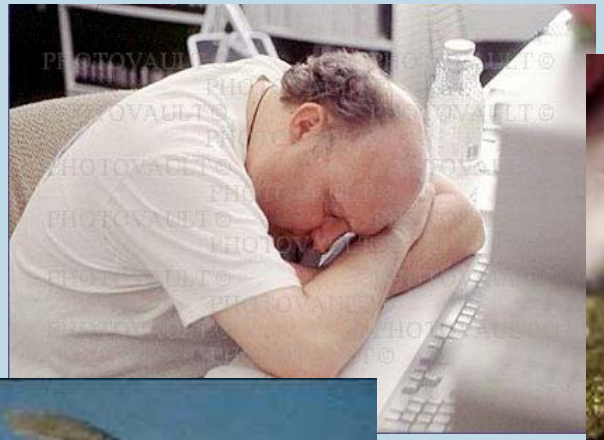
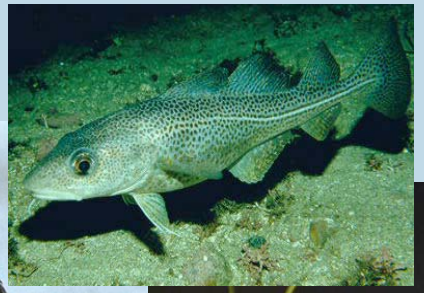
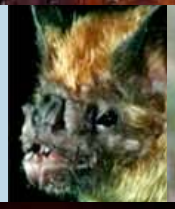
Circadian rhythms:

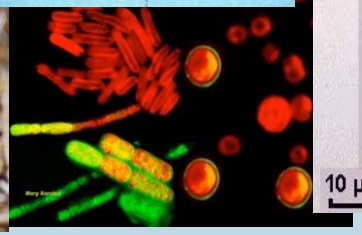
How do cells “compute”
temperature compensation?

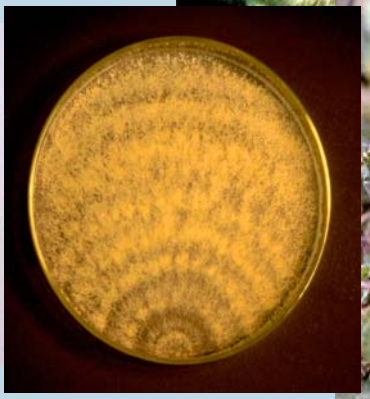




Circadian rhythms are important in daily and seasonal adaptations of organisms to their environments







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Properties of circadian rhythms

• circadian rhythms are generated within the single cell and can occur under constant environmental conditions (**free-running conditions**).

• they can be **phase shifted** by sudden changes in light, temperature, drugs, etc.

• they can lock to external periodic variations such as “lights on/off” or temperature variations. This property is called **entrainment.** Circadian rhythms also show **frequency-demultiplication.**

• they are involved in ‘**photoperiodicitiy**’, i.e., the organism/cell is able to sense a critical daylength and induce **vital physiological processes**, such as flowering, hibernation, migration,...

• the circadian period is **relatively** unaffected by different (but constant) temperatures. This property is called **temperature compensation** with $Q_{10} \approx 0.8\text{-}1.2$.

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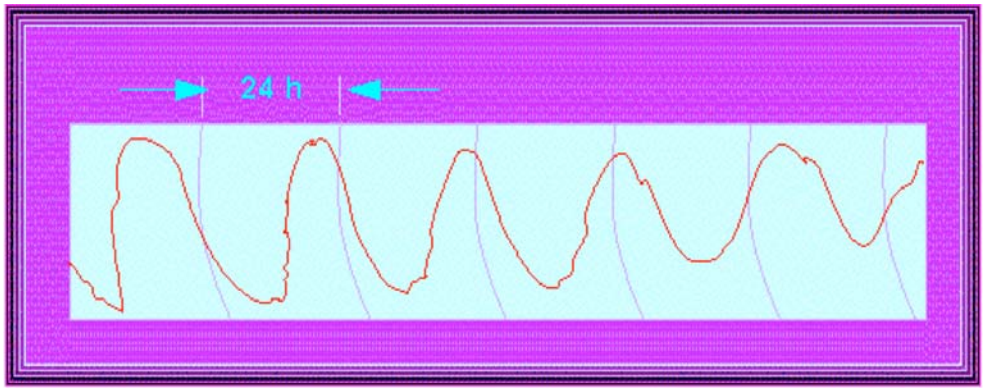
Why has temperature compensation been so difficult to explain on a molecular basis?

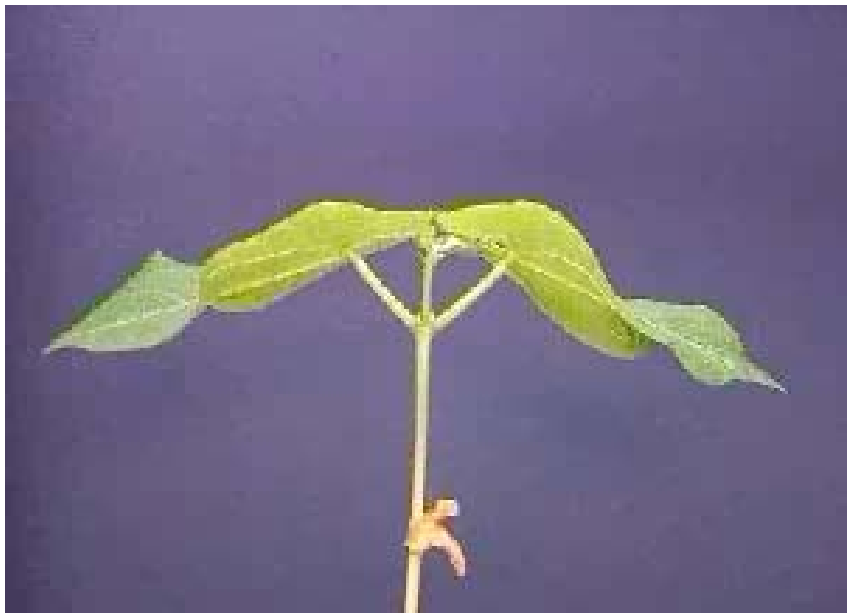
Practically all physiological reactions, enzyme catalyzed reactions, etc. are quite dependent upon temperature. Their rates increase by a factor (Q_{10}) of 2-3 when temperature is increased by 10°C ("**Van't Hoff's rule**"). This makes it difficult to point to a certain rule/mechanism how temperature compensation could work.

Examples of circadian rhythms

Leaf movements under free-running conditions (1957)

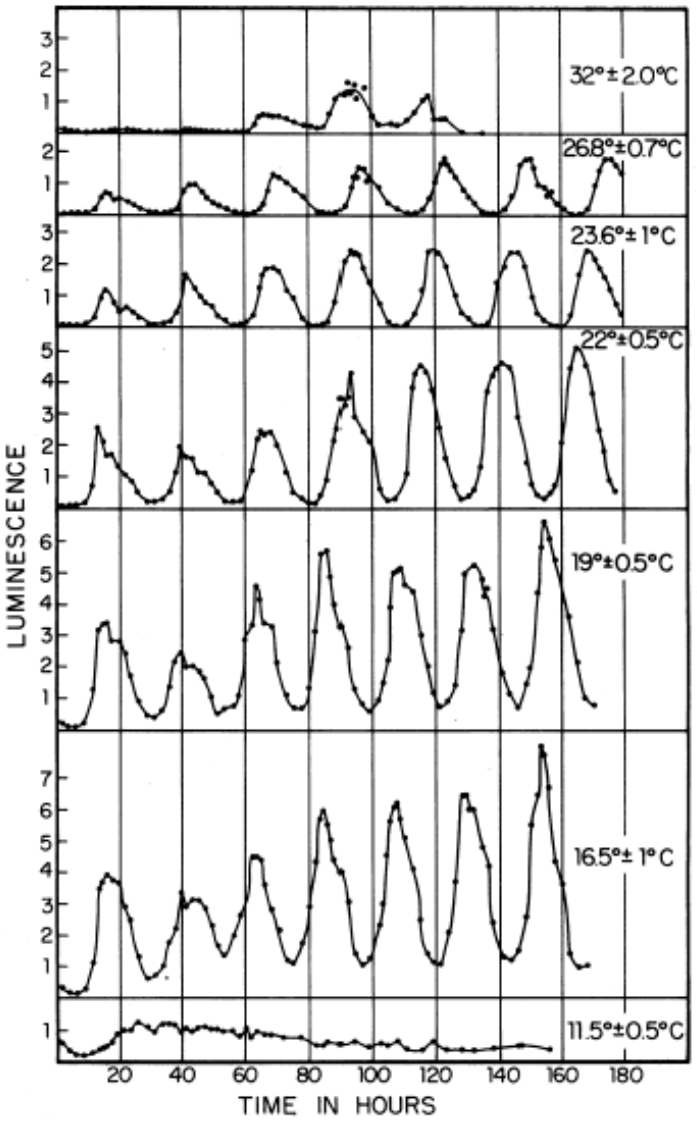


***Phaseolus coccineus*. Typical course of the circadian leaf movements under constant light (weak intensity). The phase shifts within six days by roughly 17 hours compared to the normal day. The length of one period is thus about 27 hours (circles in 24-hour-intervals; E. BÜNNING and M. TAZAWA, 1957).**



Time lapse movie of leaf movements in bean (*Phaseolus*) seedlings by Roger P. Hangarter, Indiana University.

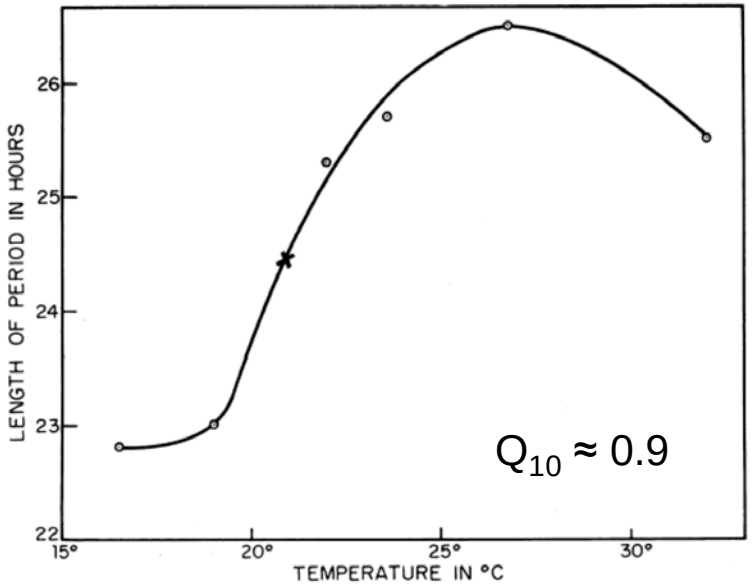
Gonyaulax bioluminescence rhythm (1957)

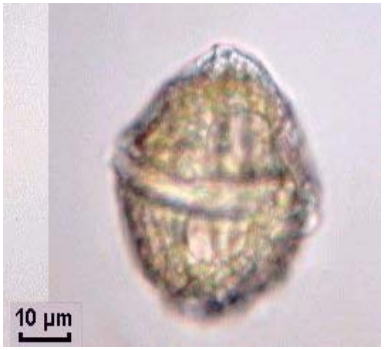


Proc Natl Acad Sci U S A. 1957 September 15; 43(9): 804–811.

ON THE MECHANISM OF TEMPERATURE INDEPENDENCE IN A BIOLOGICAL CLOCK J. Woodland Hastings and Beatrice M. Sweeney

"The experiments reported here describe the effect of temperature upon the luminescent rhythm. The results suggest that temperature independence is achieved by means of a compensation mechansism"





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Neurospora conidiation rhythm

(Pittendrigh, Bruce, Rosenzweig & Rubin: Nature, 1959)

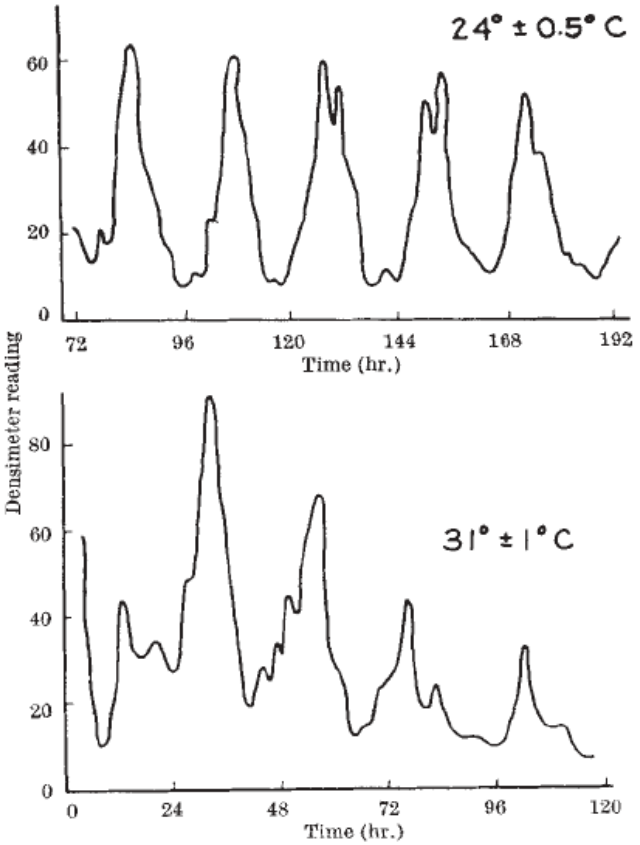

Fig. 1. Zonation in *Neurospora*. Zonation of the growth in a race-tube of a prolineless strain of *Neurospora* has been measured using a densimeter to record the relative density of mycelial growth. The time-scale shown represents hours elapsed after transfer of the race-tubes from white light to dim red light as described in the text

Citation from the 1959 paper:

The zonation of *N. crassa* thus is regulated by a rhythmic phenomenon which manifests the essential features of a biological clock[2]. The rhythm has an innate free-running period which is close to 24 hr. relatively independent of the temperature.

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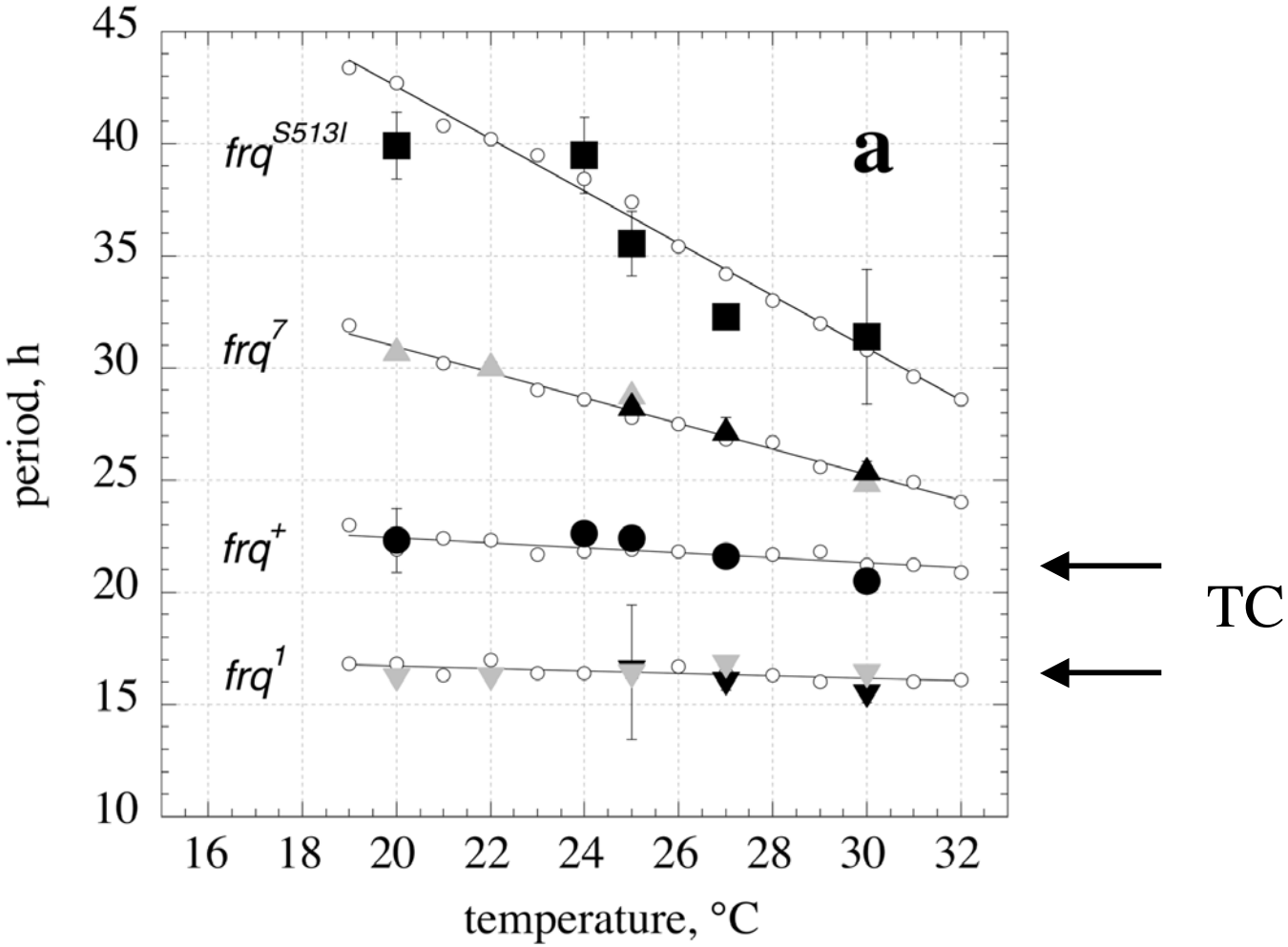
Temperature Compensation in different *Neurospora frequency* (*frq*) mutants



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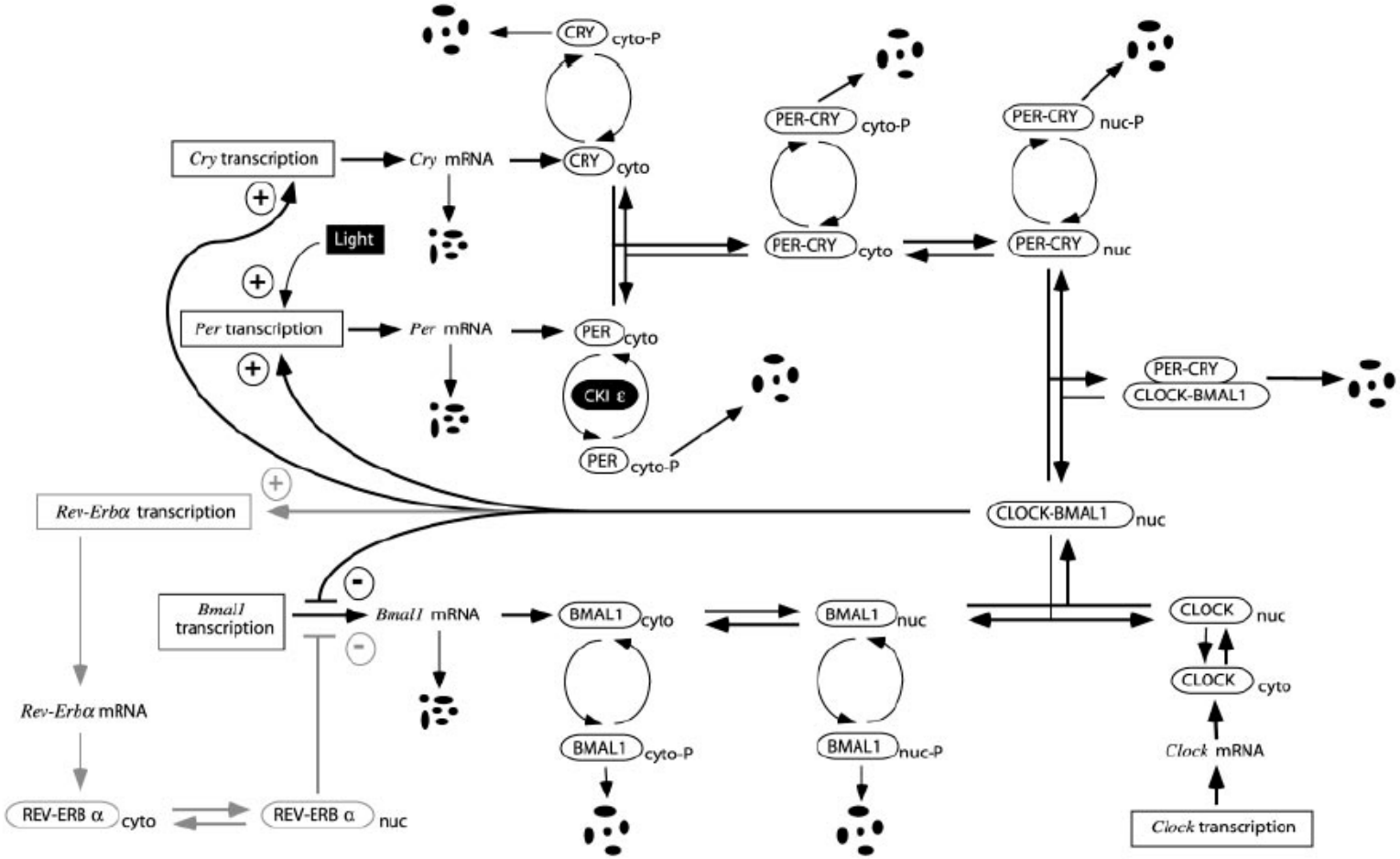
A mammalian clock model



Leloup & Goldbeter (2004), PNAS.

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Reaction hierarchies and temperature behavior

Elementary chemical reactions
(Arrhenius equation)

Stoichiometric component processes
(Arrhenius/non-Arrhenius behavior)

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A theory for temperature compensation: The antagonistic balance equation

$$P = P(k_1, k_2, \ldots, k_i, \ldots, k_N).$$

$$\frac{\partial P}{\partial T} = \sum_i \left(\frac{\partial P}{\partial k_i}\right)\left(\frac{\partial k_i}{\partial T}\right).$$

$$k_i = A_i e^{-\frac{E_i}{RT}},$$

$$\frac{\partial P}{\partial T} = \sum_i \left(\frac{\partial P}{\partial k_i}\right)\frac{E_i}{RT^2}k_i = \sum_i \left(\frac{\partial P}{\partial lnk_i}\right)\frac{E_i}{RT^2}. \qquad [12]$$

Multiplying Eq. **12** by $1/P$ and observing that $\partial P/P = \partial \ln P$, Eq. **12** can be written as

$$\frac{1}{P}\frac{\partial P}{\partial T} = \frac{\partial \ln P}{\partial T} = \frac{1}{RT^2}\sum_i \left(\frac{\partial \ln P}{\partial \ln k_i}\right)E_i = \frac{1}{RT^2}\sum_i C_i^P E_i.$$

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Balancing Categories

i) Static balance (whole net): E_i's are constant.

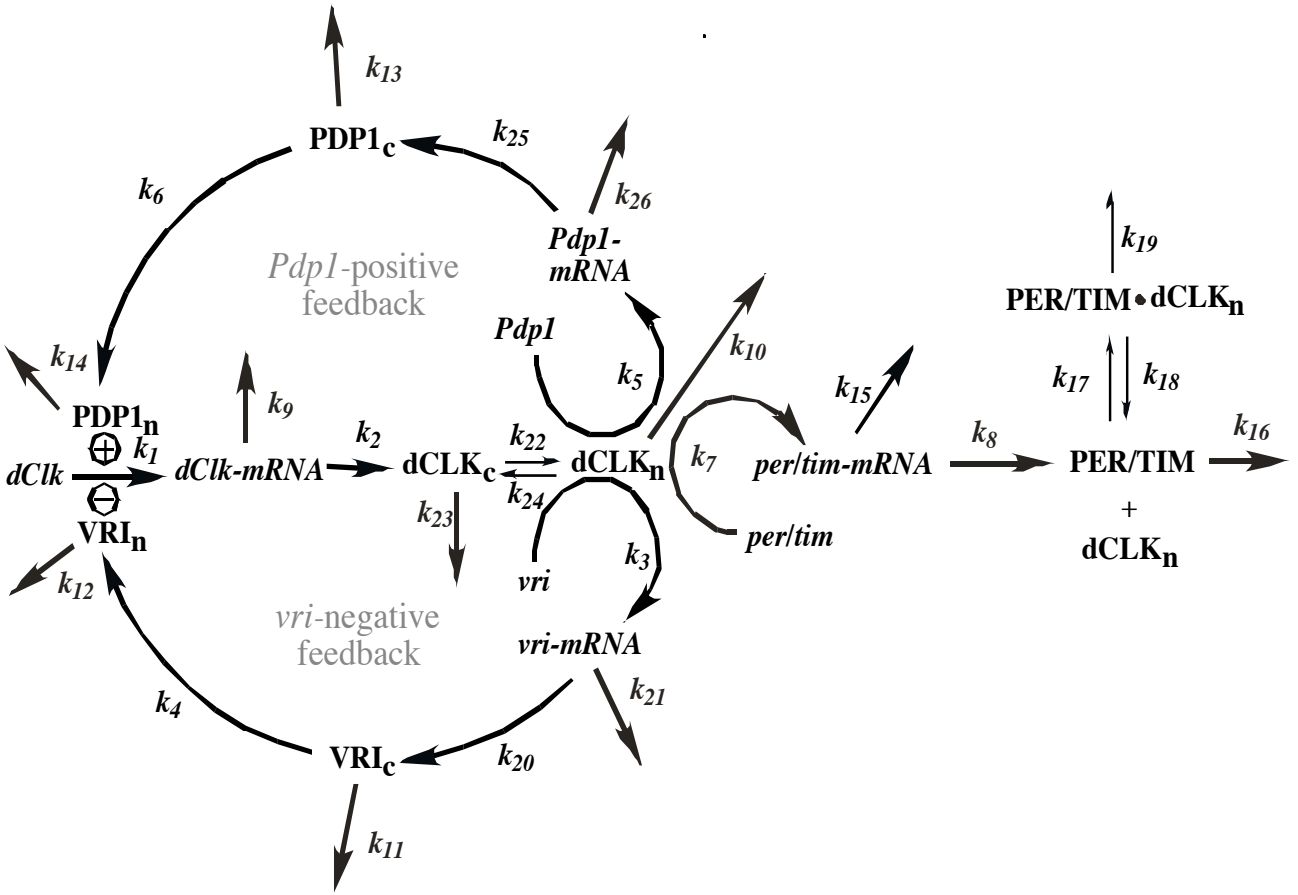
ii) Dynamic balance (whole net): E_i's are a function of T and possibly of other parts of the net.

iii) Balanced (static or dynamic) subnets [in terms of elementary or stoichiometric component processes].

iv) Robust TC: switching between stable limit cycle and stable steady state. Only a few balancing parameters.

v) Robust perfect adaptation: Sensor dependent TC (with zero C_i's), as suggested in chemotaxis.

A model of the *Drosophila* circadian clock



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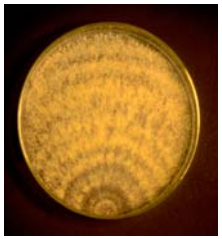
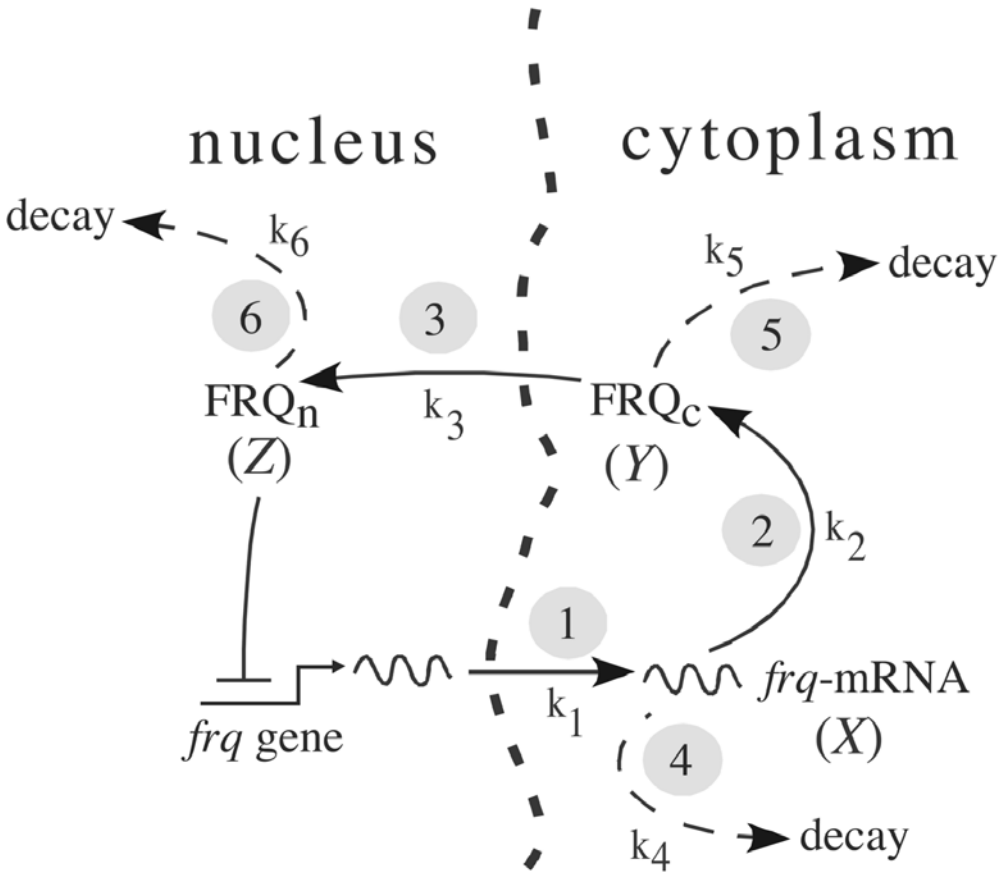
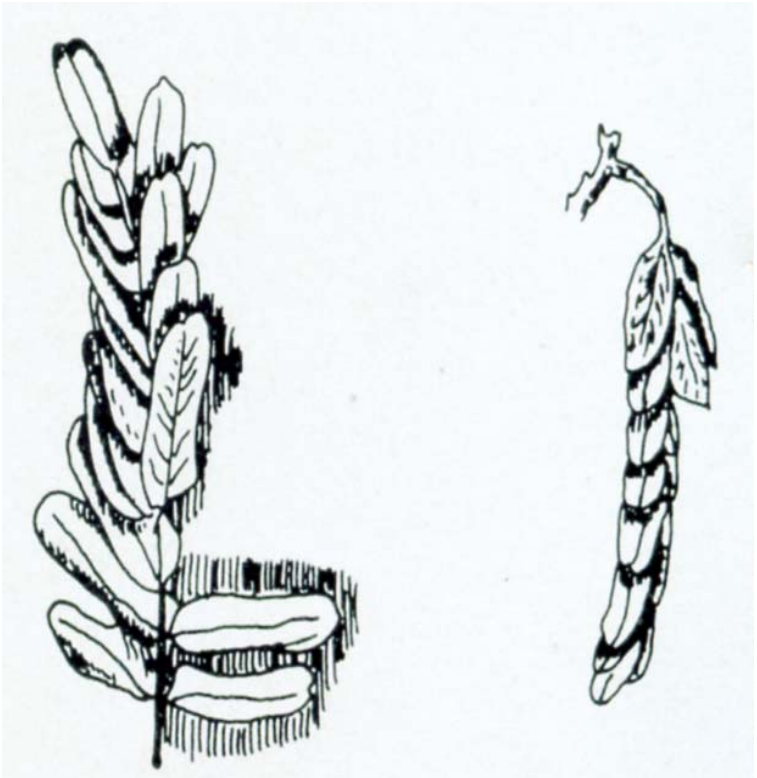
Goodwin-type model of the *Neurospora* circadian clock





Androsthenes (from Thasus) observes that plants ”sleep” (325 BC)



day night

Examples of temperature compensated rhythms

(from E. Bünning: The Physiologcal Clock, Berlin, 1964)

Table 2. *Periplaneta americana, Running Activity* (BÜNNING, 1958a)

Temperature °C	Length of Periods hrs.
18	24 — 25
19—20	24.4 ± 0.1
22—23	24.5 ± 0.1
27—28	25.0 ± 0.3
29	25.8 ± 0.7
31	24 — 27

Table 3. *Gonyaulax polyedra, Rhythm of Luminescence* (HASTINGS and SWEENEY)

Temperature °C	Length of Periods hrs.
15.9	22.5
19	23.0
22	25.3
26.6	26.8
32	25.5

Table 4. *Phaseolus multiflorus, Leaf Movements* (LEINWEBER)

Temperature °C	Length of Periods hrs.
15	28.3 ± 0.4
20	28.0 ± 0.4
25	28.0 ± 1.0

Table 5. *Lizards (Lacerta sicula), Running Activity* (HOFFMANN, 1957)

Temperature °C	Length of Periods hrs.
16	25.20
25	24.34
35	24.19