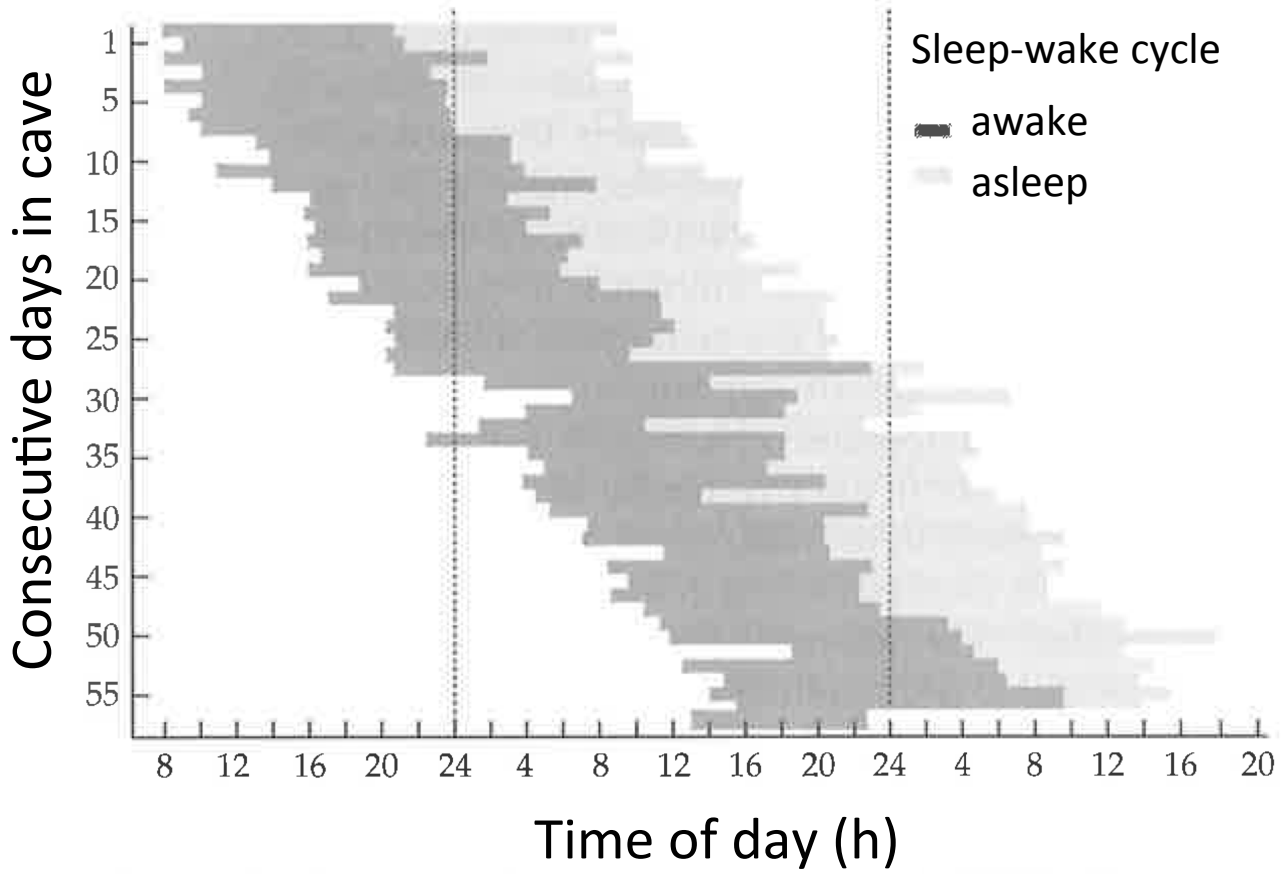
Evolution and our daily rhythms

Gen Kurosawa & Shingo Gibo (iTHEMS, RIKEN)



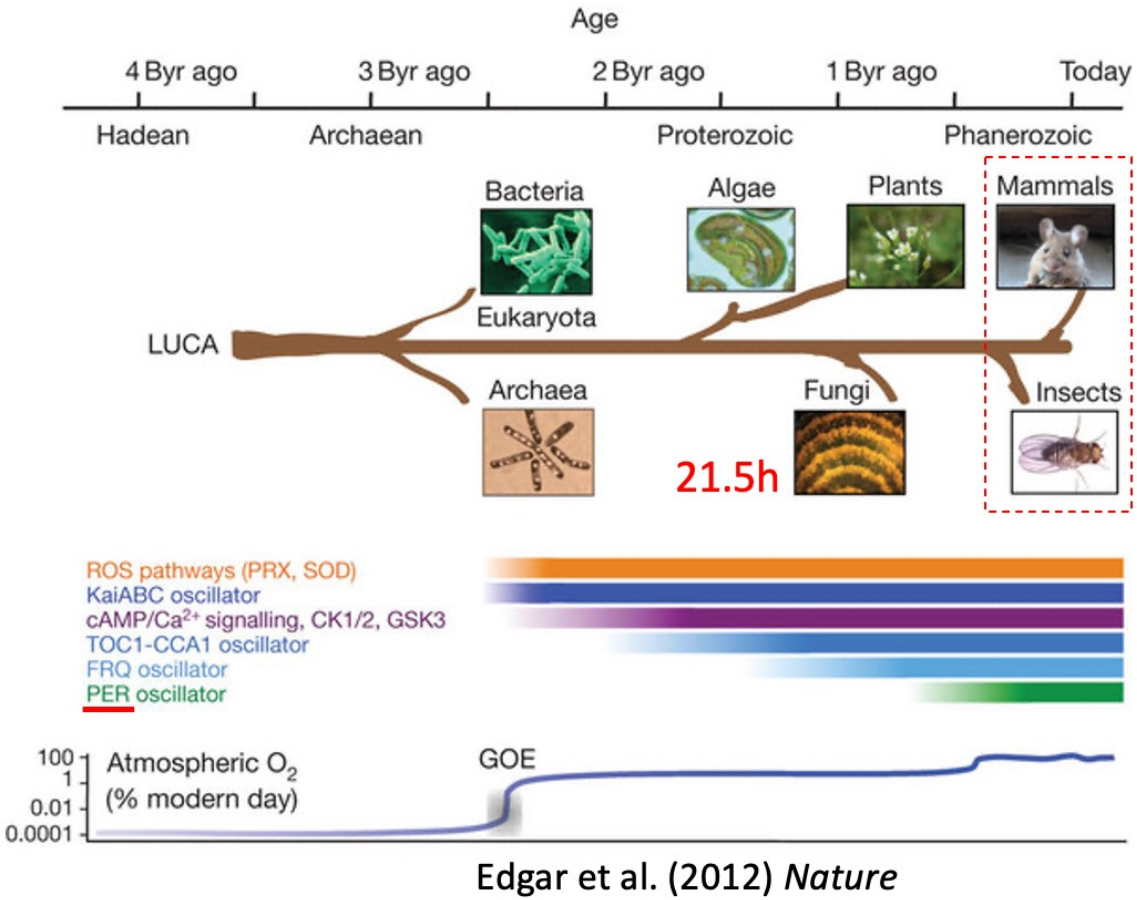
Shingo

Palmer (2002)

Gibo and Kurosawa (2019) *Biophys J*

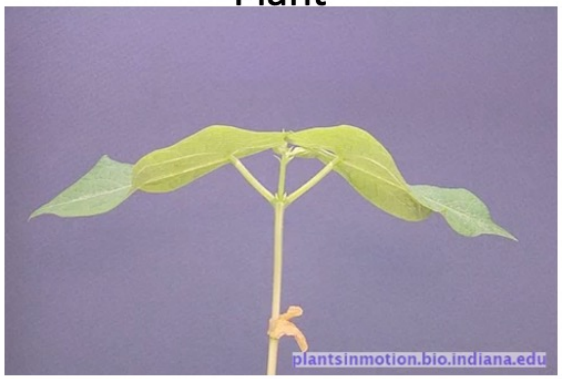
Gibo, Kunihiro, Hatsuda, Kurosawa *in prep*

Many species have daily rhythms

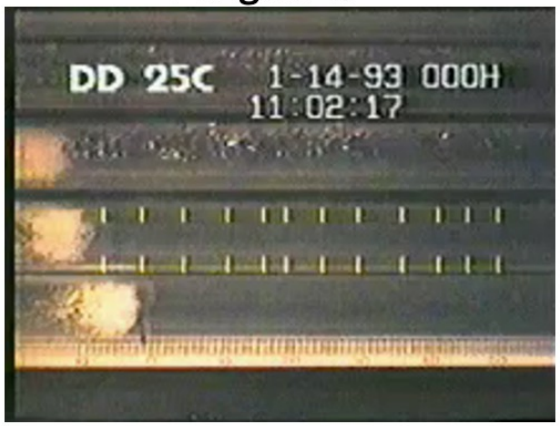


Edgar et al. (2012) *Nature*

Plant



Fungi かび

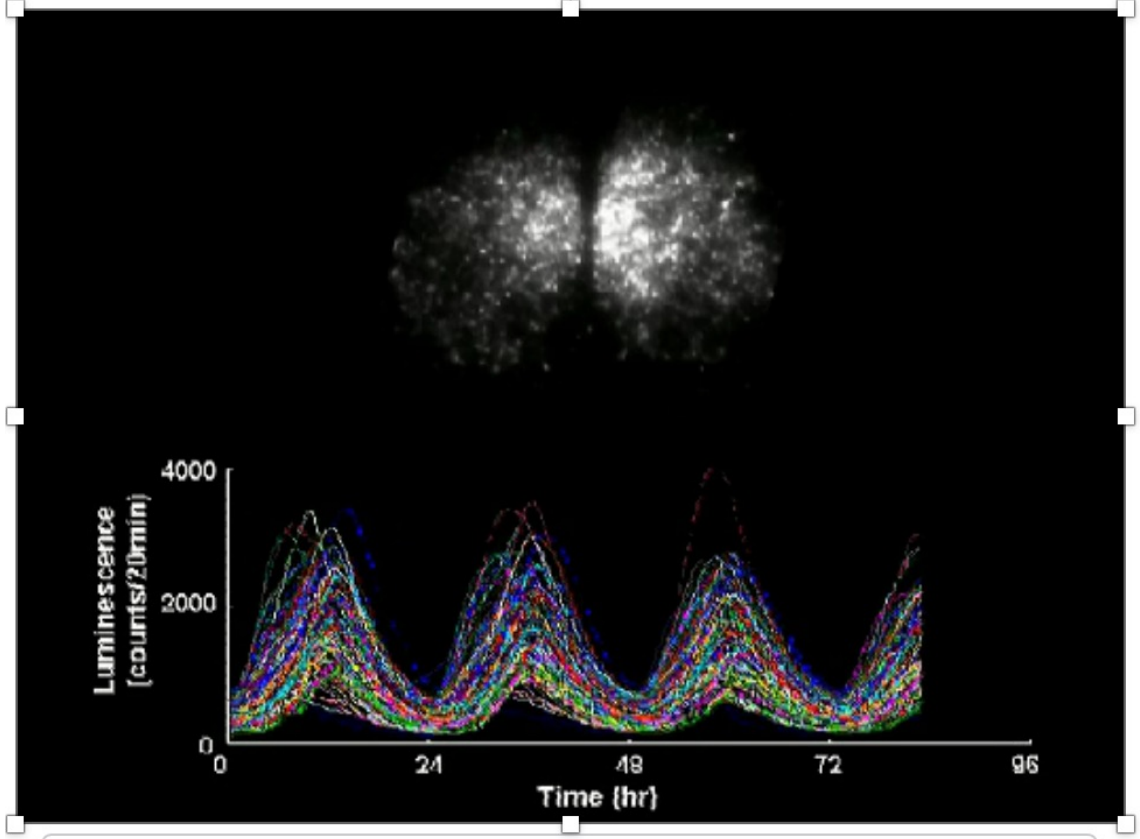


(*NB:* Number is the period of daily rhythms under constant dark)

- The comment from an astronomer at iTHEMS (Dr. Susumu Inoue)..
- The period of the earth was **~18.7h** at **1.4 billion** years ago.

Meyers & Malinverno (2019) *PNAS*

In our body, gene-activity oscillates with a period of ~24h.



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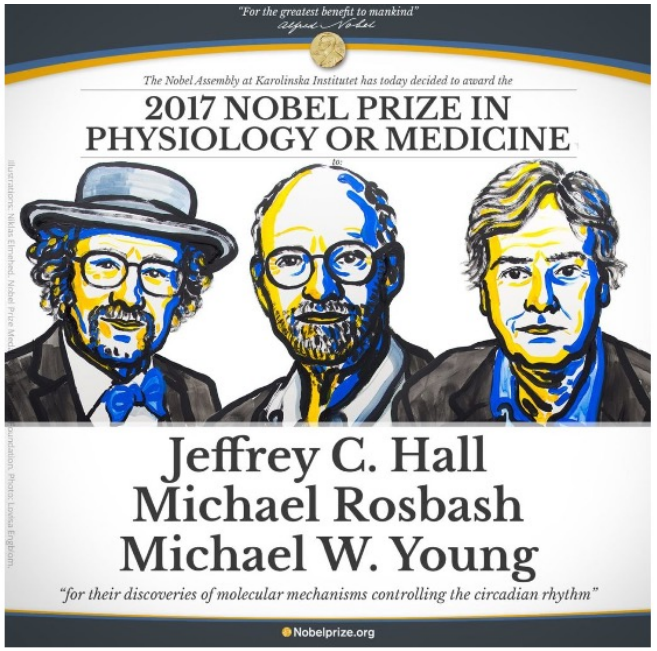
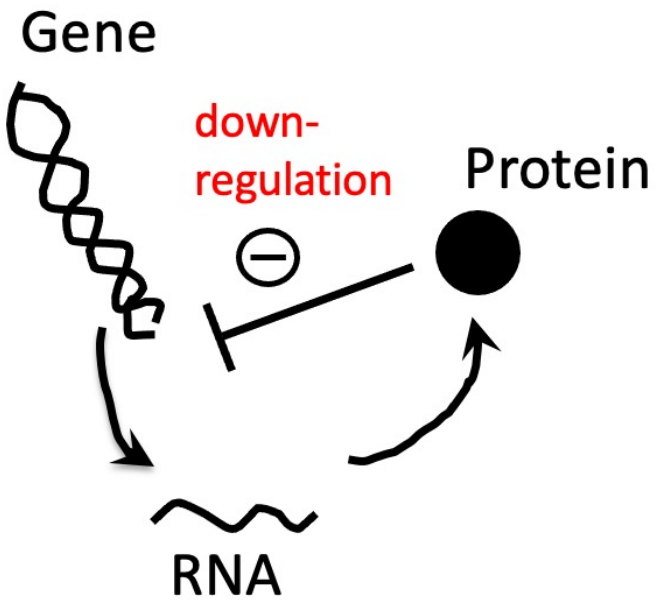
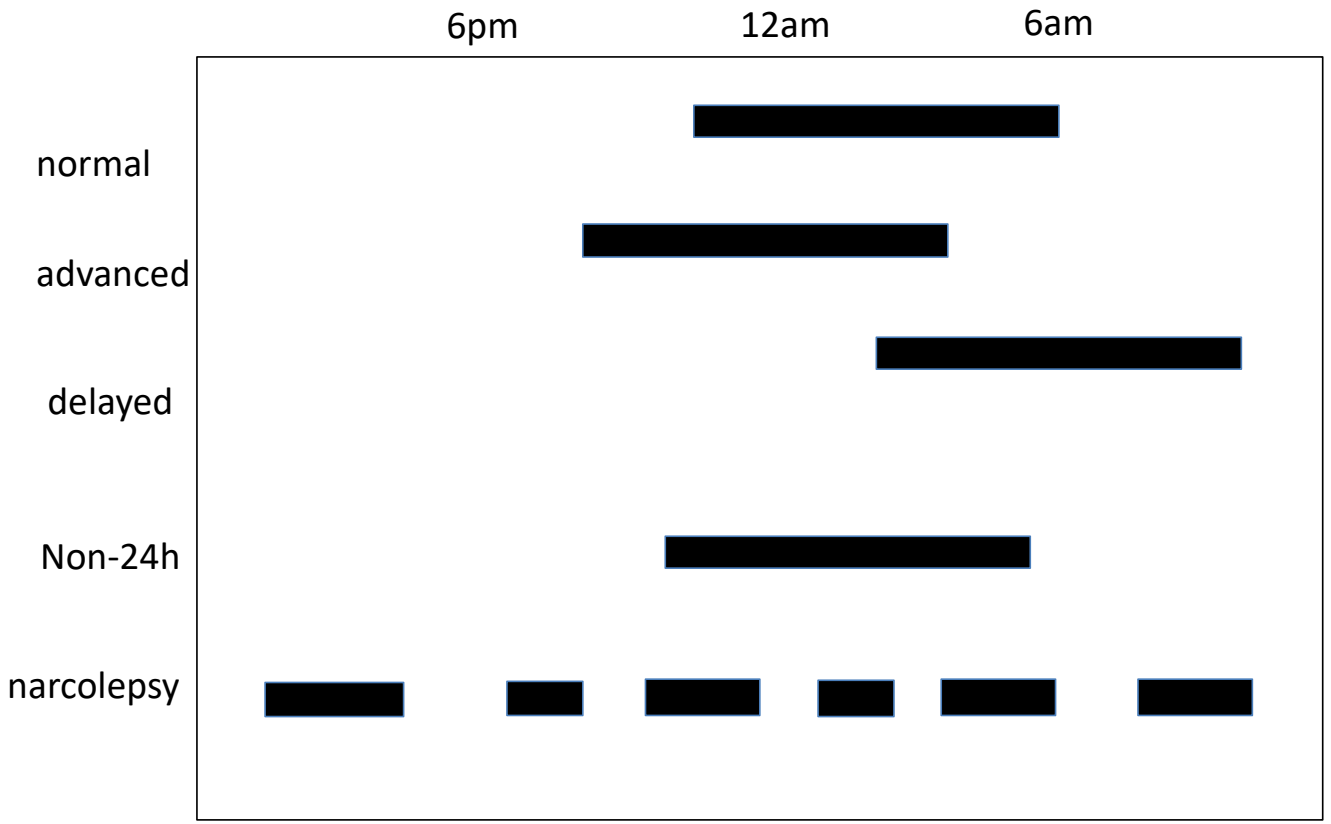




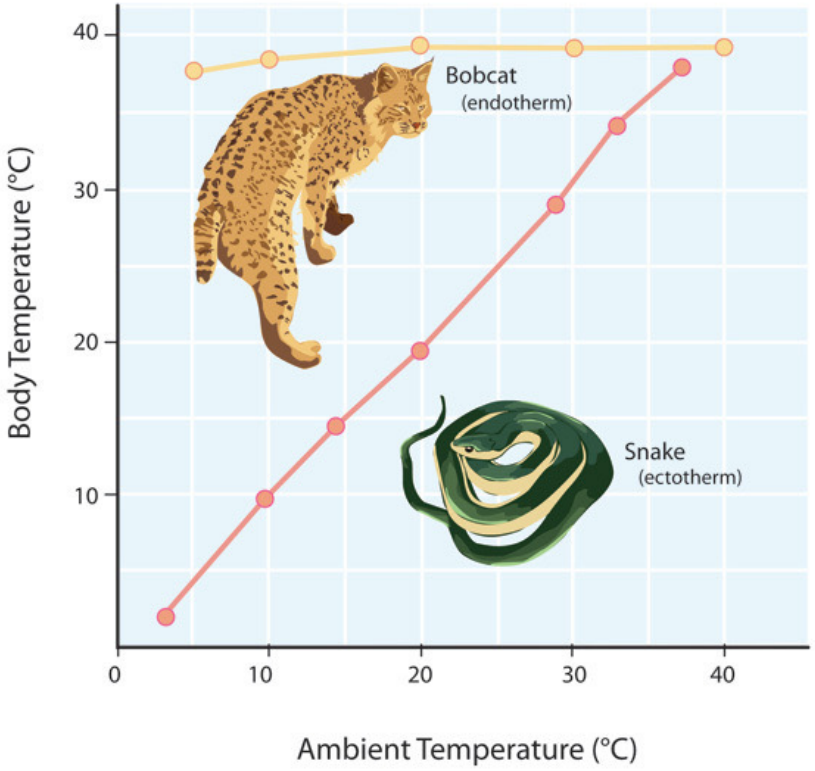
Hardin, Hall, Rosbash (1990) *Nature*

The biggest challenge in the field of daily rhythms: **understanding sleep and sleep types**



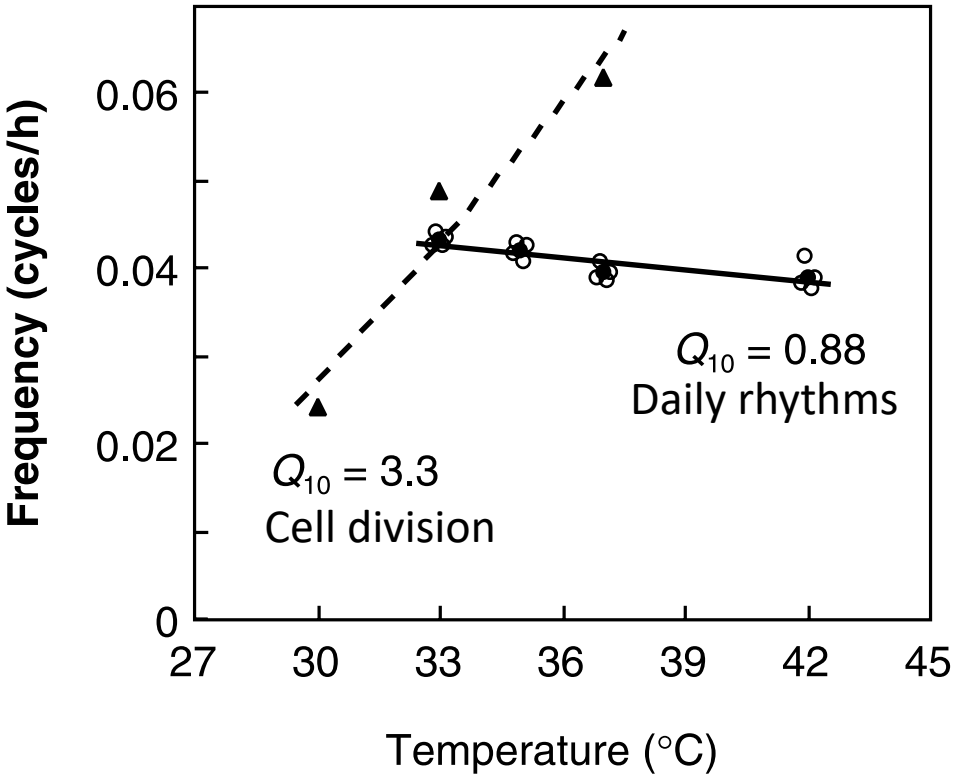
- Sleep types are related to daily rhythms.
- There are many people who are suffering from sleep disorder
- Genes are important but, environments are also important.
- Sleep types change with ages.

The biggest mystery in the field of daily rhythms:
“Why is our daily rhythms stable to temperature?”



Akin (2011)

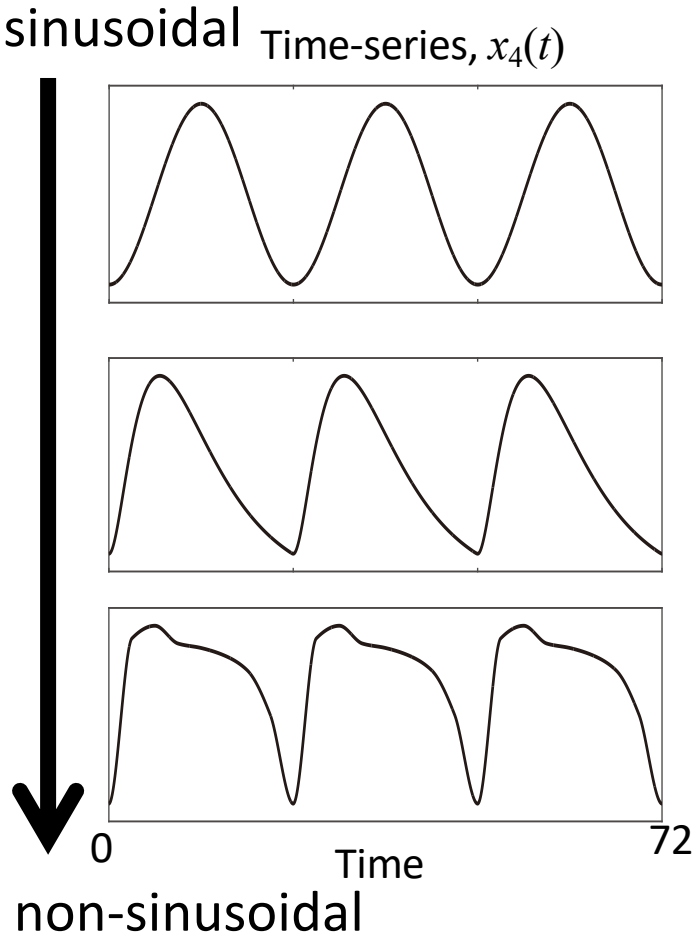
(Ex) Mammalian NIH3T3 cells



Tsuchiya,..Nishida (2003) *Genes Cells*

While enzymatic reactions usually accelerate with temperature, the period of daily rhythms is stable to temperature.

To quantitatively analyze data of daily rhythms, we focus on **waveform distortion** from sine-wave



$NS = 1.0$

$NS = 2.0$

$NS = 3.5$

$$NS = \left[\frac{\sum_{j=1}^{\infty} |a_j|^2 j^4}{\sum_{j=1}^{\infty} |a_j|^2 j^2} \right]^{\frac{1}{2}}$$

waveform of a variable

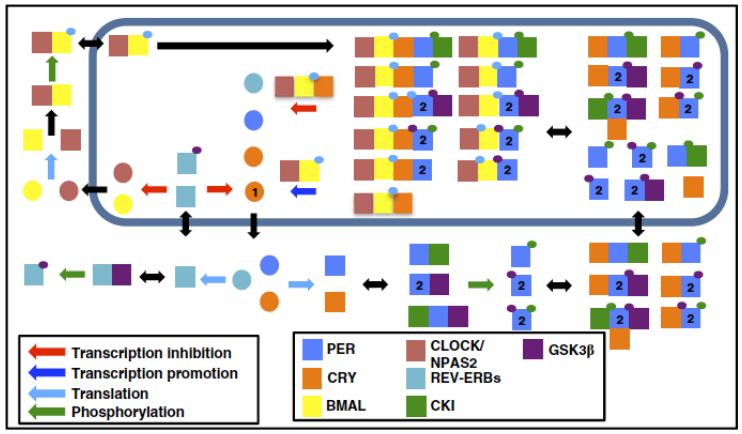
$$x_4(t) = \sum_{j=-\infty}^{\infty} a_j e^{i\frac{2\pi}{T} jt}$$

(oscillation can be expressed by sum of trigonometric function)

"We introduced the index, non-sinusoidal power (NS)"

Gibo and Kurosawa (2019) *Biophys J*

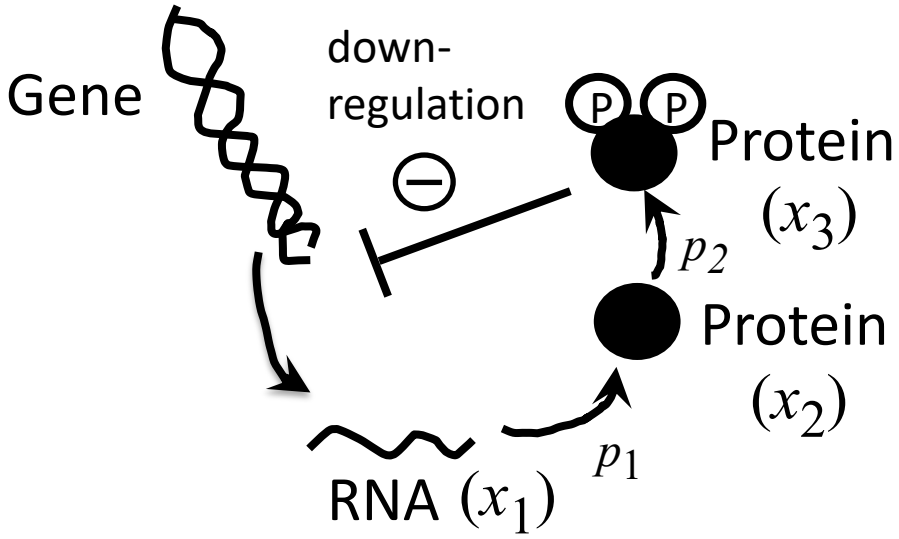
To obtain theoretical basis of **waveform**, we analyze the simple model



180 variable
Detailed model

Zhou et al. (2015)
Mol. Cell

Gibo model for circadian rhythms



simplification

$$\frac{dx_1}{dt} = f(x_3) - k_1 x_1,$$

$$\frac{dx_2}{dt} = p_1 x_1 - k_2 x_2,$$

$$\frac{dx_3}{dt} = p_2 x_2 - k_3 x_3,$$

$f(x_3)$: any function : decay

Fustin,..,Gibo,.., Kurosawa et al (2018) *PNAS*

Gibo and Kurosawa (2019) *Biophys J*

To obtain theoretical basis of **waveform**, we derived the period of daily rhythms

$$\text{Period} = \frac{2\pi}{\sqrt{k_1k_2 + k_2k_3 + k_3k_1}} \left[\frac{\sum_{j=1}^{\infty} |a_j|^2 j^4}{\sum_{j=1}^{\infty} |a_j|^2 j^2} \right]^{\frac{1}{2}}$$

NS

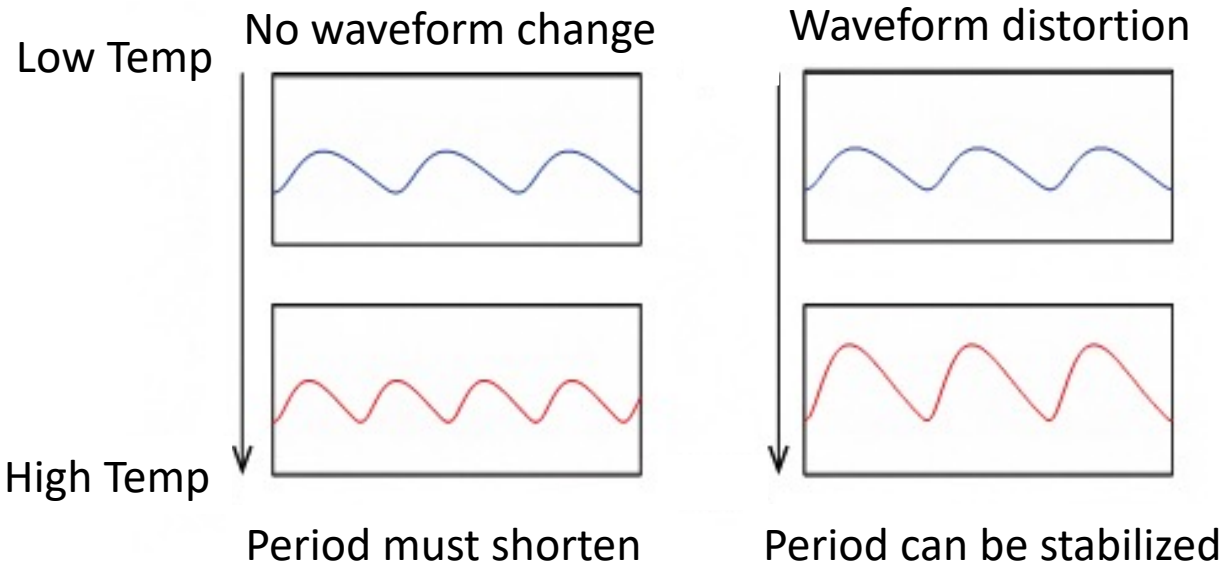
$$\text{Period} = 2\pi \left[\frac{\text{Waveform Distortion } (NS)}{\text{Quadratic eq. of rates}} \right]^{\frac{1}{2}}$$

1. Accelerated reactions tend to shorten period.
2. If accelerated reaction elongates period, waveform should become more non-sinusoidal.
3. More non-sinusoidal at higher temp for stable period.

Result 2/3

$$\text{Period} = 2\pi \left[\frac{\text{Waveform Distortion } (NS)}{\text{Quadratic eq. of rates}} \right]^{\frac{1}{2}}$$

Prediction: More non-sinusoidal waveform at higher temp generates stable period to temperature in daily rhythms.



Gibo and Kurosawa (2019) *Biophys J*

To obtain theoretical basis of **waveform**, we solved the equation by the help of physics


Shingo

Conventional perturbation approach: bad

$$x(t)= A_1 \cos \omega t + \varepsilon \, \boldsymbol{t} \, A_2 \cos 2\omega t + ..$$

where $A_i = f_i(k_1, k_2, ..)$, $\omega = g(k_1, k_2, ..)$

Renormalization-group approach

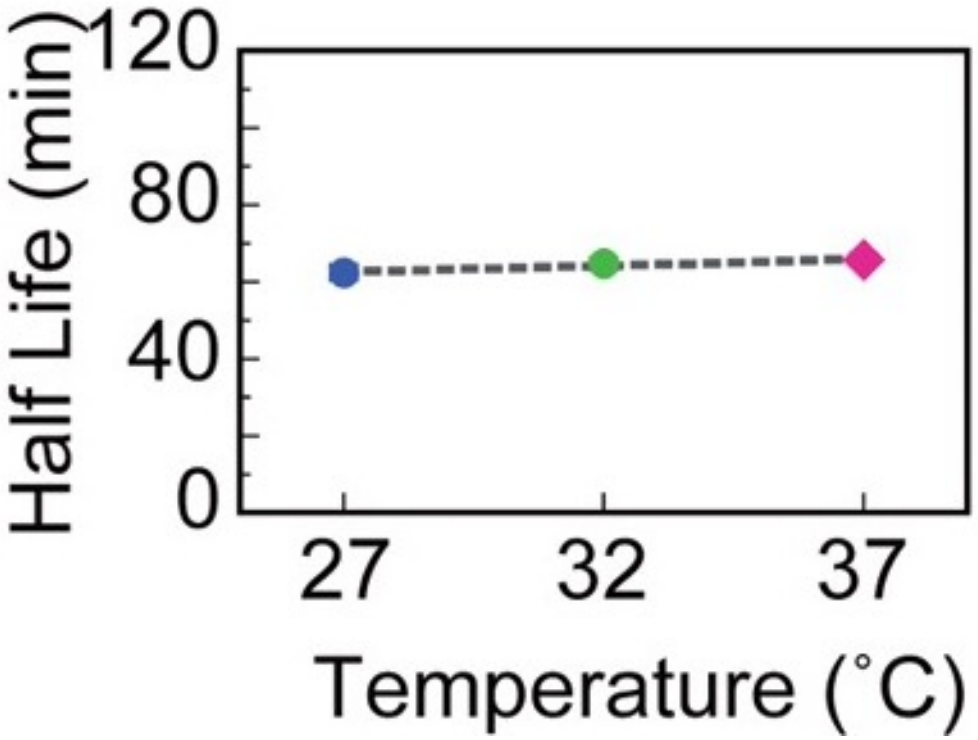
$$x(t)= A_1 \cos \omega t + \varepsilon \, A_2 \cos 2\omega t + ..$$

“Now, we can understand waveform distortion by using the language of kinetic constants (k_i)”

Gibo, Kunihiro, Hatsuda, Kurosawa *in prep*

Other hypothesis:

There should be a critical reaction for the period. If that reaction is insensitive to temp, period can be stable to temp.



Isojima et al. (2009) *PNAS*, Shinohara et al. (2017) *Mol Cell*

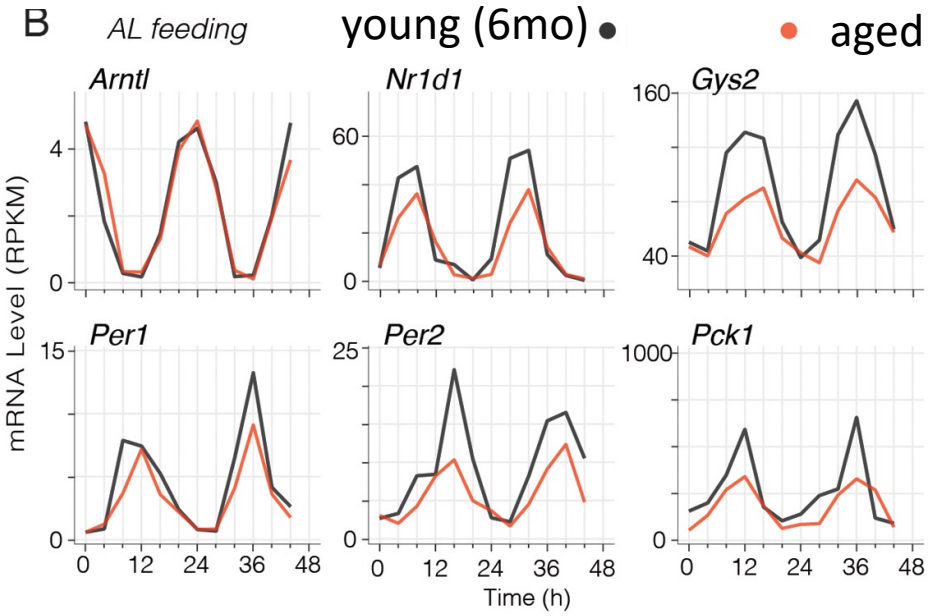
(Prof Hiroki Ueda group (RIKEN/Univ Tokyo))

Cf. Hong,.., Tyson (2007) *PNAS,* Terauchi et al. (2007) PNAS

Discussion 2/2

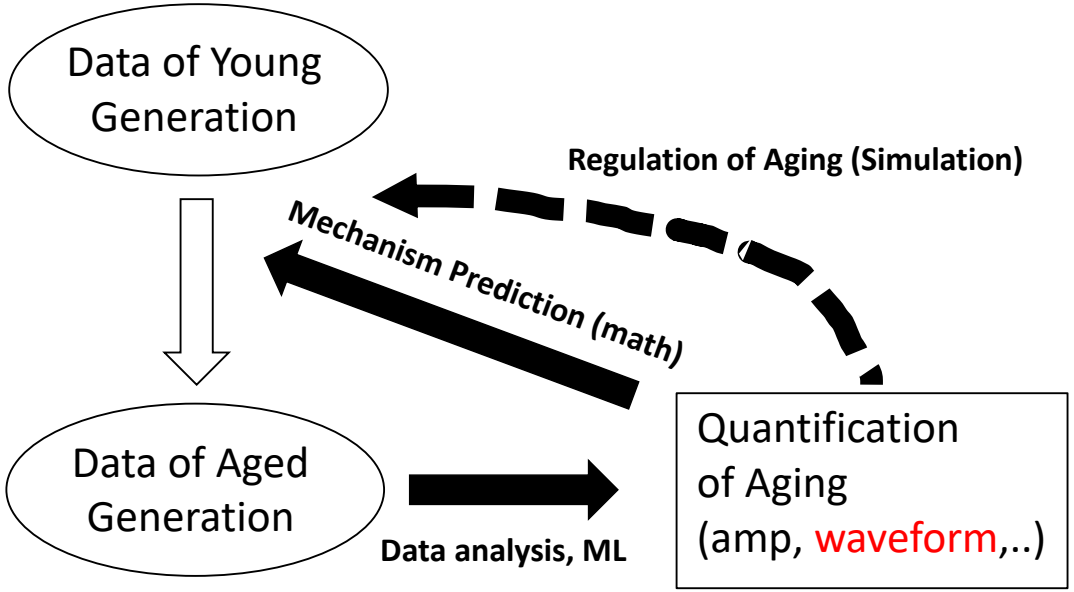
Daily rhythms in gene-activity is known to change with age. But we don't know how.

Accosta-Rodriguez et al. (2022) *Science*



(Shingo's idea)

From the analysis of waveform, cause of the change can be predicted.



Shingo

Summary

- **Challenges about daily rhythms and sleep**
  - **- sleep types**
  - **- stability of daily rhythm to temperature**

- **Waveform is an important indicator for period of daily rhythms**

- **Dr. Singo Gibo is very smart (See poster #94 about hibernation)**

Gibo and Kurosawa (2019) *Biophys J*
Gibo, Kunihiro, Hatsuda, Kurosawa *in prep*

JST CREST Biodynamics (2014-2020, PI: Prof Okamura (Kyoto U))
JST CREST Math and Info (2019-2025, PI: Prof Kawahara (Osaka U))
JSPS JP21K06105 and Continuous Support from RIKEN iTHEMS

Supplementary

Suppose that you are in a cave..
Can you wake up tomorrow w/o clock?

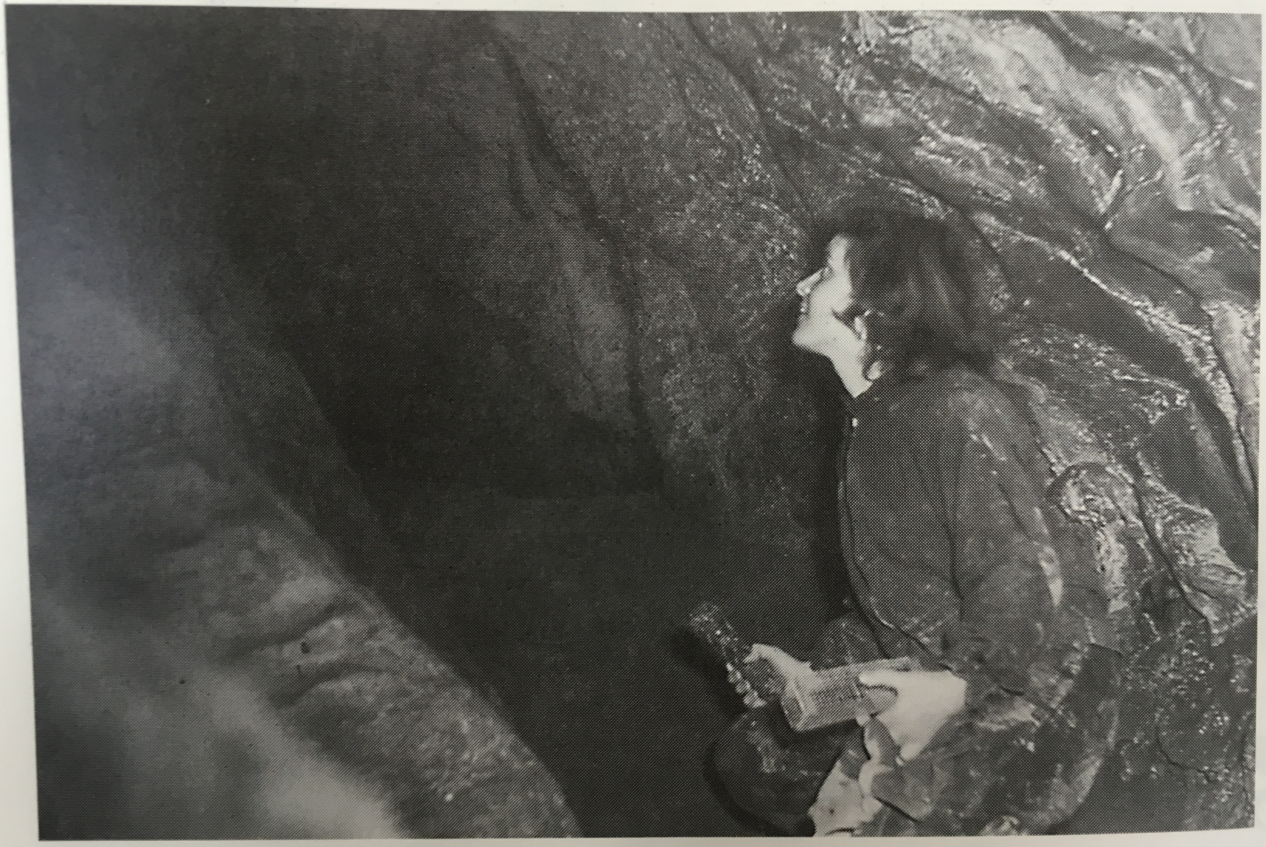


FIGURE 9.1 The environment in a cave is constant.

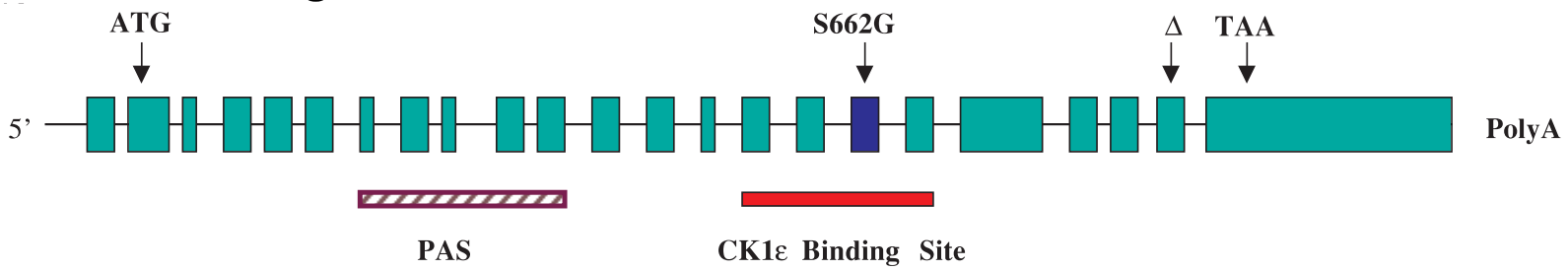
Early-bird family in the world

Dr. Fu
(UCSF)

Dr. Ptacek
(UCSF)

	Control ($n = 6$)	FASPS($n = 6$) Mean ± s.d
Sleep Onset	23:10 ± 0:40	19:25 ± 1:44
Sleep Offset[a]	07:44 ± 1:13	04:18 ± 2:00

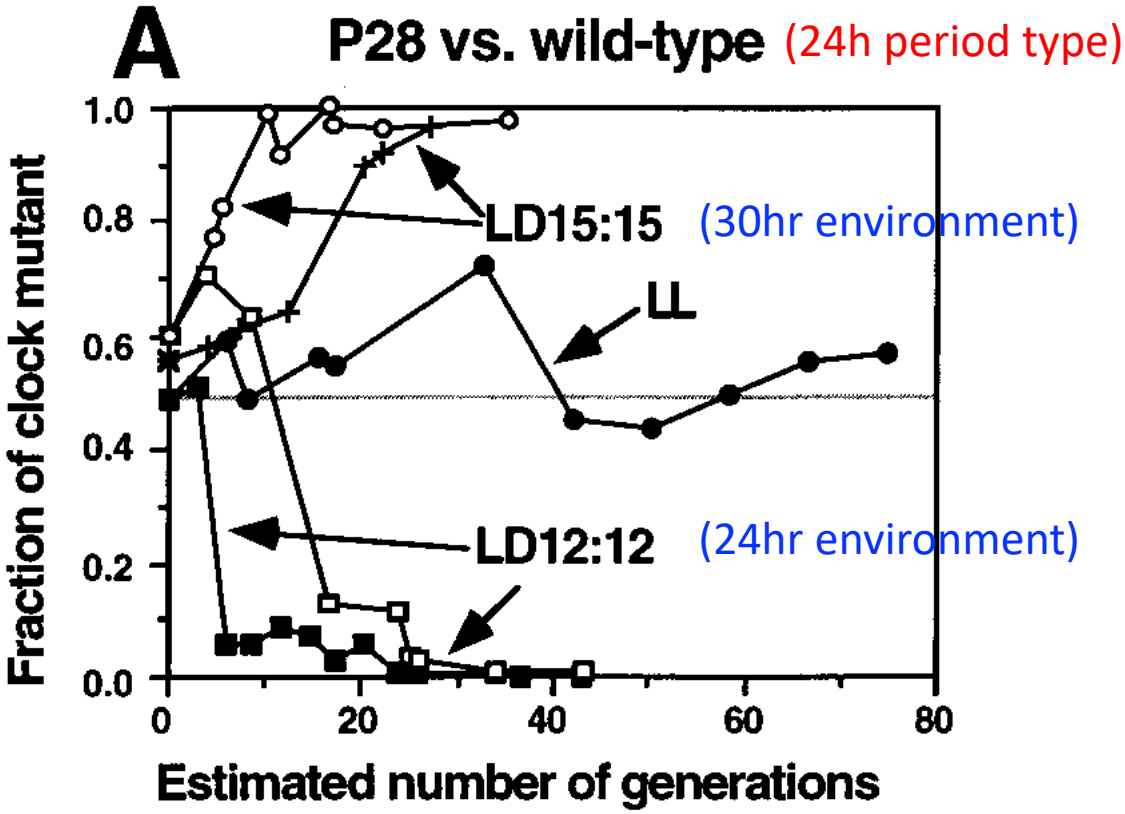
Human Per2 gene



Mutation at the binding site phosphorylation enzyme

Toh et al. (2001, 2007) *Science*

Competition experiment using an ancestor of plants



Ouyang et al. (1998) *PNAS*

"Resonance seems essential."