How do current circadian metrics relate to physiology?

- *What are these metrics measuring?*
- *Are these the outcomes of interest?*
- *If not, are these adequate proxies?*

What are we trying to measure?

Non-image forming aspects of light relevant for human health and productivity:

- Circadian impact
- Acute alertness
- Mood
- Perceptual comfort
- Downstream effects on sleep, mental and physical health
- Others?

(note, we don't actually care about the acute impact of melatonin suppression)

What are the proposed metrics actually quantitating?

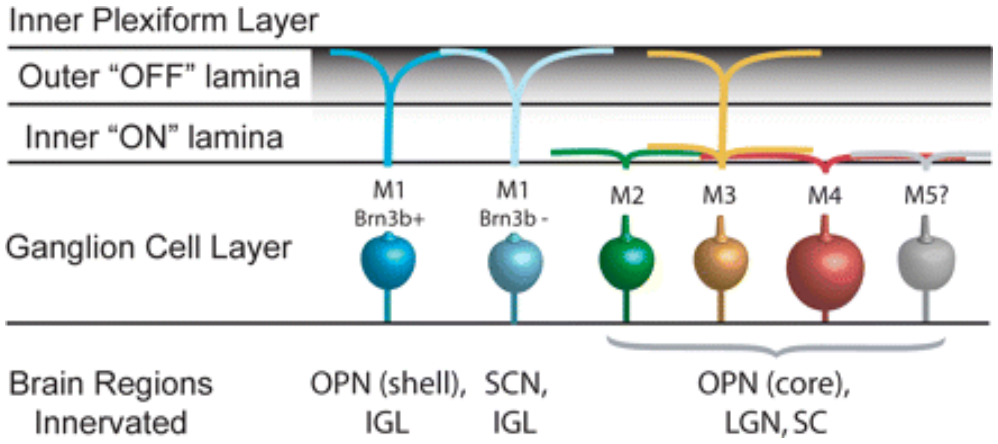
RPI Circadian Stimulus (CS)	melatonin suppression
WELL Equivalent Melanopic Lux (EML)	melanopsin action spectrum
CIE Melanopic equivalent daylight illuminance (m-EDI)	melanopsin action spectrum

WELL/CIE assume that outcomes of interest are driven solely by melanopsin
CS assumes that outcomes of interest are regulated identically to melatonin suppression

Can all of the non-image forming aspects of light be reduced to melanopsin or paralleled with melatonin suppression?

Theoretically, no

- Not just one ipRGC
- Different ipRGC use different combinations of intrinsic (melanopsin) and extrinsic (rod/cone) input (so different spectral sensitivity)



Sexton et al., 2011

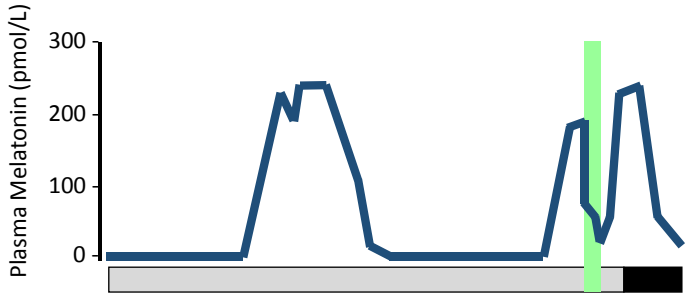
- Evidence of divergence of phase shifting and melatonin suppression response in humans:

  Zeitzer et al., 1997 (red light, shift but no suppression), Zeitzer et al. 2011 (sequence of light flashes, shift but no suppression), Rahman et al. 2018 (intermittent light, shift but no suppression)

Melatonin suppression → Sustained light exposure (melanopsin)

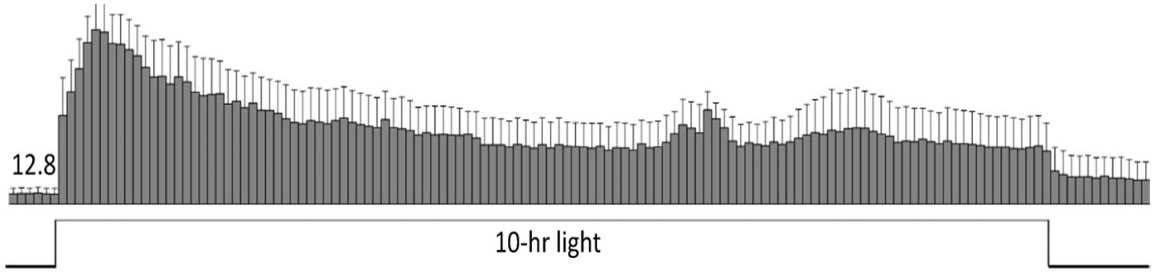
Melatonin suppression requires a *sustained* activation by light

- Removal of light stimulus results in rapid reversion of melatonin to normal levels
- Consistent with a strong involvement of melanopsin
- Melanopic irradiance seems to fit diversity of melatonin suppression from *monochromatic* stimuli very well and explain most of the variance (e.g., Brown 2020, Prayag et al. 2019)



Rapid change in melatonin in response to light

adapted from: Czeisler et al., 1995



Sustained responses possible by melanopsin in ipRGC

adapted from: Wong, 2012

Phase shifting → Integrated light exposure (melanopsin + cones)

Phase shifting can respond to *rapidly changing light levels*

- Most of the impact of continuous light happens at the beginning of the stimulus
  - Robust phase shifting responses to sequences of millisecond flashes of light (Zeitzer), intermittent light (Rimmer, Gronfier), and seconds of light (Rahman)
  - Supported by latest model of human circadian responses to light (Kronauer 2019)
- More consistent with a greater cone involvement

Are the current measures sufficient?

- *Probably not*

  More work needed on spectral sensitivity of phase shifting, alertness, etc. to complex (spectrum/temporality/magnitude) light stimuli

  High thesholds for indoor lighting are sufficient for circadian needs, but may not be ideal for visual comfort or energy utilization

  Trade-offs between these competing factors are unknown