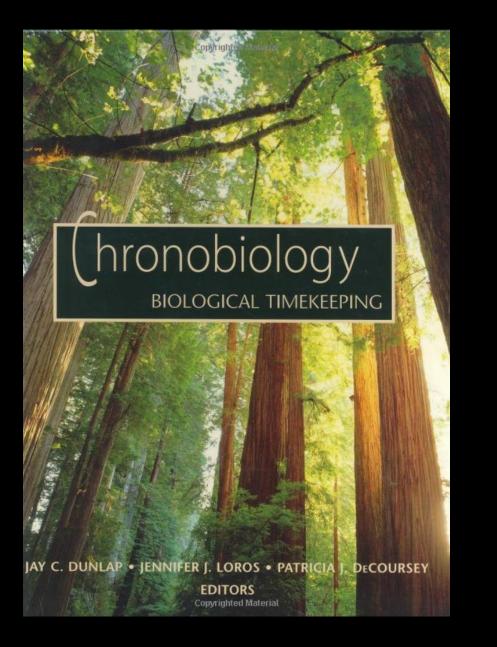


Chronobiology -- daily rhythms and seasonality in animals





"A fascinating history. . . . Literate and authoritative. . . . Marvelously exciting."

—The New York Times

TIME, LOVE, MEMORY

A GREAT BIOLOGIST AND HIS QUEST FOR THE DRIGINS OF BEHAVIOR

JONATHAN WEINER

PULITZER PRIZE-WINNING AUTHOR OF THE BEAK OF THE FINCH

https://cinchron.org/











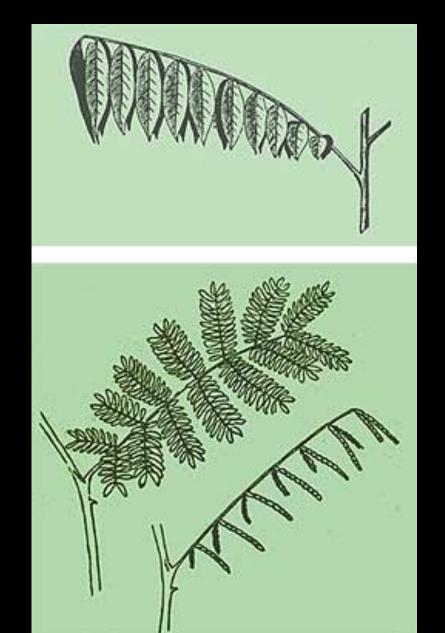


Insect Photoperiodic Timer

CRISPR/CAS9 gene editing Population genetics Insect neuropeptides

david.dolezel@entu.cas.cz



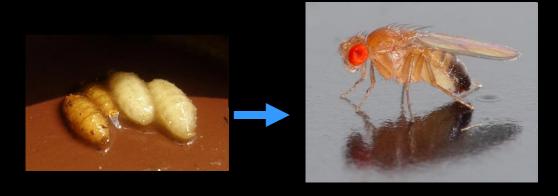


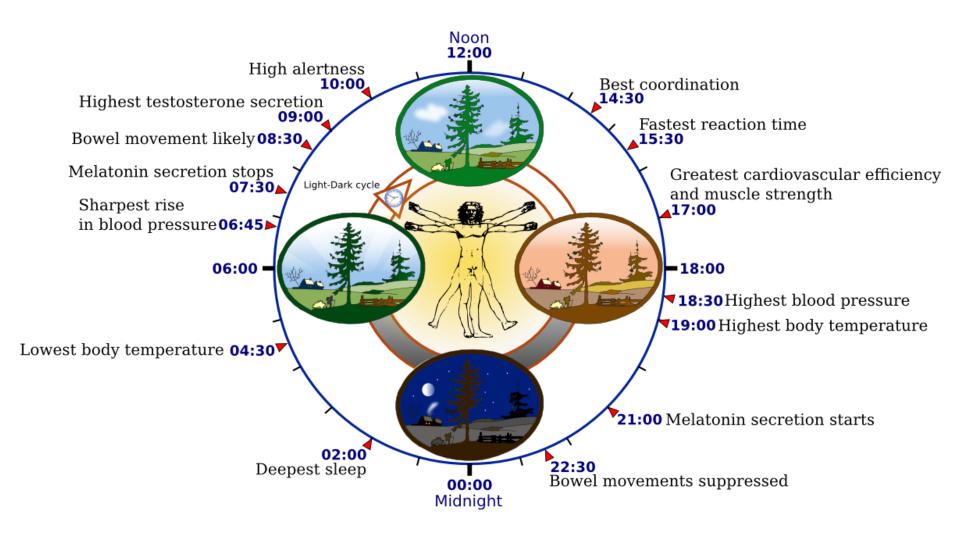
CIRCADIAN RHYTHM

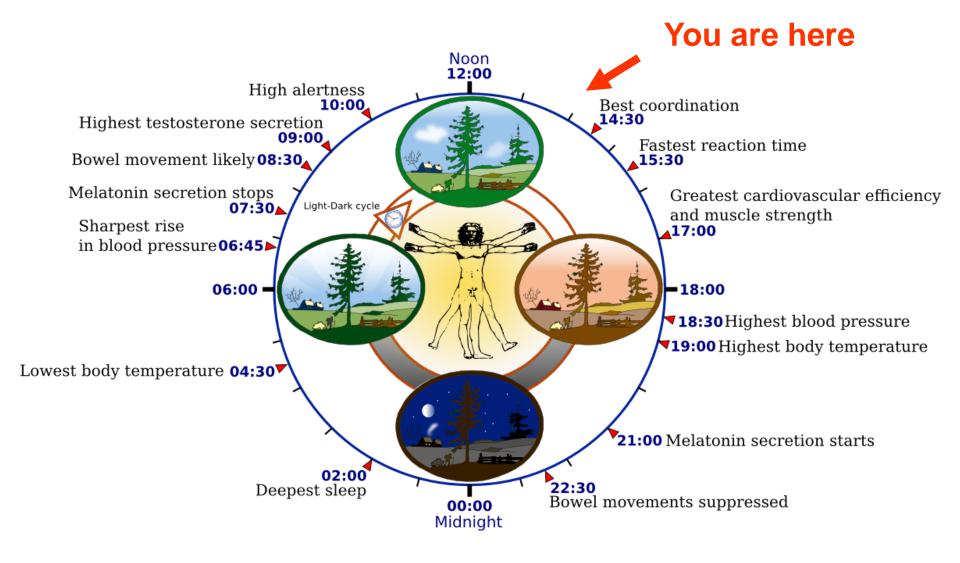
Jean-Jacques d'Ortous de Mairan, 1729

CIRCADIAN RHYTHM

















News | More Science

Out of the Zone: Jet-Lagged Baseball Teams Suffer Disadvantage

New research shows that long commutes affect a team's chances of winning

nature publishing group

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nature

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scientific correspondence

Nature 377, 583 (19 October 2002); doi:10.1038/377583a0

Baseball teams beaten by jet lag

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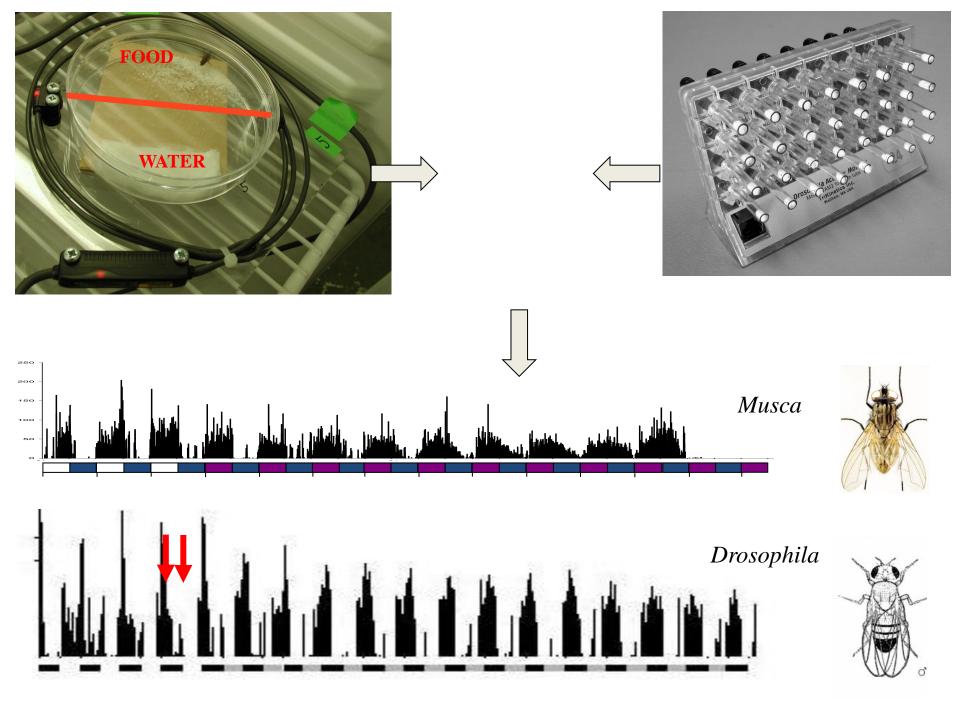
Department of Neurology, University of Massachusetts Medical School, Worcester, Massachusetts 01655, USA †Multipurpose Arthritis & Musculoskeletal Diseases Center, Department of Rheumatology and Immunology, Brigham and Women's Hospital, Boston, Massachusetts 02115, USA

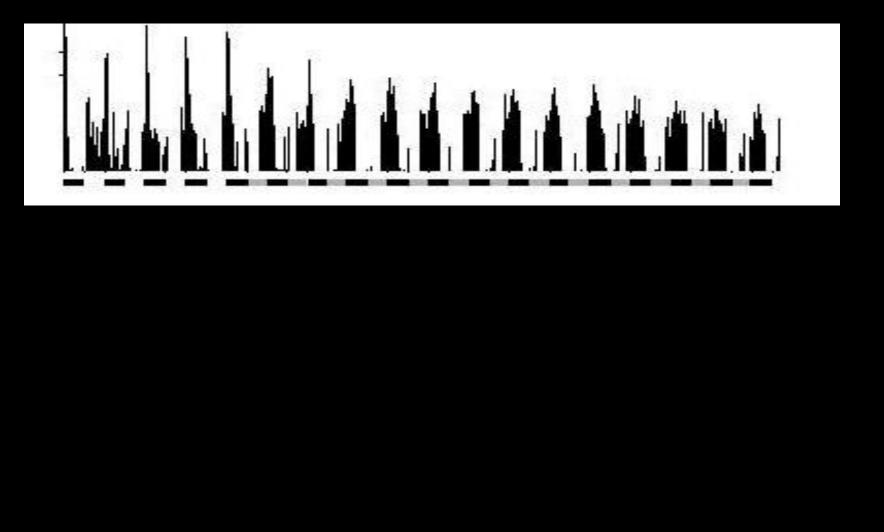
LAWRENCE D. RECHT*, ROBERT A. LEW* & WILLIAM J. SCHWARTZ*

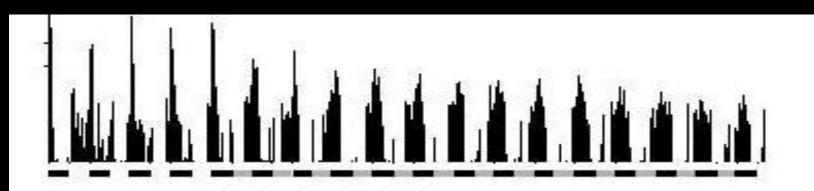


Betting on your favorite Major League Baseball team? You might want to reconsider if it has to cross three time zones to play. A new study shows that MLB teams that travel such distances to play a game could have up to a 60 percent chance of losing.



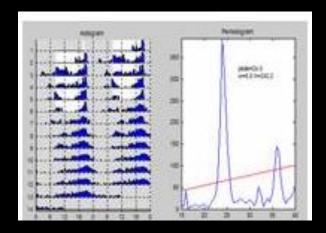


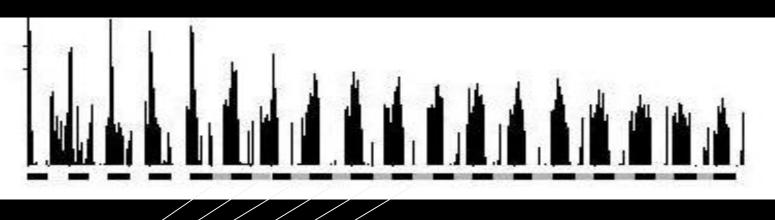




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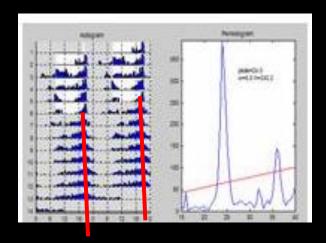


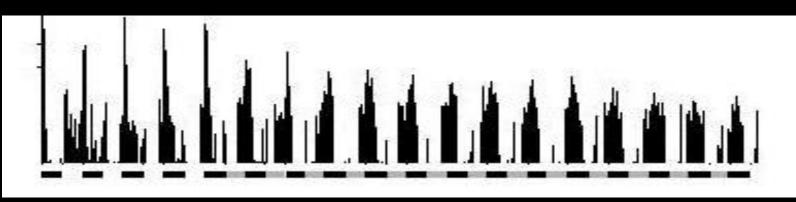


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4	×
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1	2
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3	4
2 3 4 5 6	2 3 4 5 6
5	6
6	

~24 h

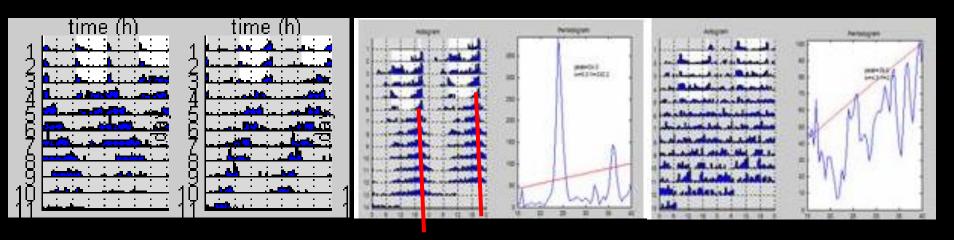


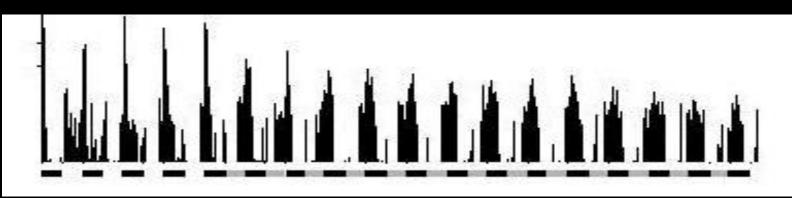


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2	2 3 4 5 6
3	4
4	5
2 3 4 5 6	6
6	

?

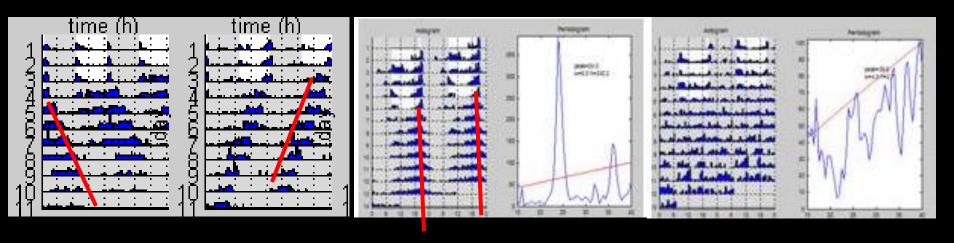
~24 h





1	2
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2 3 4 5 6	2 3 4 5 6
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5	6
6	

~24 h

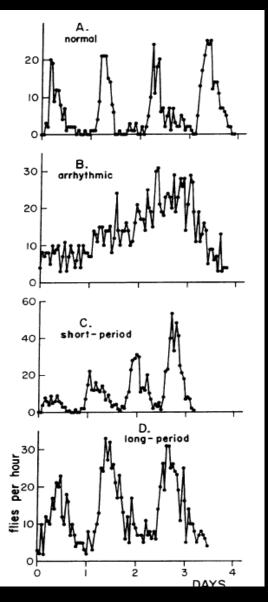


Circadian "mantra"

Circadian clocks are:

- Free running (e.g. in constant conditions)
- Entrainable (such as by light, among others)
- Temperature-compensated
- Genetically determined





Proc. Nat. Acad. Sci. USA Vol. 68, No. 9, pp. 2112-2116, September 1971

Clock Mutants of Drosophila melanogaster

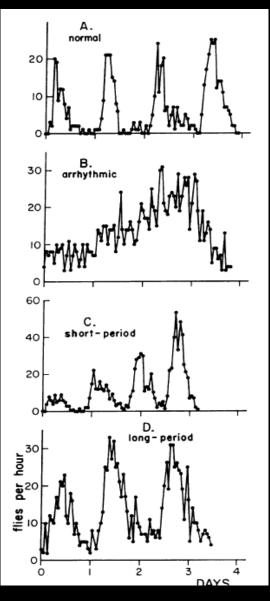
(eclosion/circadian/rhythms/X chromosome)

RONALD J. KONOPKA AND SEYMOUR BENZER

Division of Biology, California Institute of Technology, Pasadena, Calif. 91109

Contributed by Seymour Benzer, July 2, 1971





Proc. Nat. Acad. Sci. USA Vol. 68, No. 9, pp. 2112-2116, September 1971

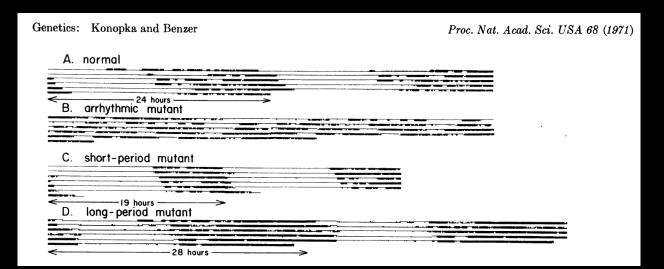
Clock Mutants of Drosophila melanogaster

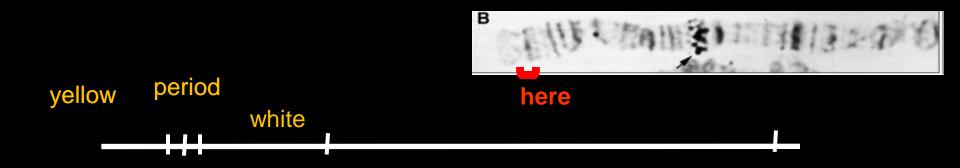
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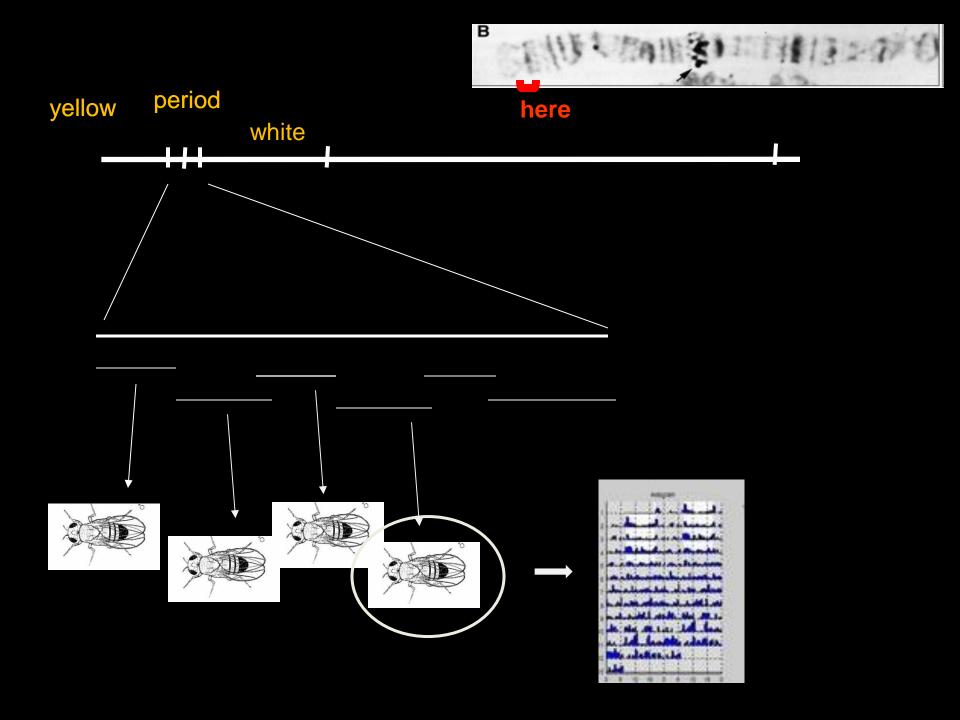
RONALD J. KONOPKA AND SEYMOUR BENZER

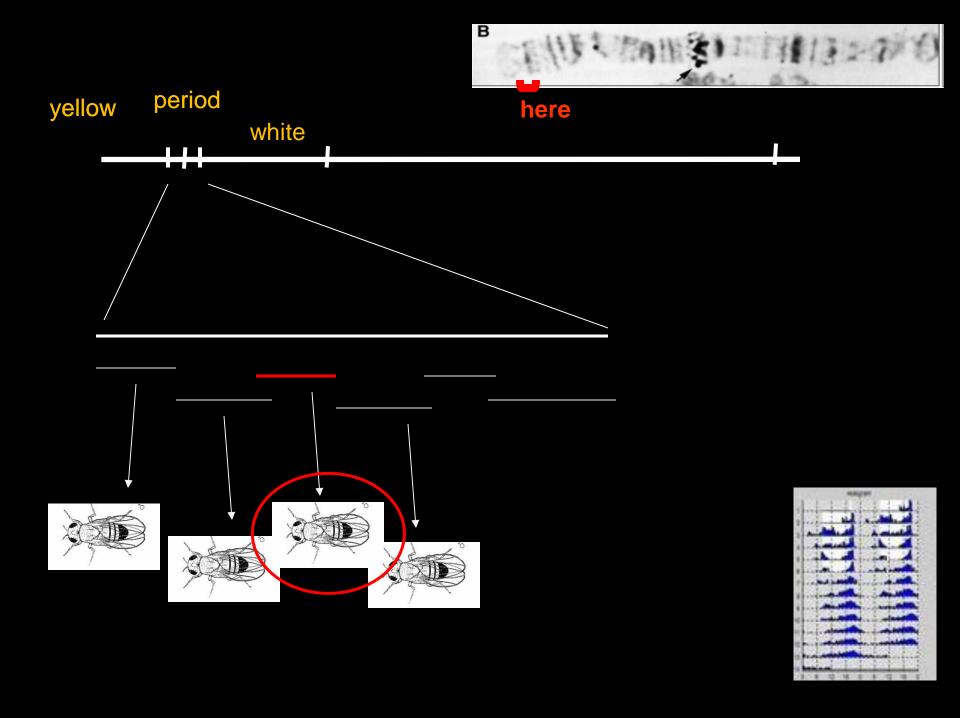
Division of Biology, California Institute of Technology, Pasadena, Calif. 91109

Contributed by Seymour Benzer, July 2, 1971

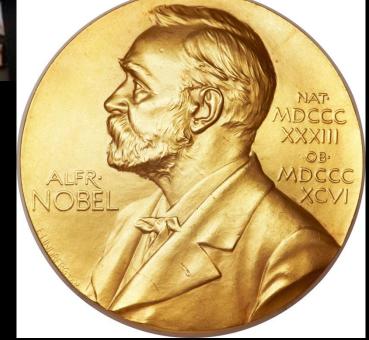






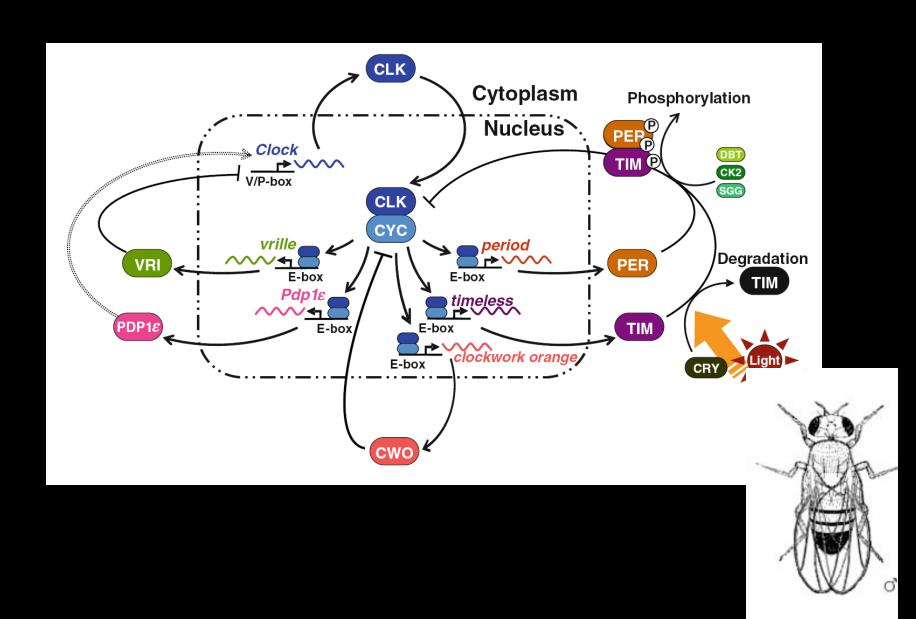


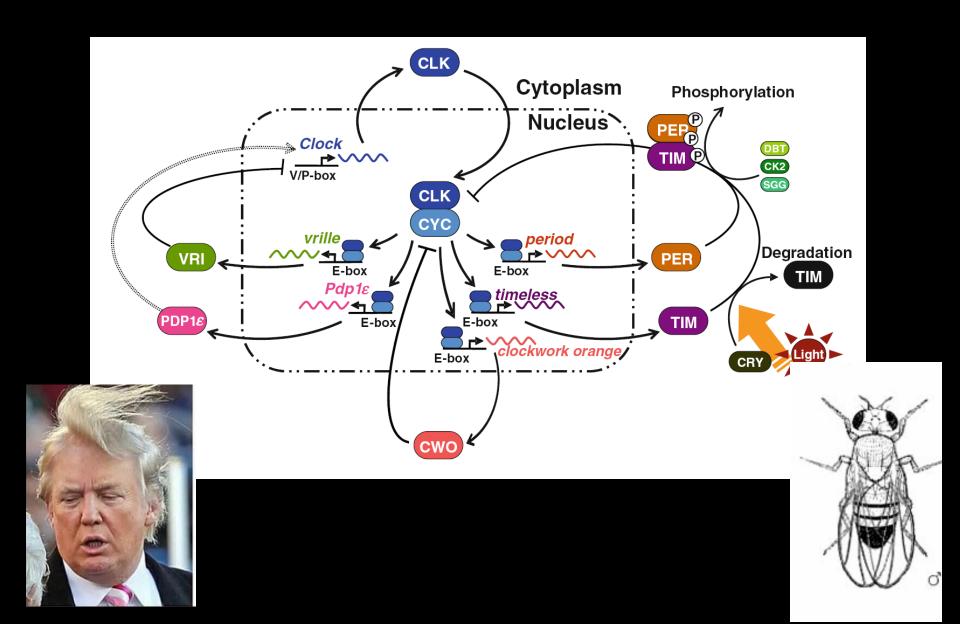


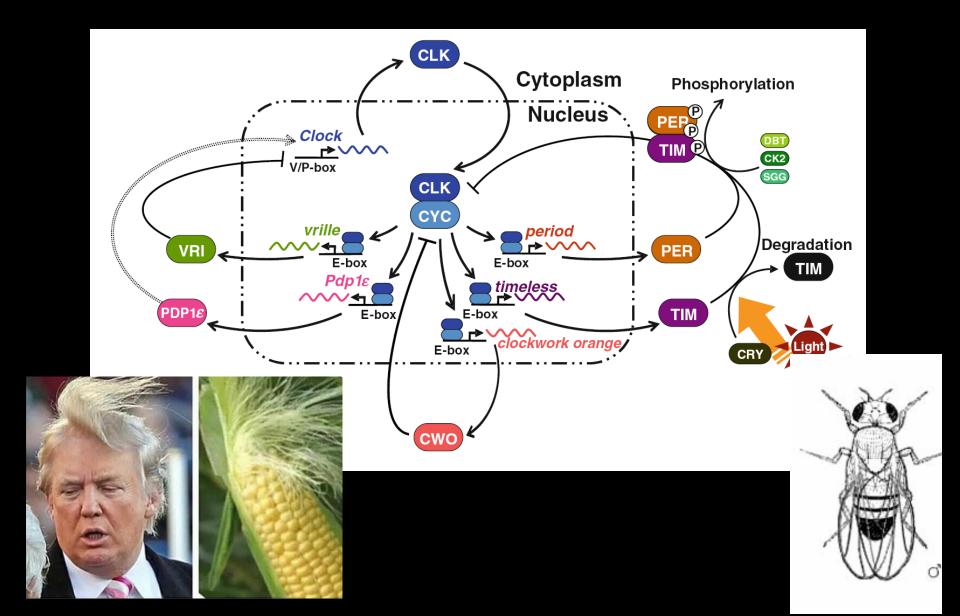


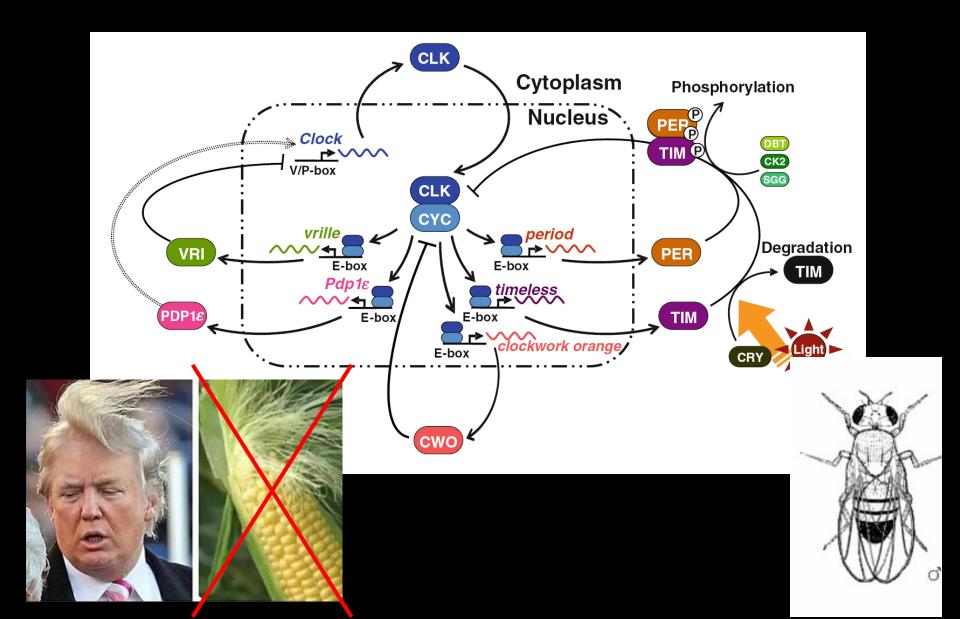






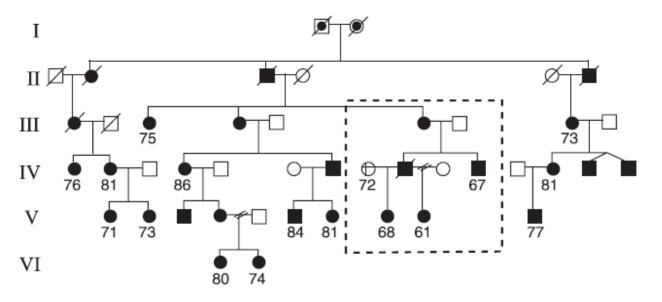






Human FASP

Fig. 1. ASPS kindred 2174. Horne-Östberg scores are shown below individuals. The dotted line marks a branch (branch 3) where the ASPS phenotype does not cosegregate with the mutation. Circles, women; squares, men; filled circles and squares, affected individuals; empty circles and squares, unaffected individuals. Unknown in-



dividuals (not meeting strict criteria for being "affected" or "unaffected") were eliminated from this pedigree for the sake of simplicity.

Human FASP

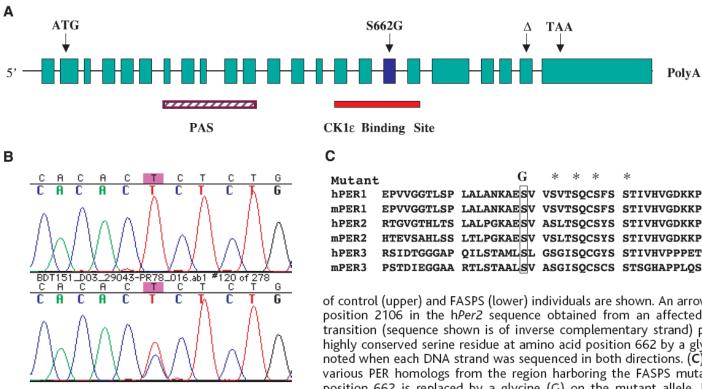
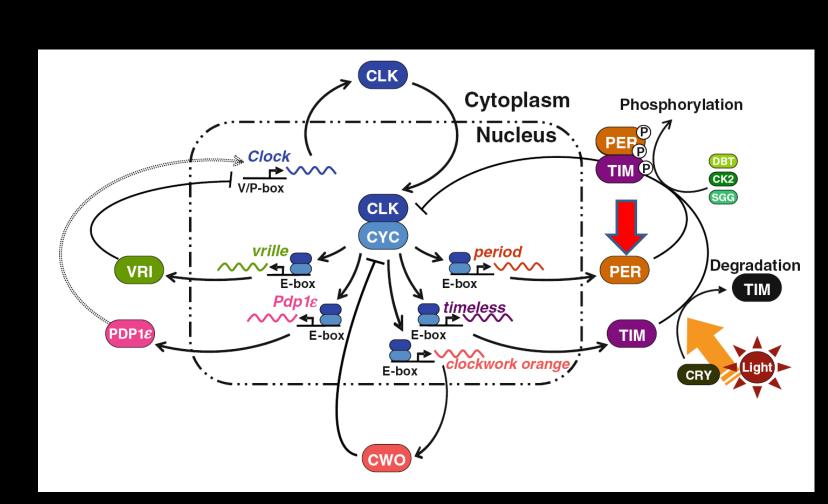
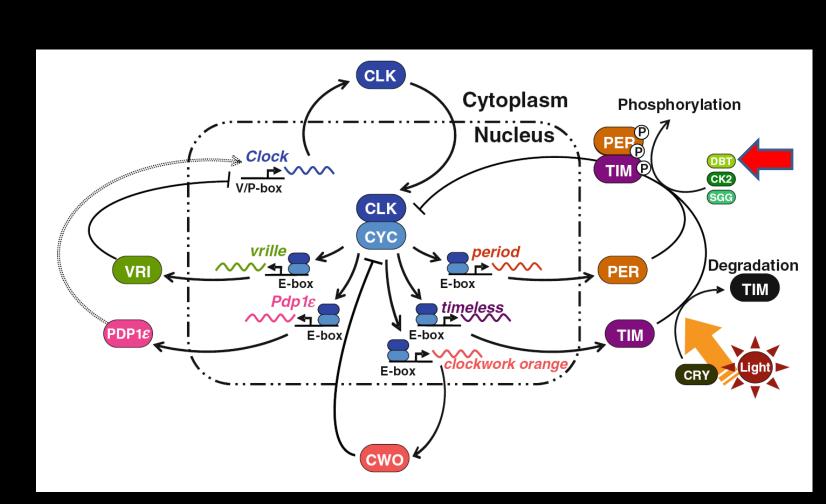


Fig. 2. (A) Genomic structure of hPer2. The hPer2 gene contains 23 exons (colored rectangles). The intervening introns are not drawn to scale. The mutation in kindred 2174 (S662G) occurs in exon 17. The " Δ " above exon 22 shows the location of the sequence error (a 1 base pair deletion) in the hPer2 cDNA GenBank sequence. (B) The hPer2 mutation in kindred 2174. DNA sequences from the hPer2 gene

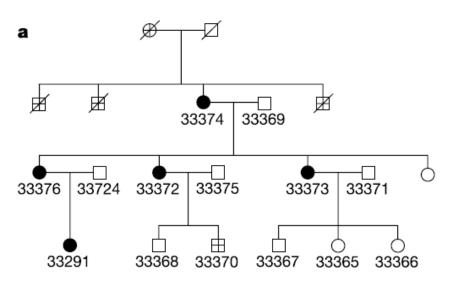
PolvA

of control (upper) and FASPS (lower) individuals are shown. An arrow marks a double peak at position 2106 in the hPer2 sequence obtained from an affected individual. This A to G transition (sequence shown is of inverse complementary strand) predicts substitution of a highly conserved serine residue at amino acid position 662 by a glycine. A double peak was noted when each DNA strand was sequenced in both directions. (C) Amino acid sequence of various PER homologs from the region harboring the FASPS mutation (37). The serine at position 662 is replaced by a glycine (G) on the mutant allele. Four asterisks mark four subsequent conserved serine residues each with two intervening amino acids.





Human FASP



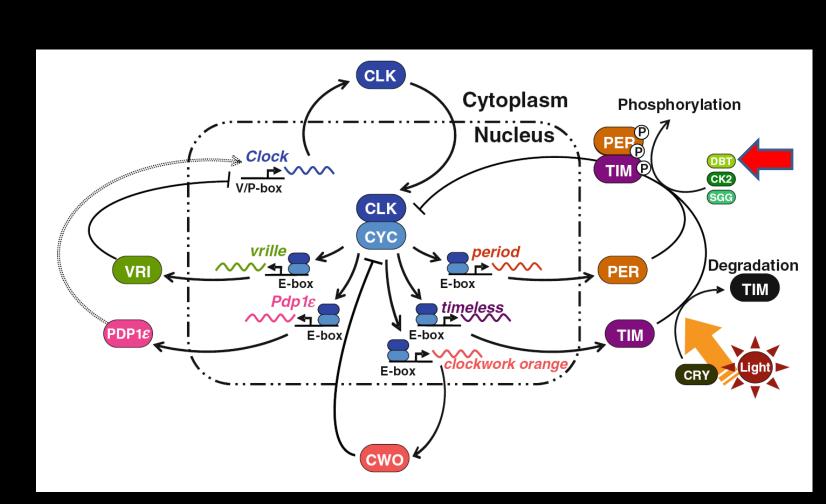
Functional consequences of a *CKI* δ mutation causing familial advanced sleep phase syndrome

Ying Xu 1* , Quasar S. Padiath 1* , Robert E. Shapiro 2 , Christopher R. Jones 3 , Susan C. Wu 1 , Noriko Saigoh 1 , Kazumasa Saigoh 1 †, Louis J. Ptáček 1,4 & Ying-Hui Fu 1

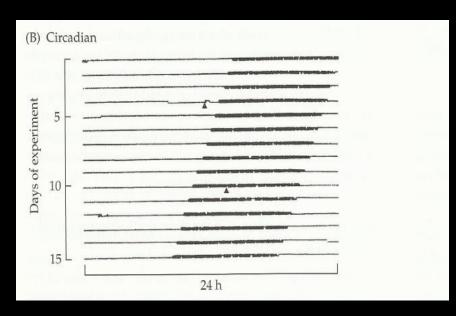
b

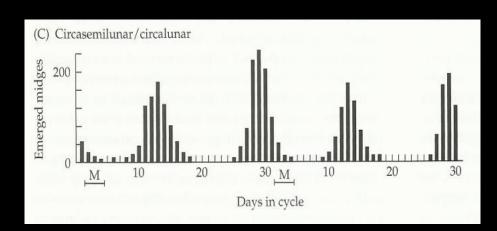
```
hCK1δ GEEVAIKLECVKTKHPQLHIESKIYKMMQ mCK1δ GEEVAIKLECVKTKHPQLHIESKIYKMMQ hCK1ε GEEVAIKLECVKTKHPQLHIESKFYKMMQ mCK1ε GEEVAIKLECVKTKHPQLHIESKFYKMMQ Dbt GEEVAIKLECIRTKHPQLHIESKFYKMMQ
```

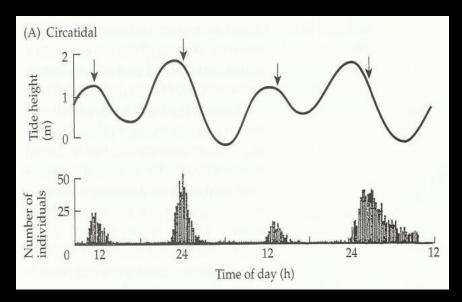
Figure 1 CKlδ-T44A FASPS pedigree and the amino acid alignment around the mutation. **a**, FASPS kindred 5231. Circles represent women, squares denote men, filled circles and squares show affected individuals; empty circles and squares show unaffected individuals. The individual marked with a cross is 'probably affected' but was conservatively classified as unknown. Diagonal lines across symbols indicate deceased individuals. **b**, Alignments for *Drosophila* Dbt and mouse (m) and human (h) CKlδ and CKlɛ proteins. The T44A mutation is highlighted.

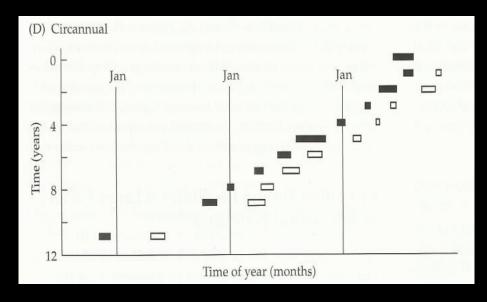


NON-CIRCADIAN RHYTHMS







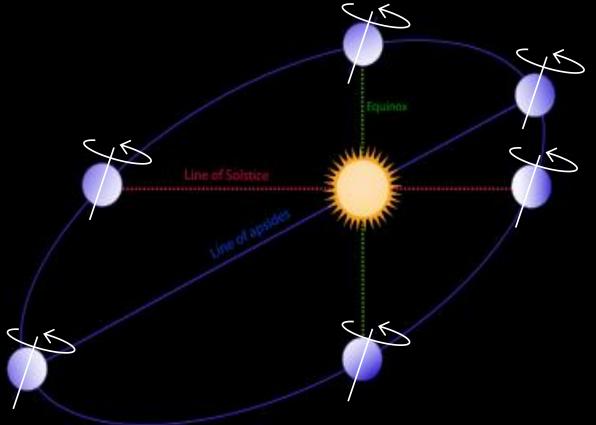


SEASONALITY: THE PHOTOPERIODIC TIMER (CLOCK)



Northern spring/ Southern fall

Northern winter/ Southern summer

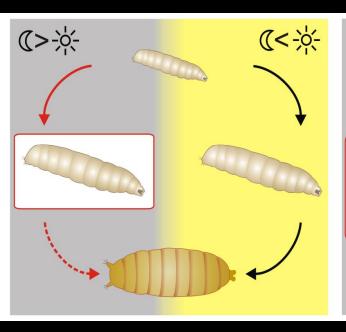


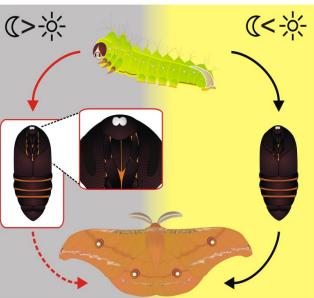
Northern summer/ Southern winter Northern fall/ Southern spring

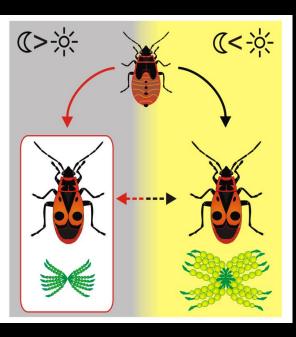
Insect diapause

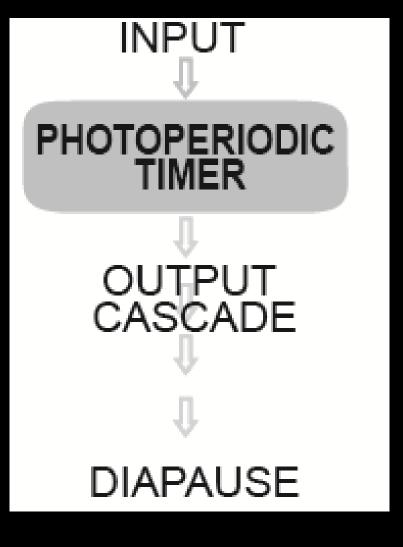
Larval diapause (*Chymomyza* costata)

Pupal diapause (Antheraea pernyi) Adult diapause (*Pyrrhocoris* apterus)





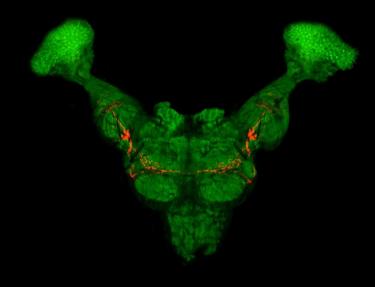




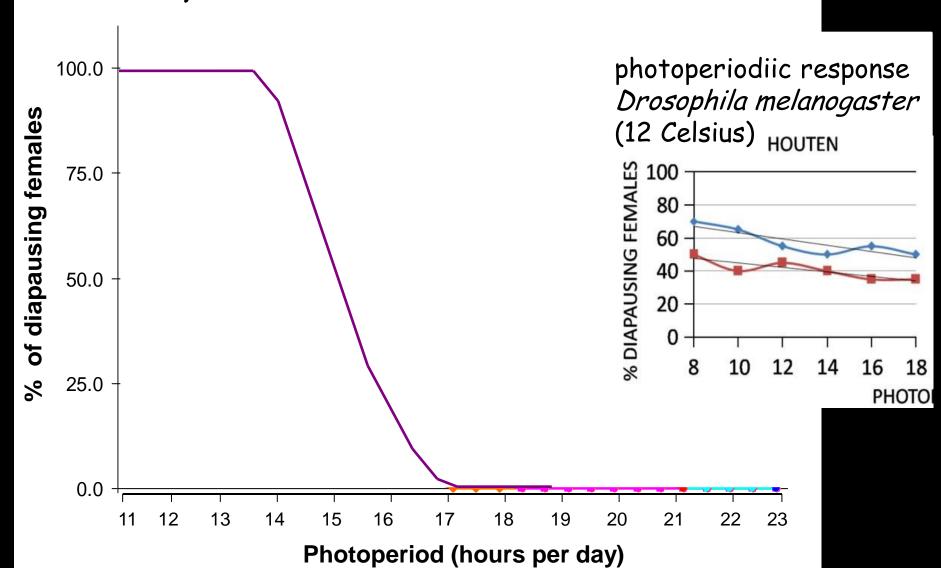
Diapause is an ultimate physiological output far downstream of the photoperiodic timer

Pyrrhocoris apterus





Photoperiodic response in *P. apterus* (25 Celsius)



PHOTOPERIODIC TIMER (photoperiodic clock)

Runs at constant conditions (DD)

 Measures photoperiod or nightlength (day-length)

PHOTOPERIODIC TIMER (photoperiodic clock)

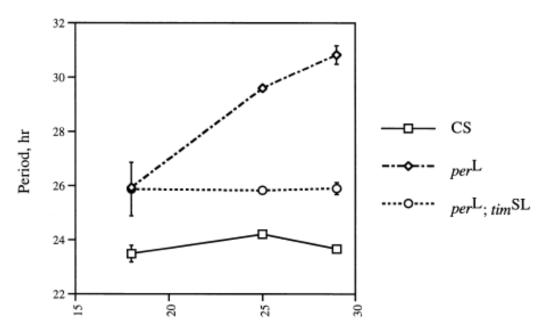
- Runs at constant conditions (DD)
- Free running period close to 24hrs
- Measures photoperiod or nightlength (day-length)
- No free running period

PHOTOPERIODIC TIMER (photoperiodic clock)

Runs at constant conditions (DD)

- Measures photoperiod or nightlength (day-length)
- Free running period close to 24hrs
- No free running period

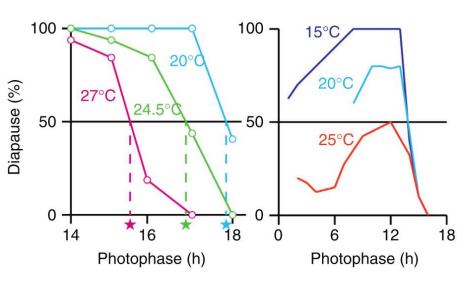
Temperature compensated



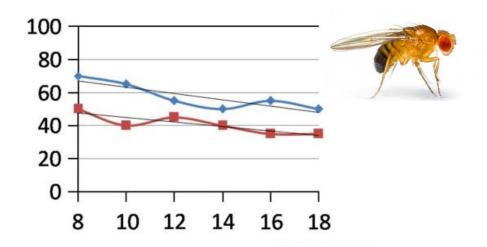
- Runs at constant conditions (DD)
- Free running period close to 24hrs
- Temperature compensated

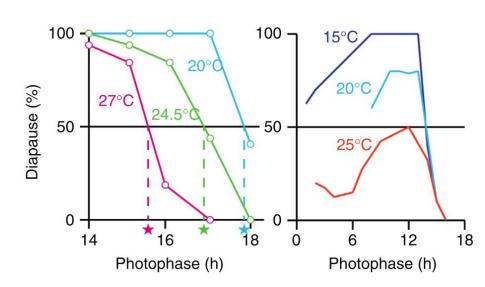
PHOTOPERIODIC TIMER (photoperiodic clock)

- Measures photoperiod or nightlength (day-length)
- No free running period
- Temperature is important factor influencing photoperiodic response curve

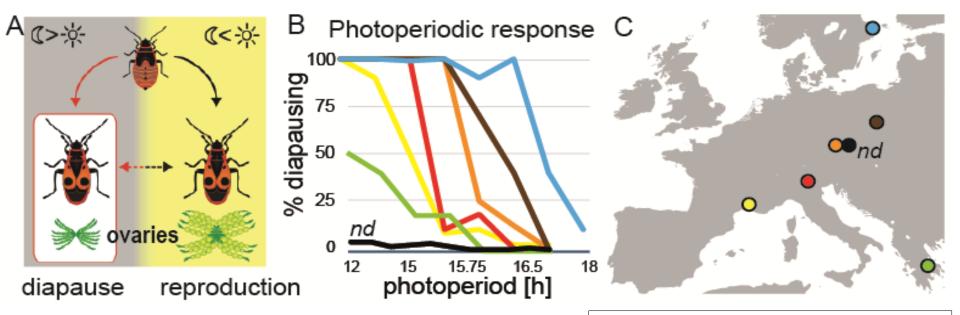


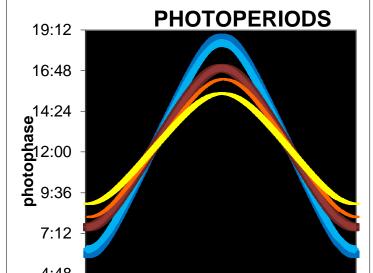
PHOTOPERIODIC TIMER (photoperiodic clock)





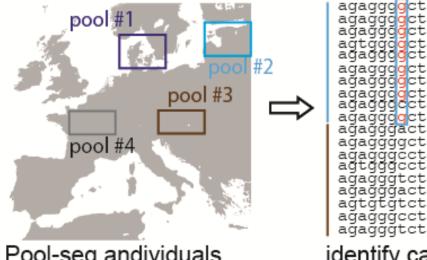
A big experiment in Nature: geographic variability





How to study natural adaptations? – distinguish important changes from unimportant variability

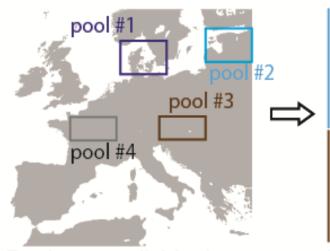
- Genetic variability behind the biology you are studding
- Genetic variability behind something else
 (important & interesting, but for someone else)
- Random variability, bottleneck, founder effect
- Technical artifacts & various limitations



Pool-seq andividuals (with known CPP)

agaggggctctttqqacc agagggcctctatggacc agagggtctcttttggacc

identify candidate pool-specific SNPs

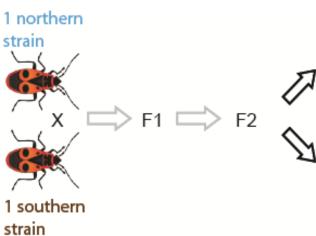


Pool-seq andividuals (with known CPP)

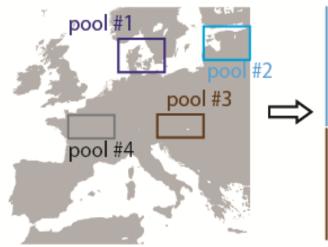
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agagggtctcttttt

identify candidate pool-specific SNPs





phenotype & genotype F1 and F2 bugs

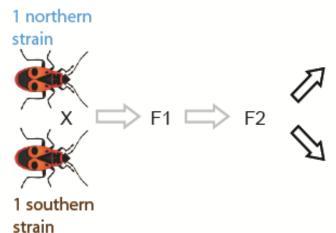


Pool-seq andividuals (with known CPP)

agaggggctctttggacc agagggtctcttttggacc

identify candidate pool-specific SNPs





phenotype & genotype F1 and F2 bugs

- too many candidates?
- Novel genes?
- a few clear candidates
- cis-regulatory regions
- allelic variants
 - AA change

variants associating with CPP

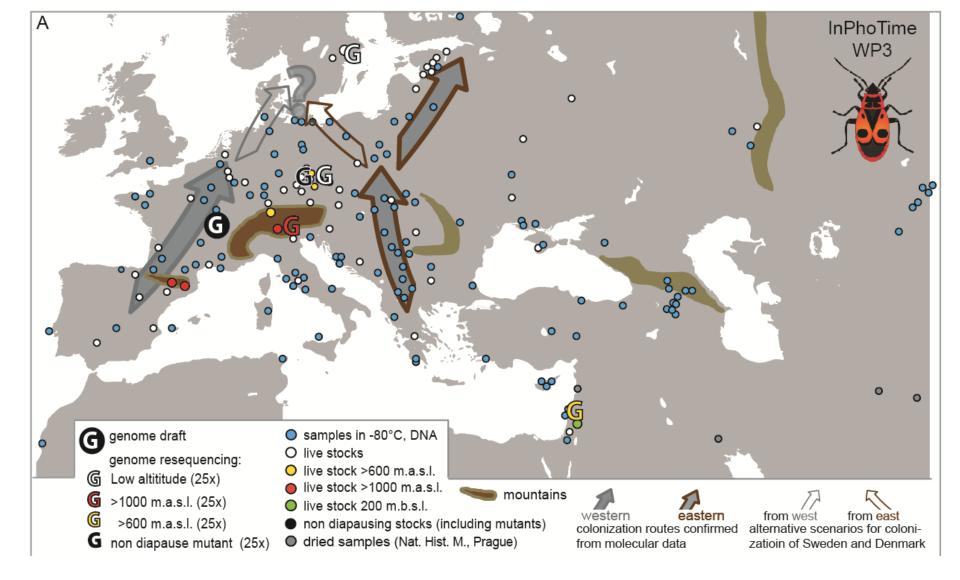
test function by reverse genetics

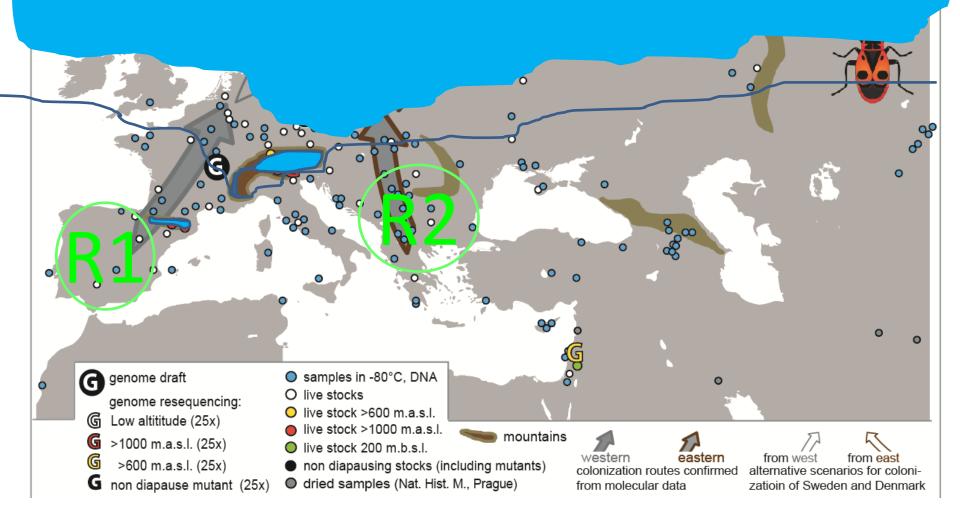


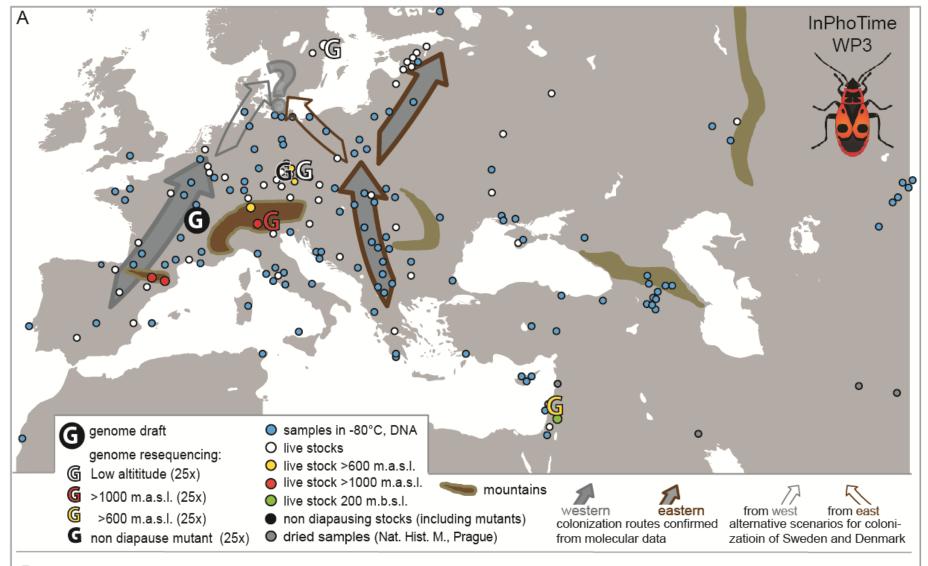
RNAi

genome

editing







B Sweden Estonia Latvia Czech Rep. Italy-mts. Israel

CRYPTOCHROME2 (CRY2)
TVQKASKCVIGTDYPLPM
TVQKASKCVIGTDYPLPM
TVQKASKCVIGTDYPLPM
TVQKASKCIIGTDYPLPM
TVQKASKCIIGTDYPLPM
TVQKASKCIIGTDYPLPM
TVQKASKCIIGTDYPLPM

PERIOD (PER)

 $ext{NNDPVTP}^{\mathbf{T}} ext{IPNHETQ}$

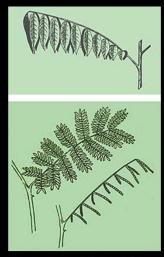
NNDPVTPTIPNHETQ NNDPVTPAIPNHETQ NNDPVTPAIPNHETQ

Fig. 10 Preliminary data supporting WP3.

- (A) Western and eastern colonizations routes in Europe will serve as a uniques source for latitudinal and altitudinal genetic variants in the photoperiodic timer.
- (B) Geographic variants of CRY2 and PER proteins



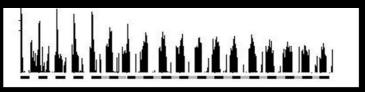




CIRCADIAN RHYTHM

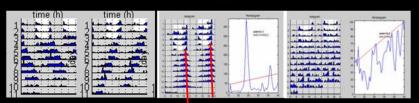
Jean-Jacques d'Ortous de Mairan, 1729

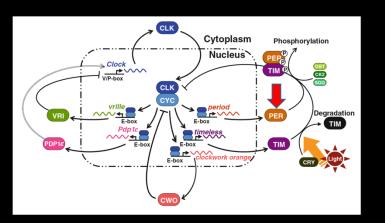




1	2
2	3
3	4
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2 3 4 5	6
6	

~24 h

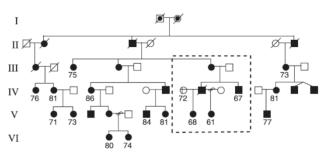




Human FASP

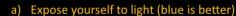
Summary

Fig. 1. ASPS kindred 2174. Horne-Östberg scores are shown below individuals. The dotted line marks a branch (branch 3) where the ASPS phenotype does not cosegregate with the mutation. Circles, women; squares, men; filled circles and squares, affected individuals; empty circles and squares, unaffected individuals. Unknown in-

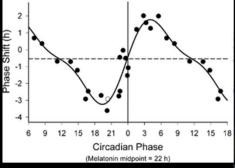


dividuals (not meeting strict criteria for being "affected" or "unaffected") were eliminated from this pedigree for the sake of simplicity.

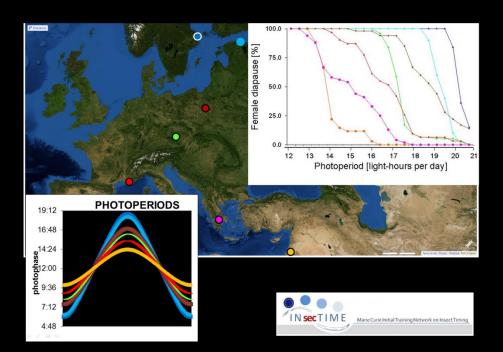
You leave SF in the afternoon (3 p.m.) arriving to London at 7a.m. (of London time), what do you do to entrain to the new regime? Time difference is 8 hrs.



b) Hide from light









https://cinchron.org/

https://cinchron.org









- CIRCADIAN CHRONOBIOLOGY -



- SEASONAL CHRONOBIOLOGY -



- METABOLIC CHRONOBIOLOGY -



- COMMERCIAL CHRONOBIOLOGY -



Insect Photoperiodic Timer

CRISPR/CAS9 gene editing Population genetics Insect neuropeptides

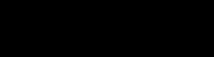
david.dolezel@entu.cas.cz



Acknowledgment

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Adam Bajgar
Jonna Kotwica-Rolinska
Milena Damulewicz
Jan Provaznik
Olina Bazalova
Lenka Chodakova
Martin Pivarci
Hanka Vaneckova
Jan Martinek









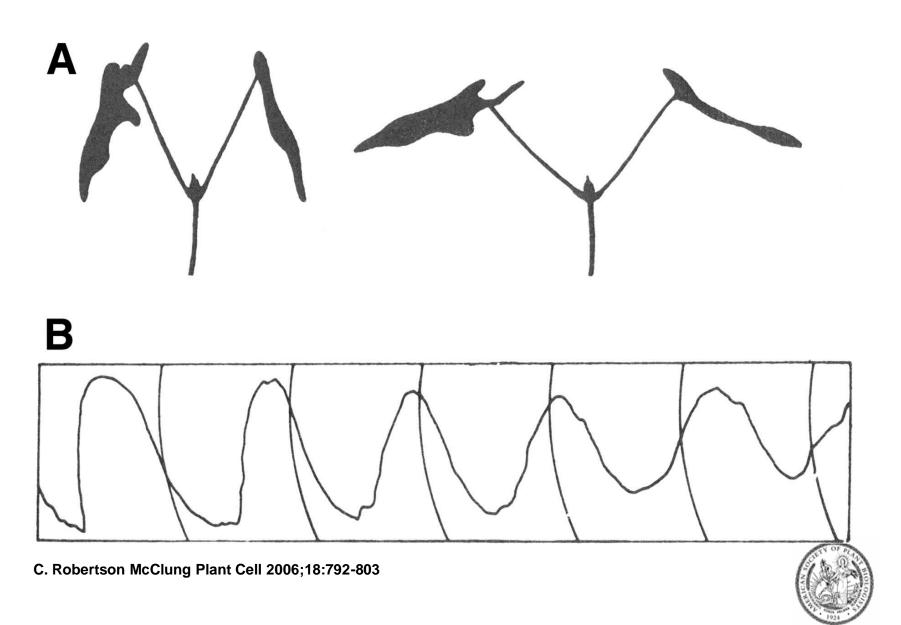


EMBL Heidelberg

- Vladimír Beneš
- Jonathon Blake

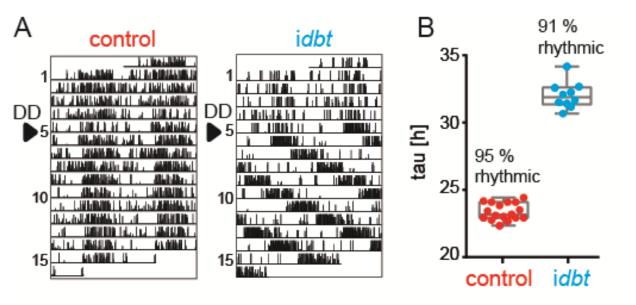
Currently we have one or two PhD positions

Leaf Movements of a Representative Species.(A) Sleep movements of Phaseolus coccineus.



No circadian clock *versus* altered circadian clock

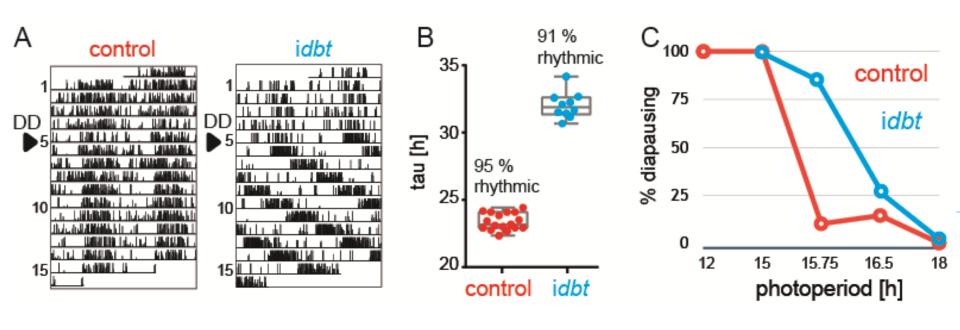
Circadian clock



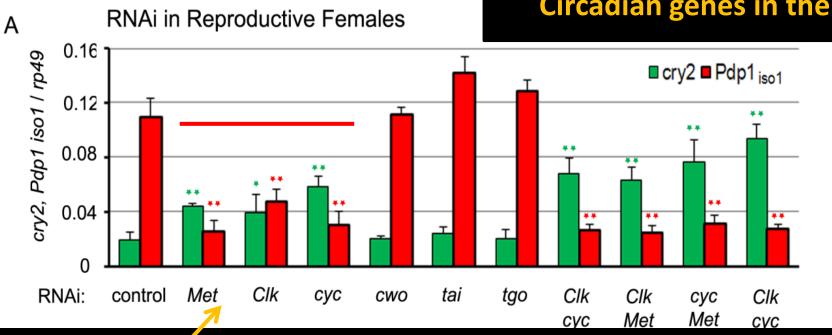
No circadian clock *versus* altered circadian clock

Circadian clock

Photoperiodic timer



Circadian genes in the gut



JH (juvenile hormone)

