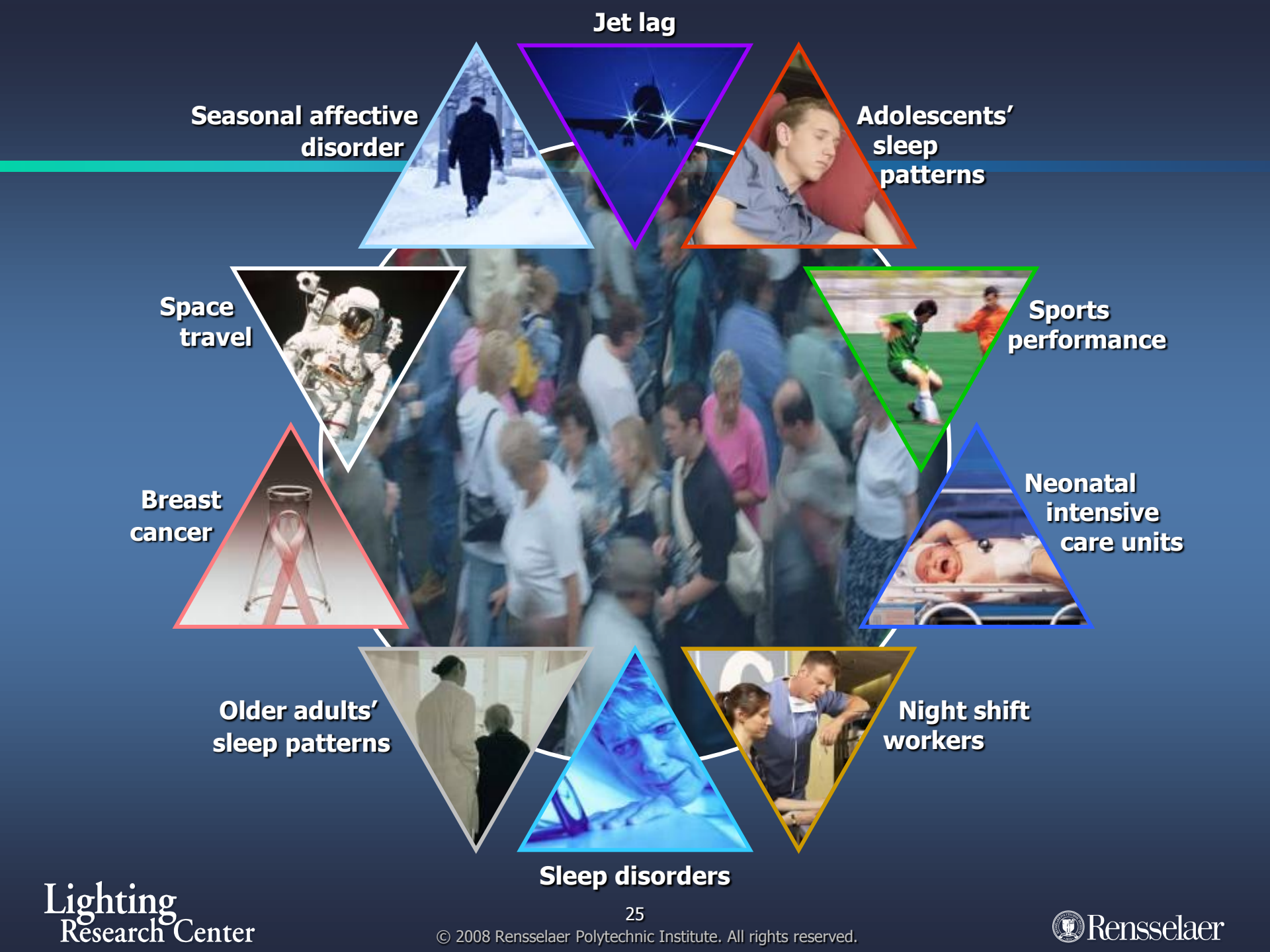
Putting it all together

- The mathematical model proposed by Rea and colleagues
  - Has been able to predict circadian responses (melatonin suppression by light and alertness) for various light sources
  - Is consistent with the neuroanatomy and neurophysiology of the retina
    - It accounts for spectral opponency
  - However, the model does not account for timing/duration of exposure, photic history, pupil areas, and regeneration of ipRGCs by long wavelength light

Putting it all together

Light source	Photopic lumens/watt	Circadian stimulus/watt
Incandescent	12	12
CFL 2700K	55	38
T8 fluorescent 3000K	100	109
T8 fluorescent 4100K	100	67
T8 fluorescent 6500K	90	184
T8 fluorescent 7500K	55	90
Metal halide	95	86
White LED	35	82
Blue LED	15	295

Photopic lumens/watt (lm/W) and circadian stimulus/watt (CS/W) for some electric light sources. Values of CS/watt were arbitrarily normalized to a black body radiator of 2856 K at 1000 lux at the eye. In this way, values for both lm/W and CS/W become equal for a common incandescent light source.



Lighting Research Center

Rensselaer

What is next?

- Integrate intensity, spectrum, timing duration, distribution and light history
- Development of a personal light meter that can measure "light" for the circadian system

Thank you!

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