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# From Bench to Bedtime: Entraining Policy to Science

— Day 1 —

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Jackie Lin, Rachel Swope

# We are the initial cohort of MAHPING Pedagogy Fellows!



- MAHPING: The Morehouse and Harvard Program in Neuroscience Growth
- Pedagogy Fellows: Seven graduate students across both institutions come together to learn inclusive teaching strategies and co-teach a course at both Harvard and Morehouse
- We chose to design and teach a course on applying circadian biology to policy decisions
- Website: [bit.ly/mahping](https://bit.ly/mahping)

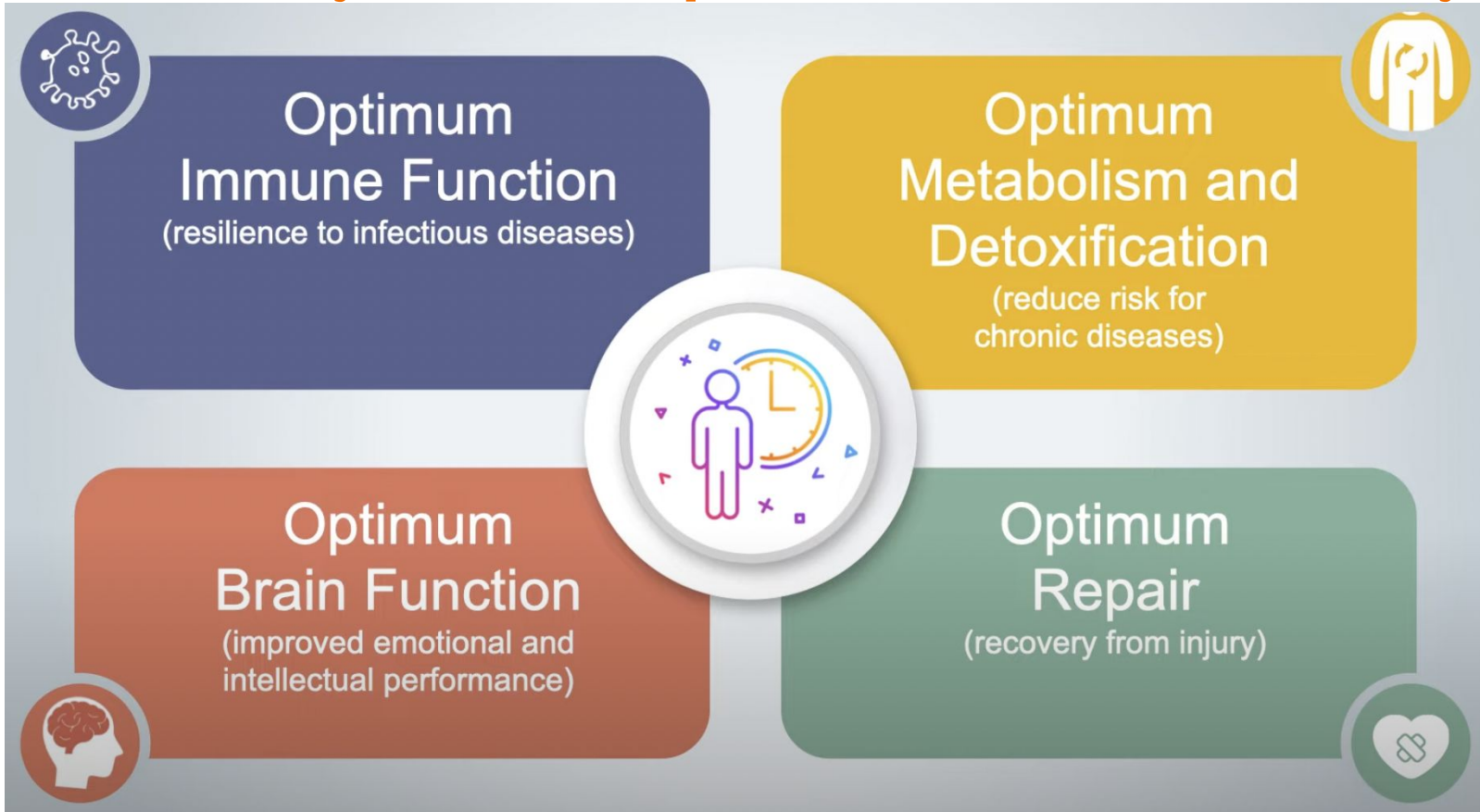
## Get to know your class

- Are there any bona fide circadian biologists here?
- What model organisms do we all work on?
- What reasons do we have for taking this course?

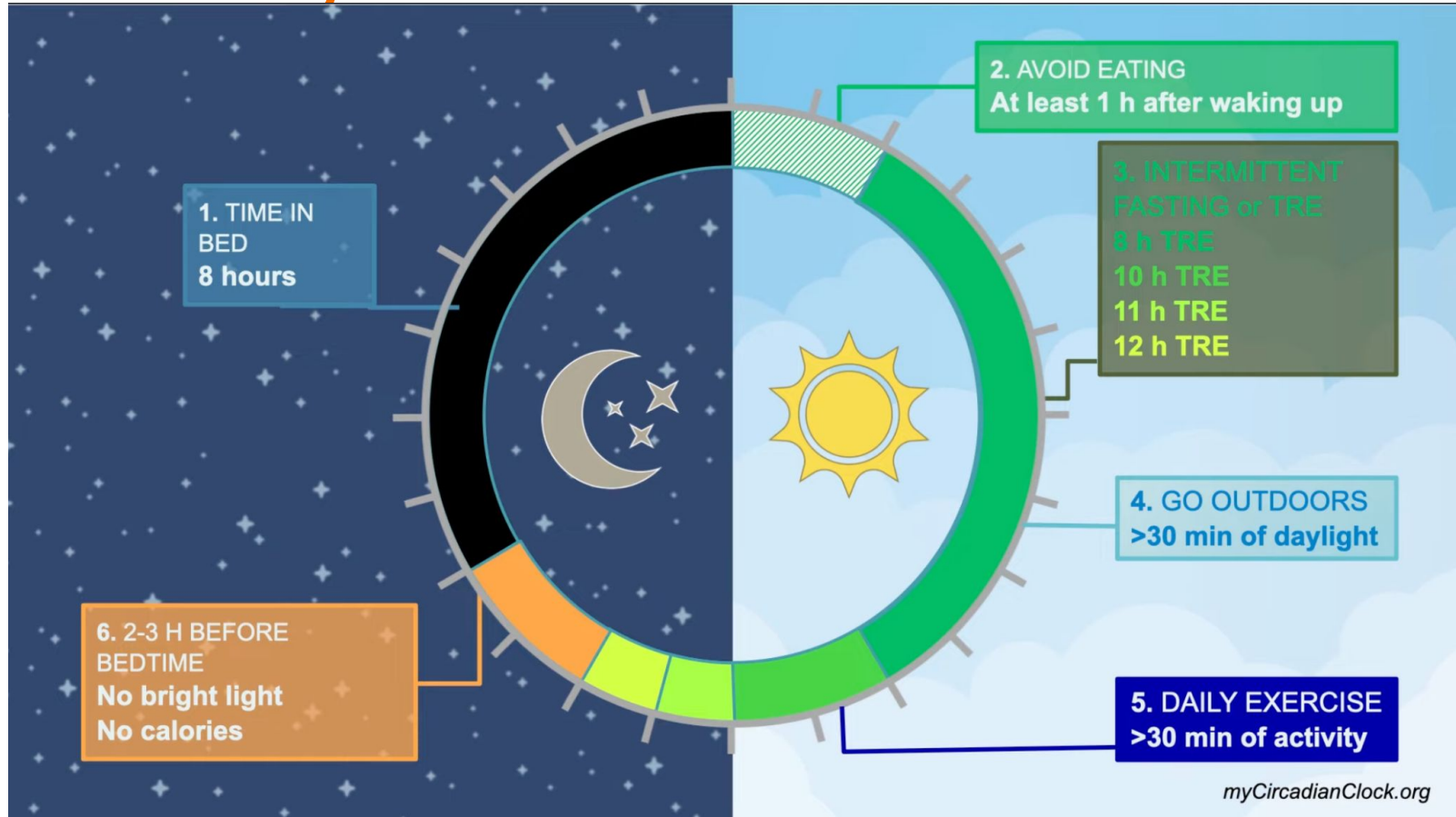
# Day 1: Why do circadian rhythms matter?



# Circadian rhythms underpin health in numerous ways



# Circadian rhythms can be reinforced or interfered with



## Day 1

Introduction to what circadian rhythms are and how they are maintained

## Day 2

Examination of the effects of circadian rhythm disruptions on health

## Day 3

Exploration of policies related to circadian rhythms



# Course Schedule

## Day One

- What are circadian rhythms, and why do they matter?
- Autoinhibitory transcriptional networks allow for temporal gene regulation
- How environmental stimuli like light can “entrain” the circadian clock
- How the brain coordinates circadian rhythms in the periphery

## Day Two

- How does circadian biology impact shift workers?
- Shift work as a historical phenomenon
- How to leverage circadian biology to improve health outcomes in shift workers
- Exploring the psycho-social ramifications of shift work

## Day Three

- How should future policies be informed by circadian biology?
- The current status of DST and school start times in the USA
- How to better support health and productivity outcomes using circadian biology

# Learning Objectives

At the end of Day 1, students can ...

- ❑ define circadian rhythms and entrainment in layman's terms.
- ❑ outline the steps in the autoinhibitory transcriptional network that creates circadian rhythms.
- ❑ draw out the path through which light, an external cue, entrains the SCN.
- ❑ predict the effect on circadian rhythms if exposed to light during early and late night.
- ❑ explain the role of melatonin as an external cue to entrain the clock.
- ❑ identify peripheral clocks and the bodily functions they regulate.

## Think-Pair-Share:

**How would you define circadian rhythms for the public?**

Take 2 mins to discuss with a partner then I'll ask for volunteers.

# How would you define circadian rhythms for the public?

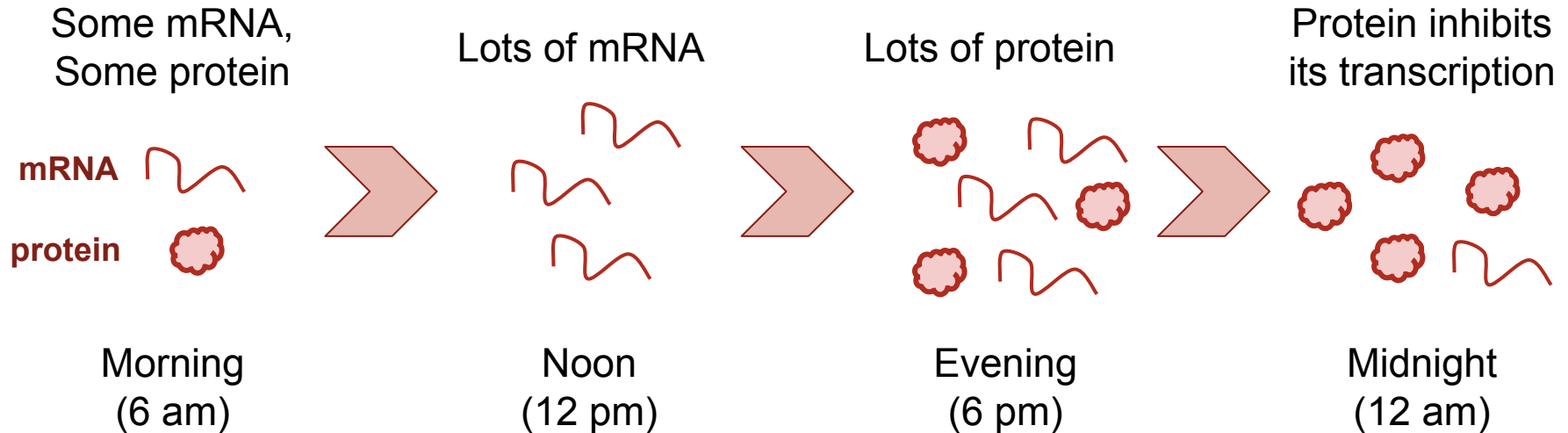


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# How does a cell keep track of time?

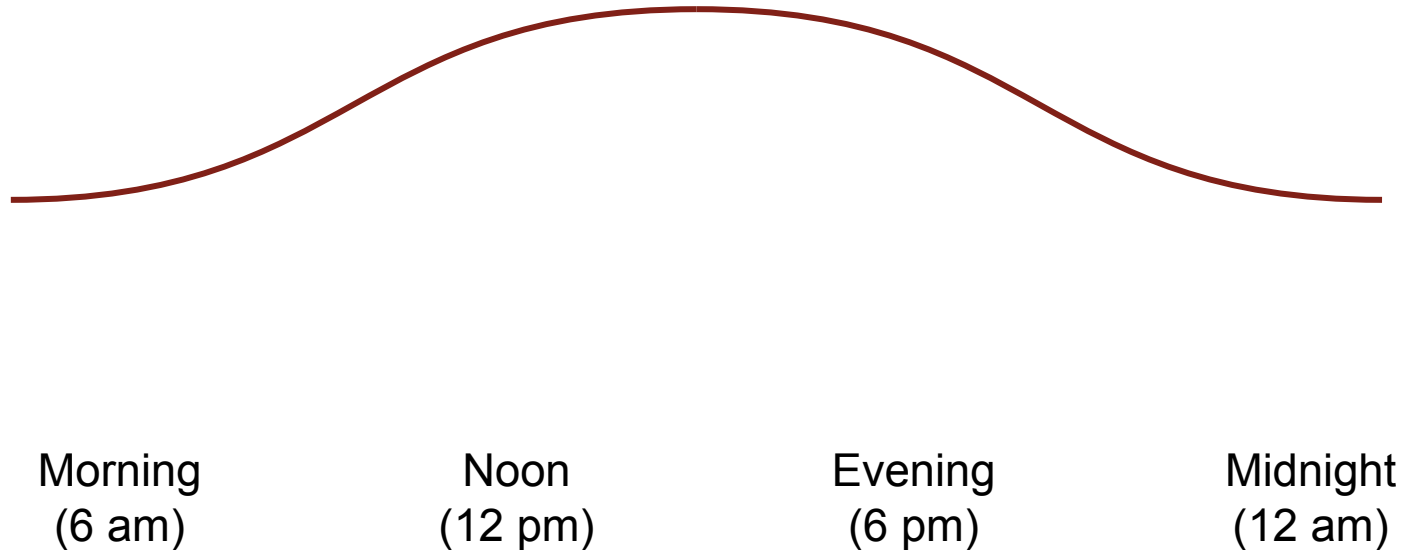
**Big idea:** cells use an auto-inhibitory transcriptional feedback loop, in which proteins are transcribed, feedback to inhibit their transcription, and then degrade over a ~24 hr period to regulate circadian rhythms.



# How does a cell keep track of time?

Levels of mRNA or protein correspond with time of day.

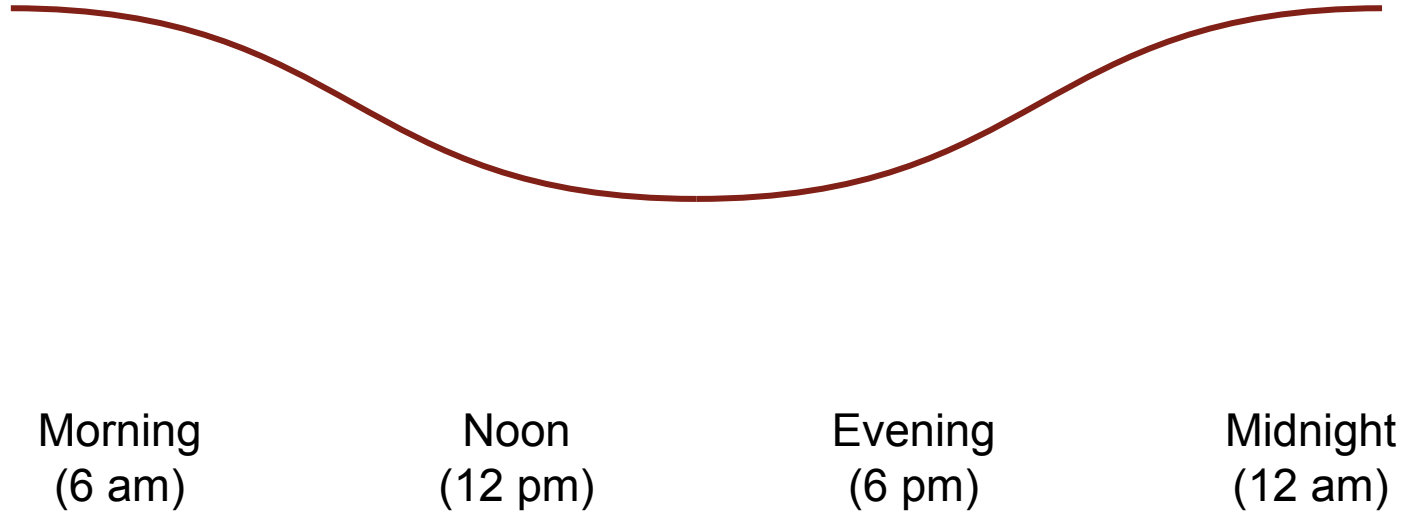
mRNA  
level



# How does a cell keep track of time?

Levels of mRNA or protein correspond with time of day.

protein  
level



# Pairs of genes and proteins regulate circadian rhythms

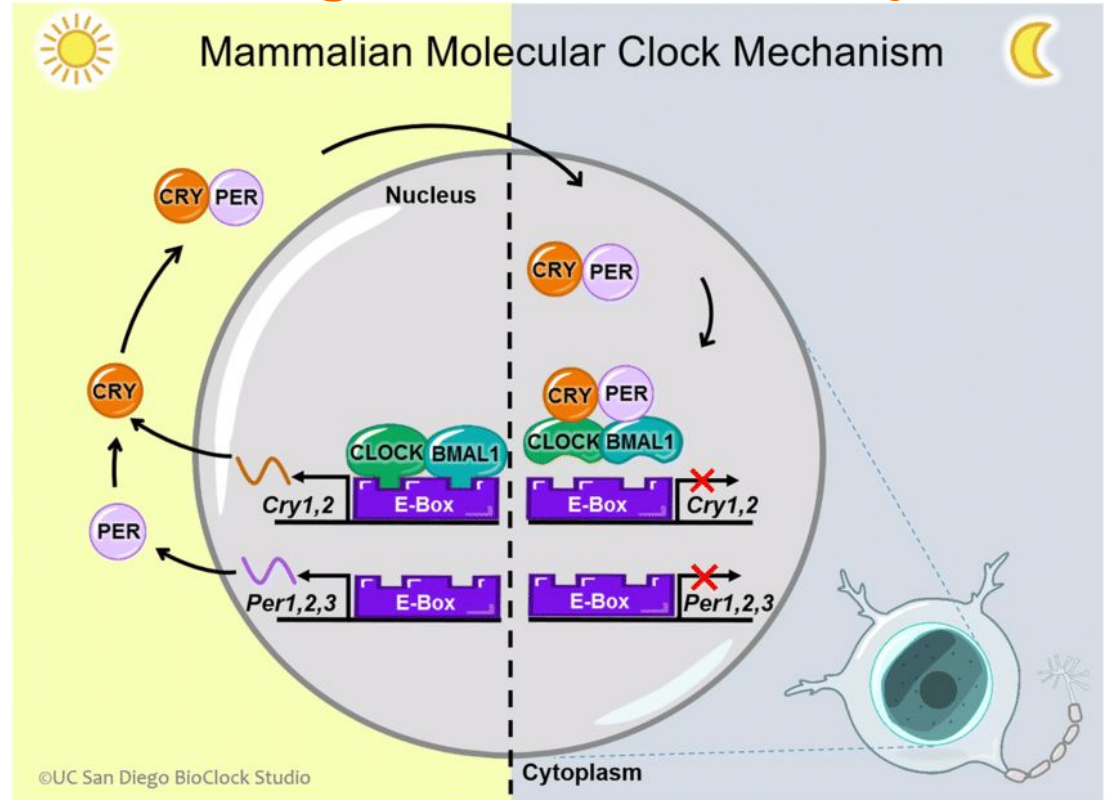
PROTEIN / gene

PER / *per*

CRY / *cry*

BMAL1

CLOCK



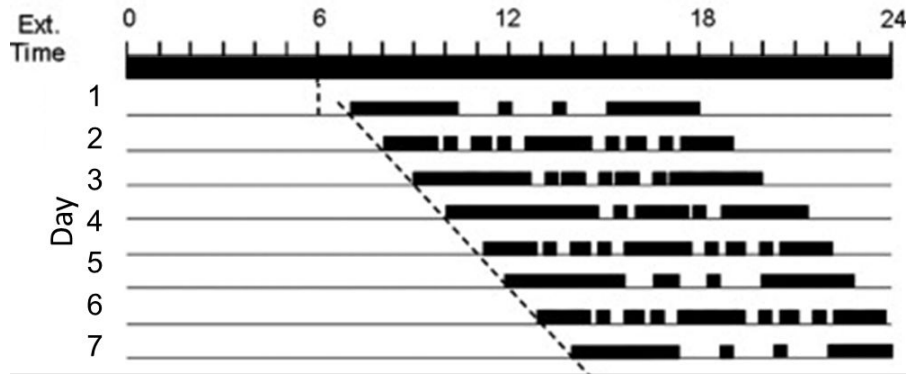


## **Worksheet:**

**Work in pairs or small groups to outline the steps of the auto-inhibitory transcriptional network.**

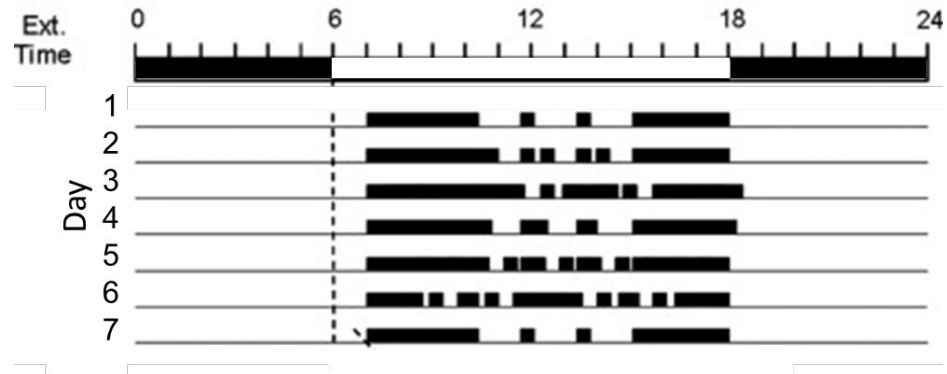


## Circadian rhythm is $> 24\text{h}$ in constant darkness



Actogram of human in constant darkness

## Circadian clocks can be entrained by external cues



Actogram of human entrained by light

## **Poll Everywhere:**

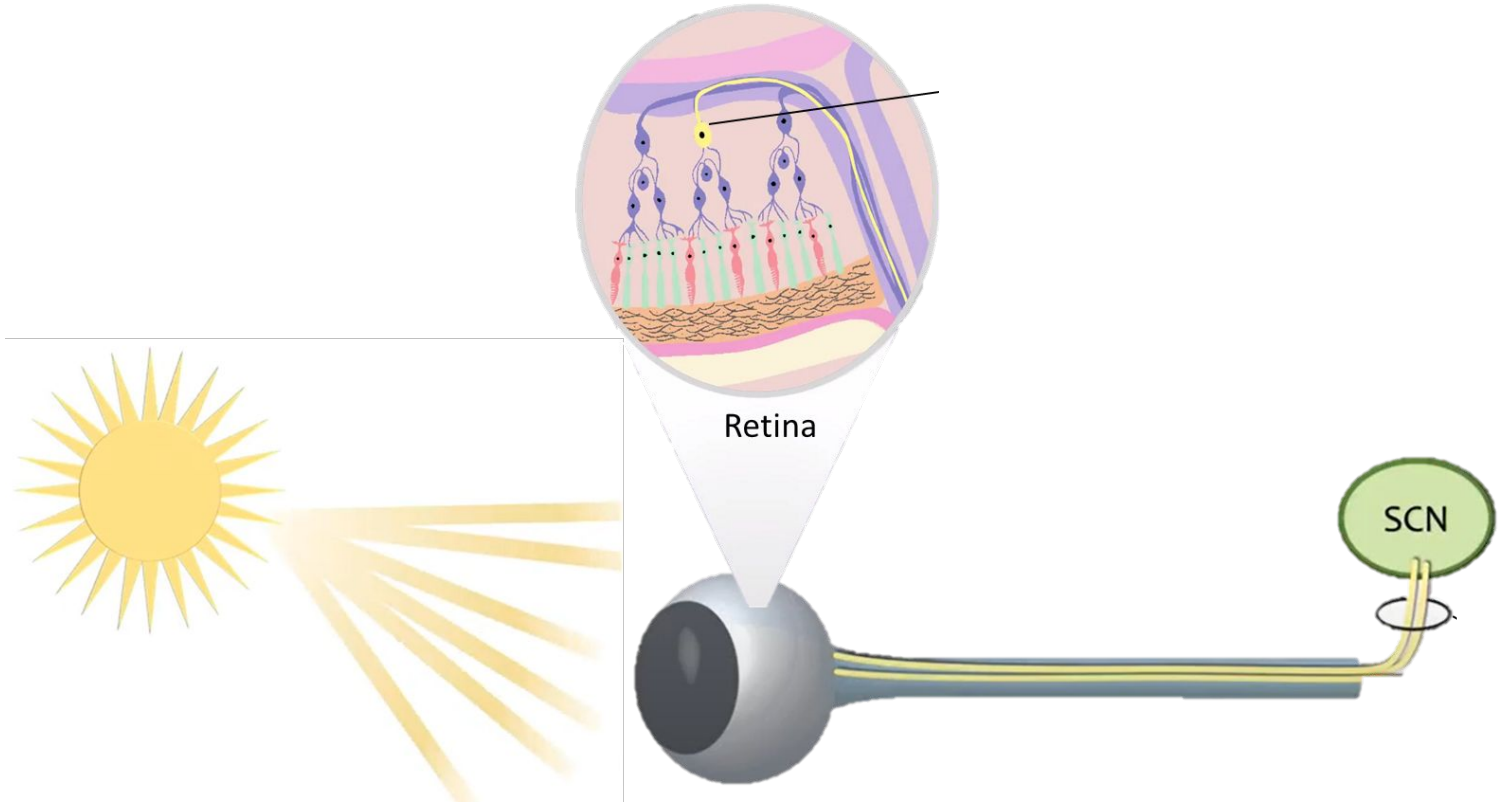
**How would you define entrainment of the circadian rhythm for the public?**

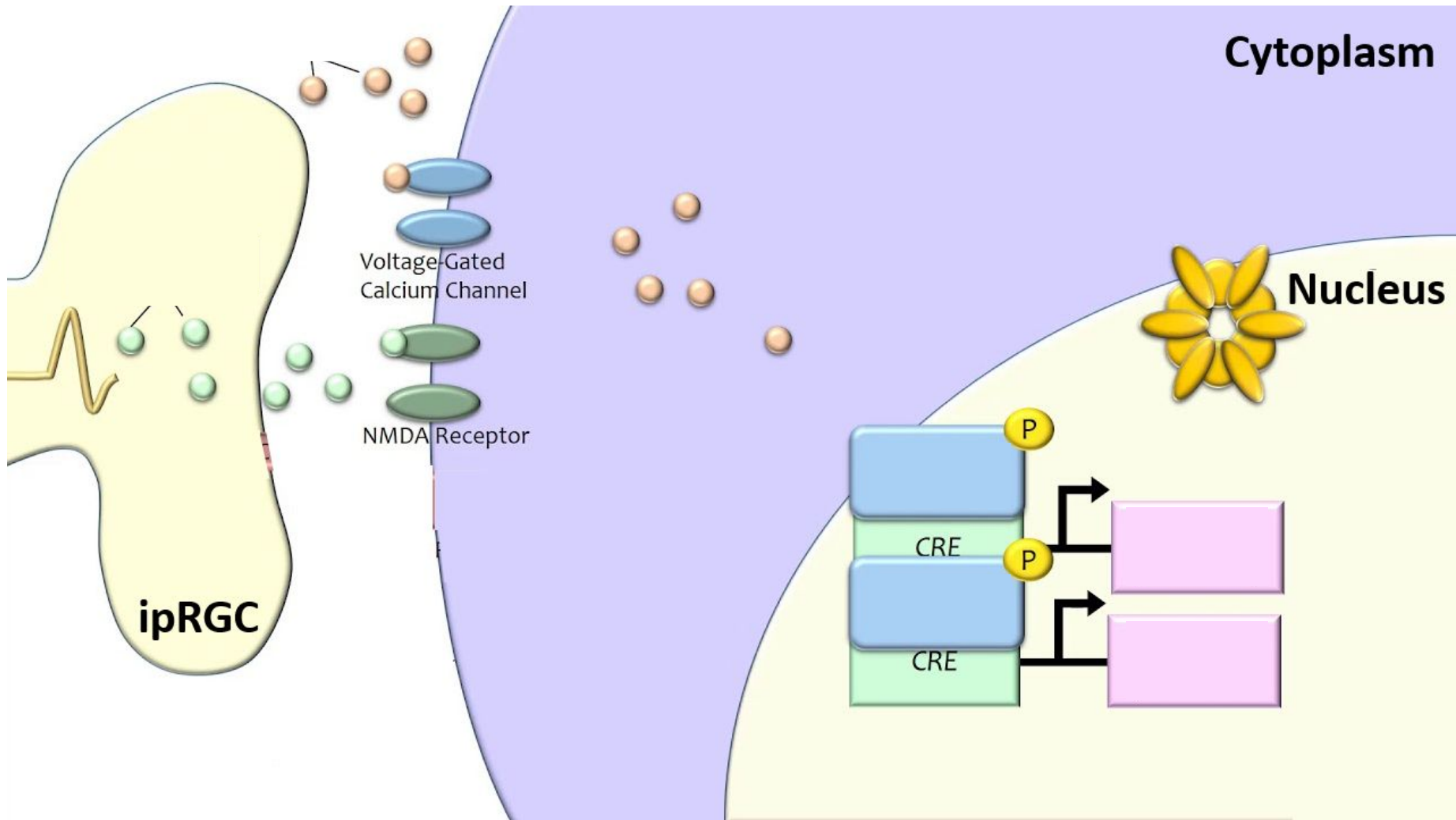
# How would you define entrainment of circadian rhythms for the public?



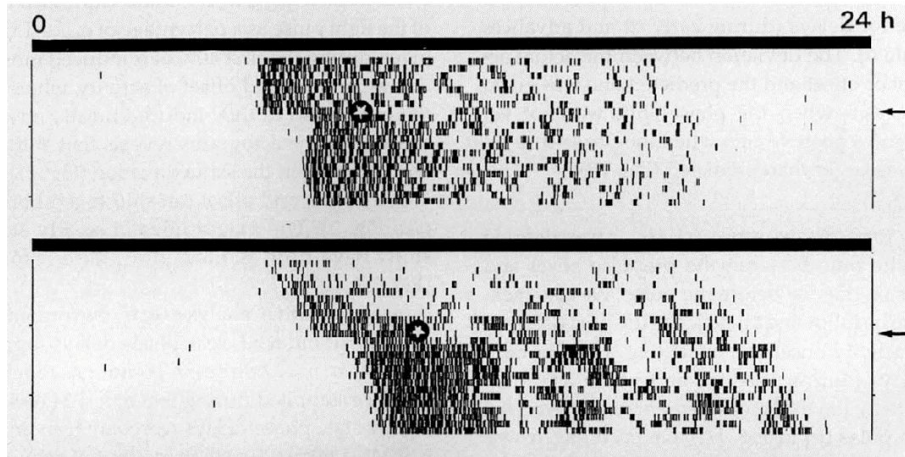
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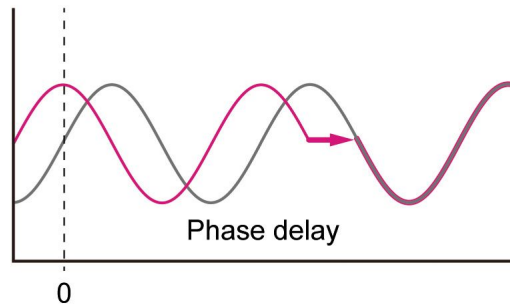




# Effects of light on circadian rhythms: Phase Delay

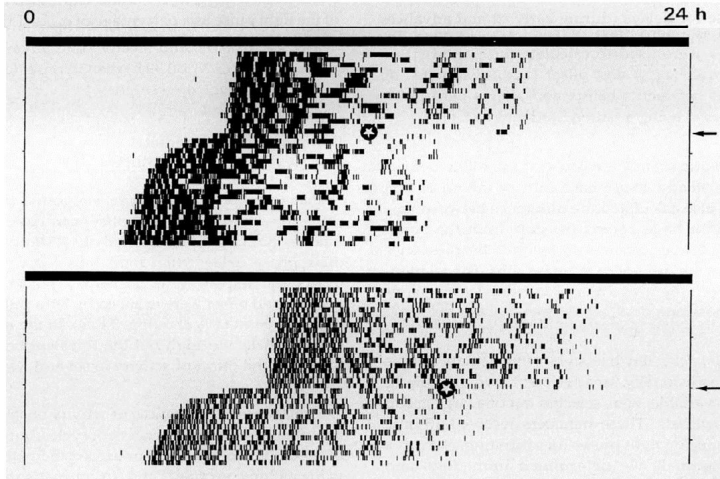


- Occurs when exposed to light during first half of the night
- Activity starts **later** in the day

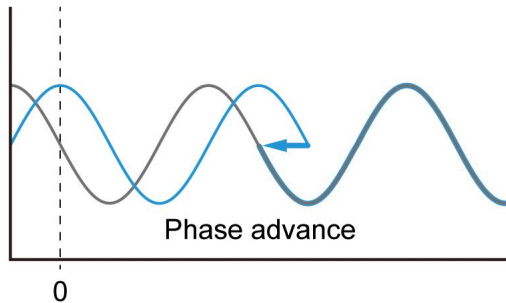




# Effects of light on circadian rhythms: Phase Advance

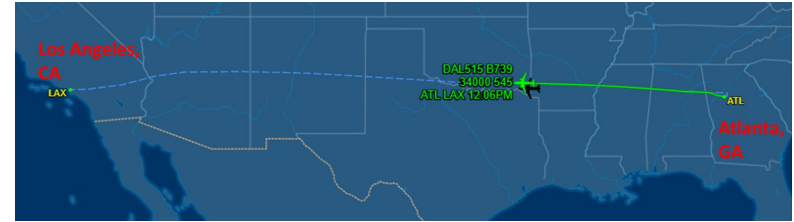


- Occurs when exposed to light during second half of the night
- Activity starts **earlier** in the day



# Example of Phase Shift: Jet Lag

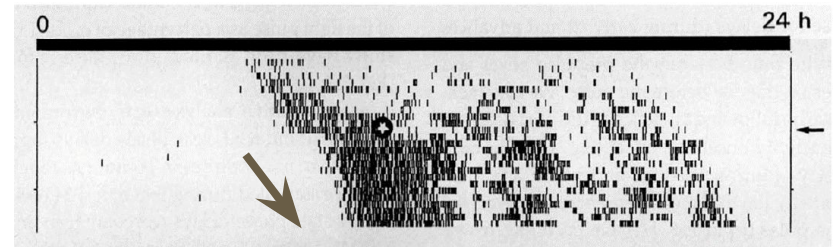
## Phase Delay-Travel Westward



Travel from Atlanta, GA to Los Angeles, CA

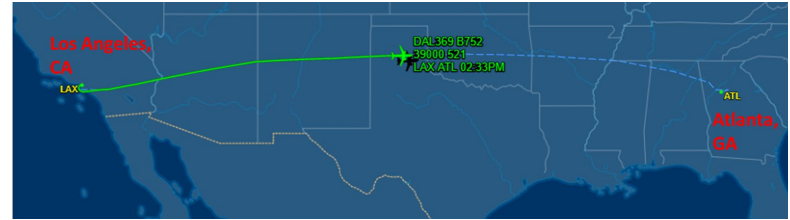


Light exposure in the **first half** of the night.

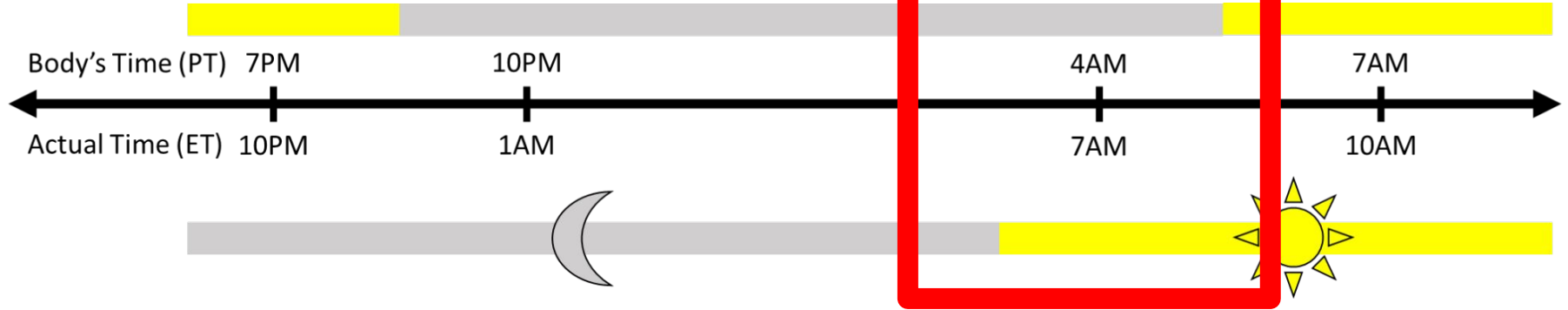


# Example of Phase Shift: Jet Lag

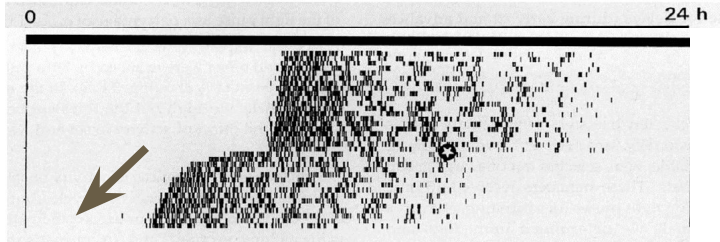
## Phase Advance- Travel Eastward



Travel from Los Angeles, CA to Atlanta, GA

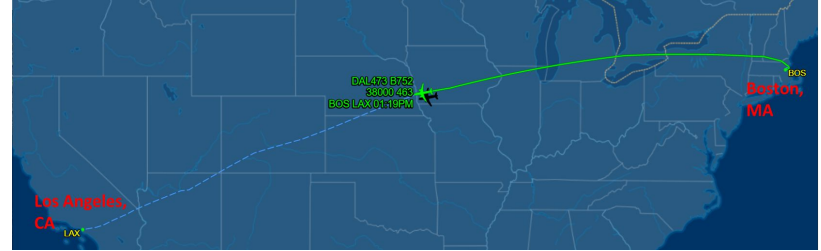


Light exposure in the **second half** of the night.

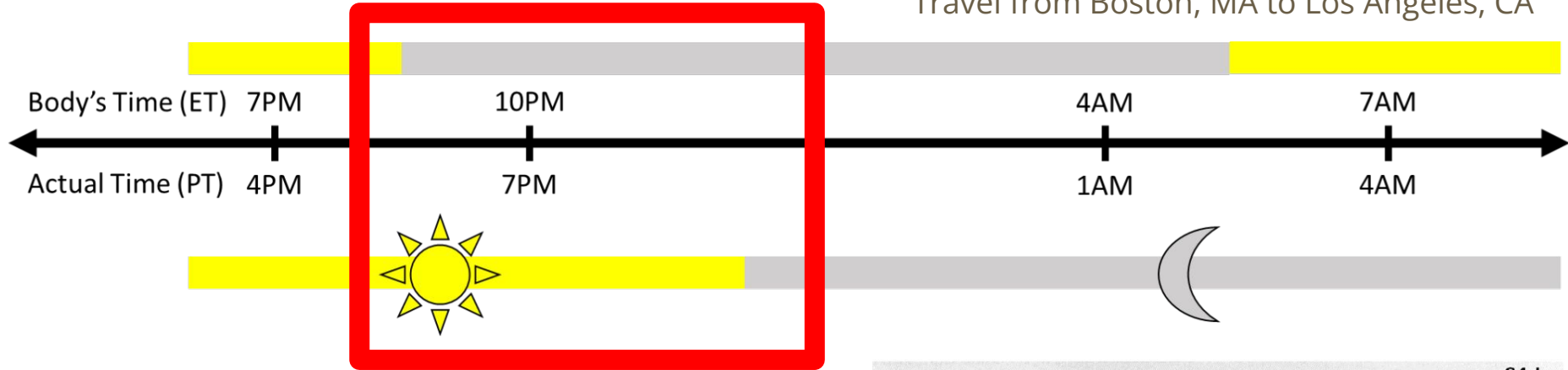


# Example of Phase Shift: Jet Lag

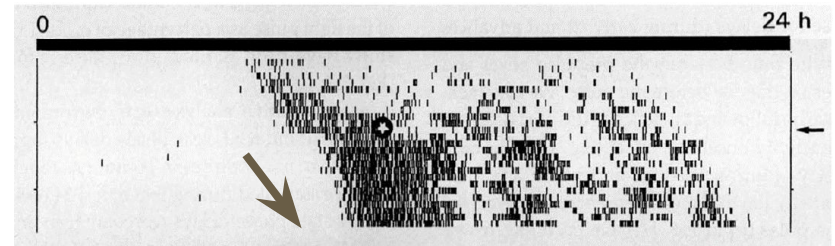
## Phase Delay-Travel Westward



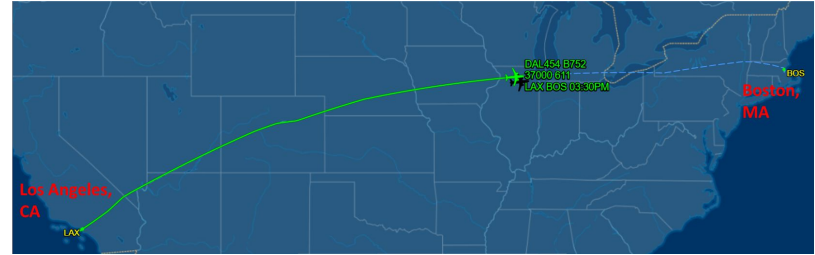
Travel from Boston, MA to Los Angeles, CA



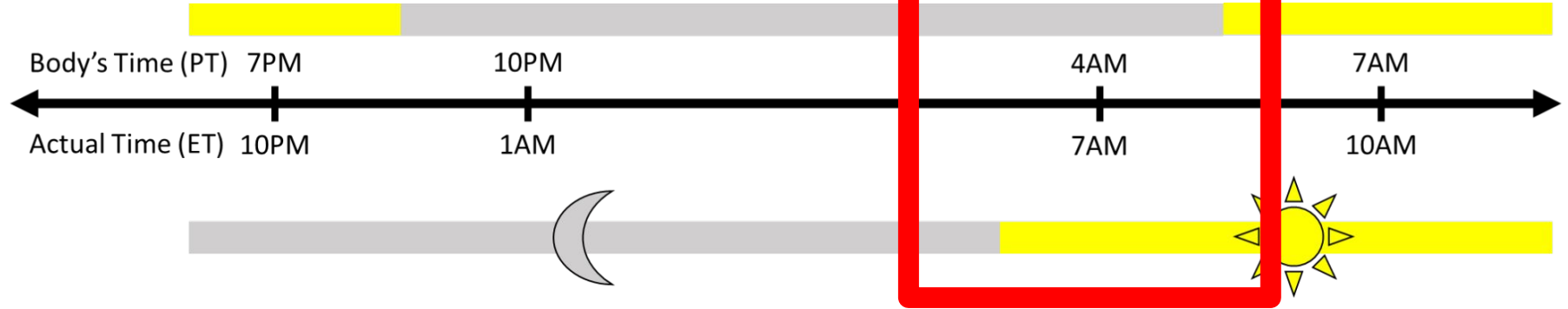
Light exposure in the **first half** of the night.



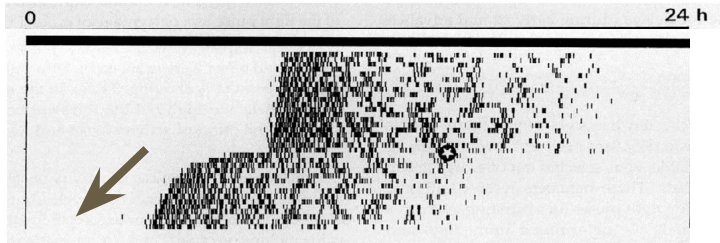
# Example of Phase Shift: Jet Lag Phase Advance- Travel Eastward



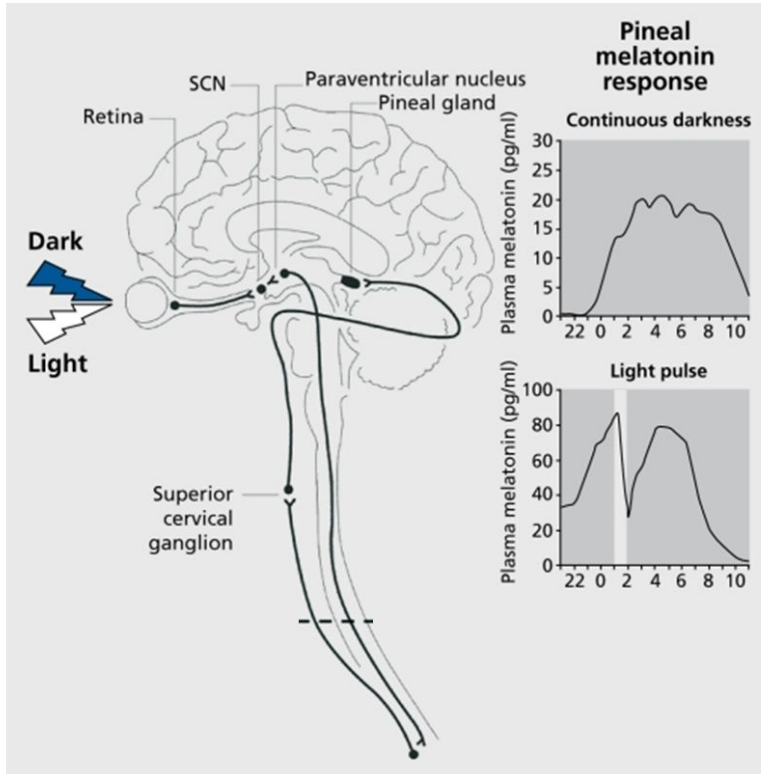
Travel from Los Angeles, CA to Boston, MA



Light exposure in the  
**second half** of the night.



# Melatonin is a molecule involved in the sleep-wake cycle

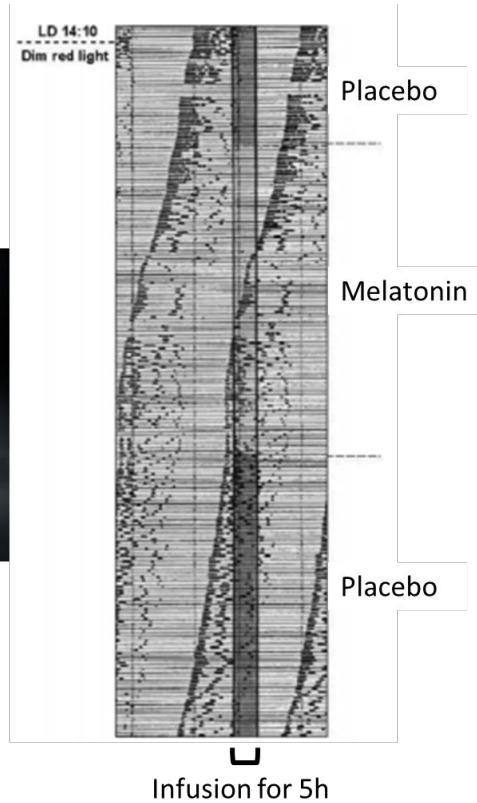


- Released from the pineal gland during darkness
- Inhibited in the presence of light

# Exogenous melatonin can be an external cue for entrainment...



In constant darkness

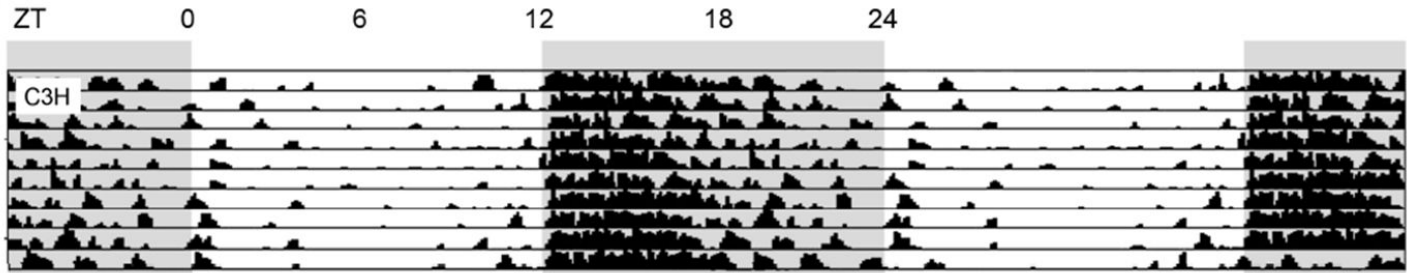


- When placebo was administered, circadian rhythm was  $< 24\text{h}$
- When melatonin was administered, circadian rhythm was  $\sim 24\text{h}$
- Once melatonin administration was stopped, circadian rhythm went back to  $< 24\text{h}$

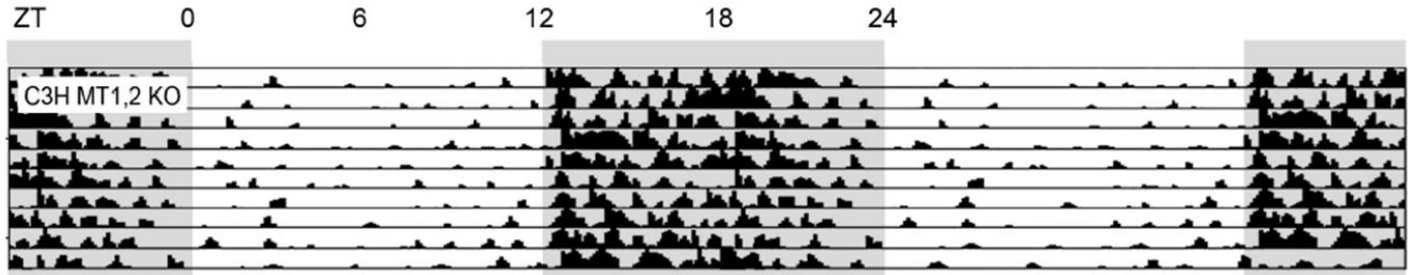
# ... but it is not essential for entrainment



✓ melatonin



✗ melatonin

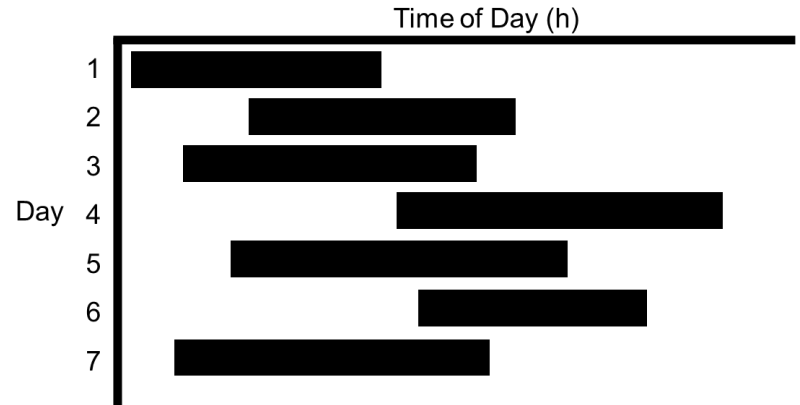


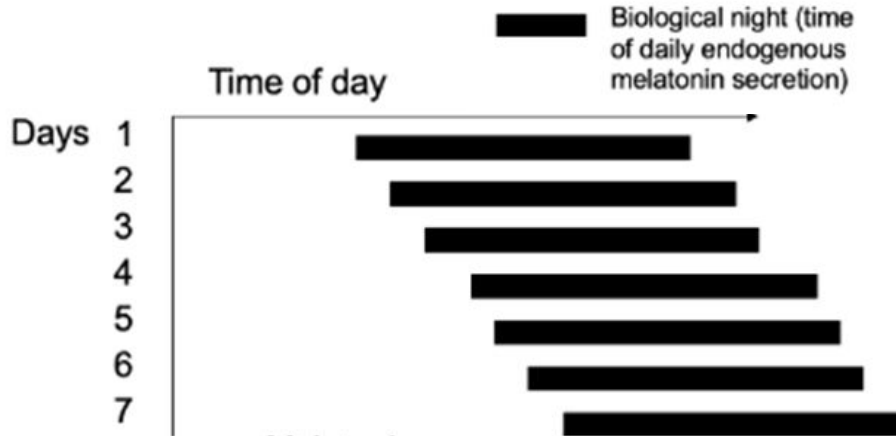


# Group Activity:

Sketch a 7-day actogram of a ...  
Scenario 1: totally blind person's circadian rhythm  
Scenario 2: totally blind person's circadian rhythm who is taking melatonin

Example:





### Circadian rhythm of a totally blind person

- SCN is not entrained by light
- Circadian rhythm is not 24h

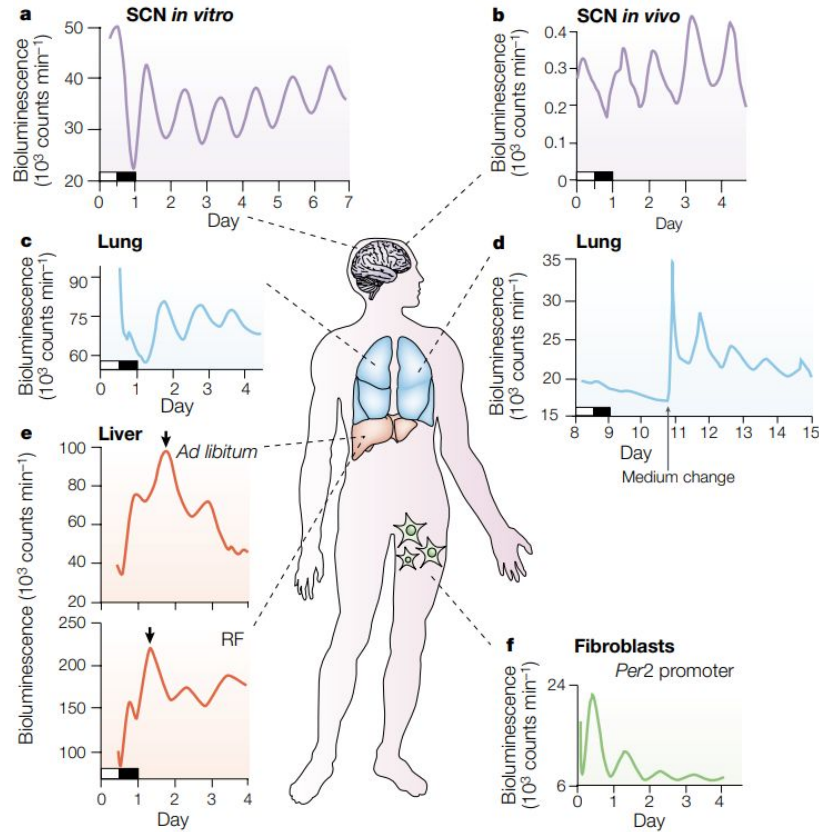
# Clocks are everywhere!

- While the master timekeeper is in the brain, many cells in your body change their activity according to the time of day.
- While the brain contains the master timekeeper that can inform processes in the periphery, almost every cell in the body has its own clock!

# Where in the body would you expect to find circadian rhythms?

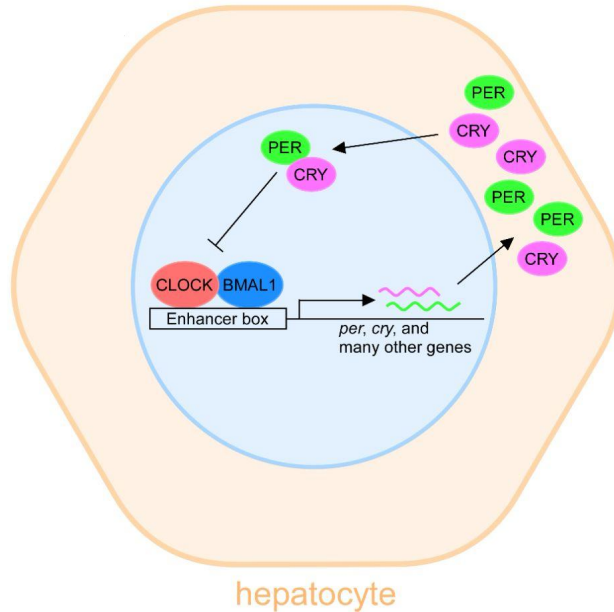


# Nearly all tissues in the body have peripheral clocks.

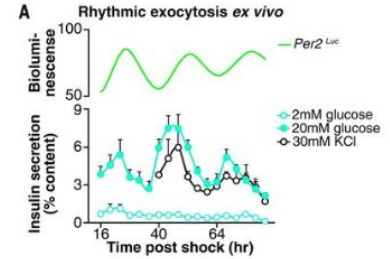
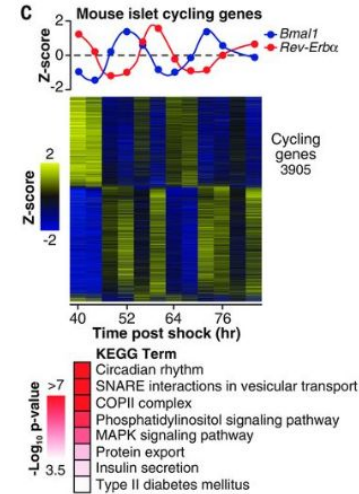
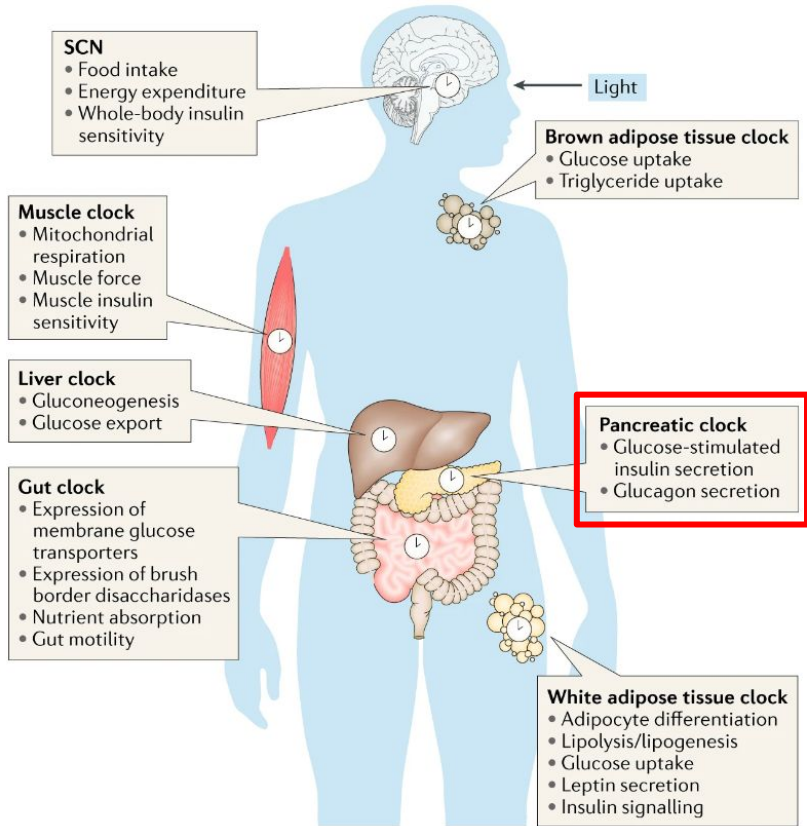


**Other examples:** immune system, heart, vasculature, bone, gut, pancreas, muscle, other brain regions, etc.

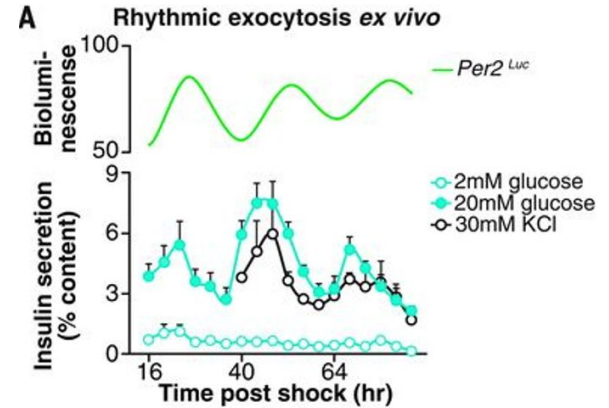
# What is a peripheral clock?



# Peripheral clocks regulate metabolism.



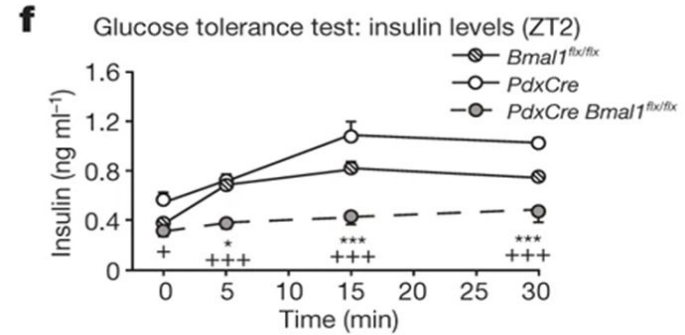
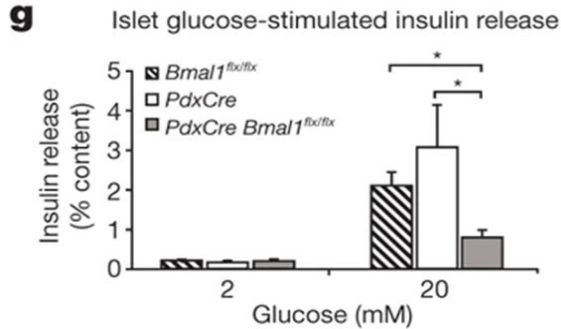
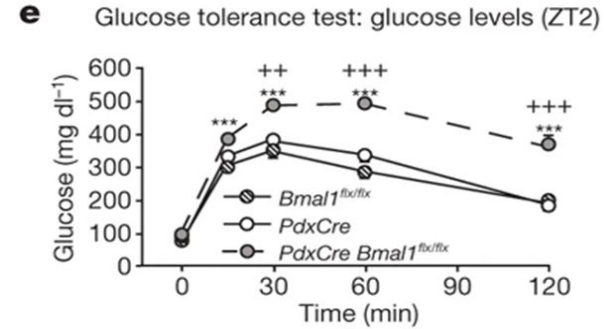
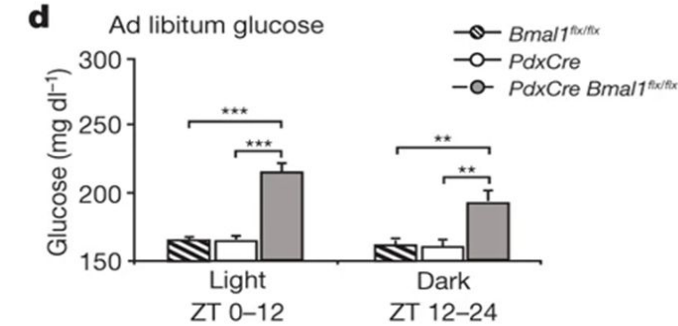
Predict how deleting the peripheral clock **from only the pancreas** will change insulin secretion and blood glucose levels in mice. Discuss with a partner for 2 min before we discuss as a group!



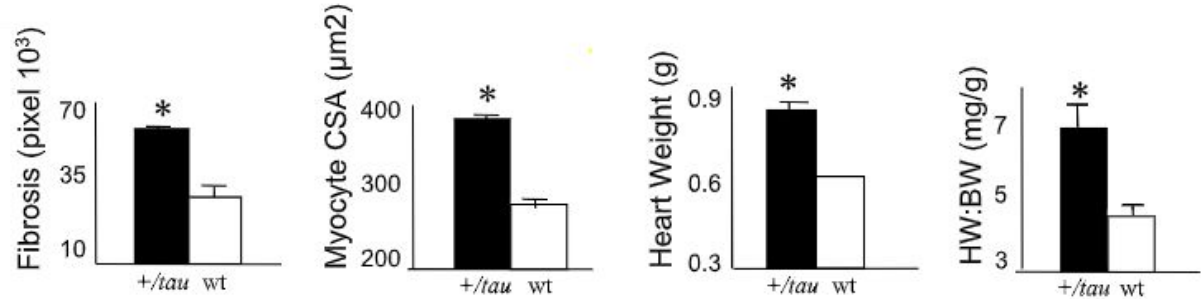
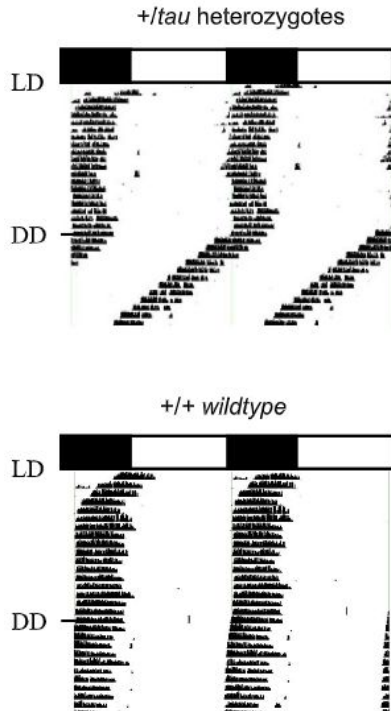
Perelis, M., et. al. (2015) *Science*.



# the result is diabetes!

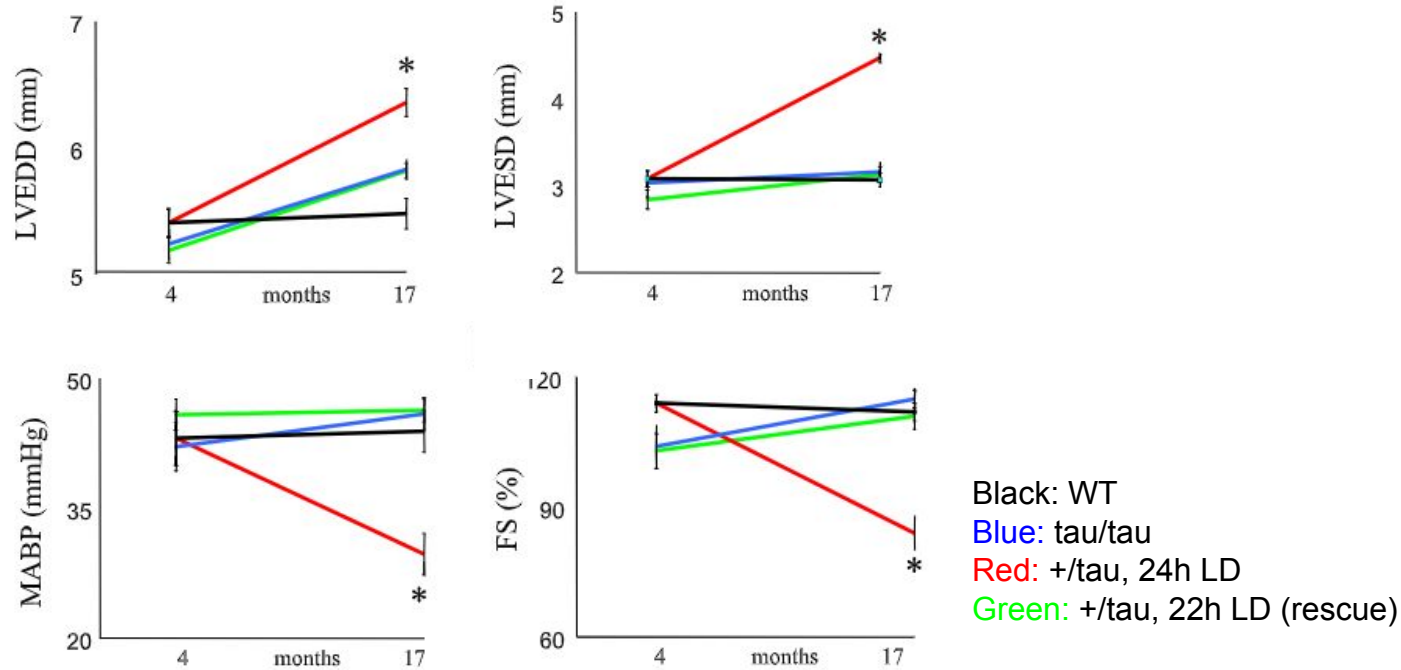


# Chronic mismatch between genotype and LD cycles causes scarring and enlargement of the heart in hamsters.



+/*tau* hamsters have a **shorter** circadian rhythm (22h LD cycle) than WT animals (24h)

# Cardiovascular defects can be rescued by switching +/-tau hamsters to a 22h LD cycle!



## Sneak Peek of Day 2: What is shift work?

Shift work is a work schedule that falls outside of the hours of 7am - 6pm. Can be fixed or rotating.

Examples: healthcare workers, pilots and flight attendants, police officers, truck drivers, etc.

Consider. How might shift work be similar or different from the genetic manipulations of peripheral clocks we discussed?

**Predict.** What is a disease or health issue you expect to be related to shift work? Discuss with a partner for 2 min and add your ideas to the Poll Everywhere!

# What is a disease or health issue you expect to be related to shift work?



# What is one new thing you learned today?



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