Lecture 21

summary

3.5 Stochastic bifurcations in genetic networks

$N=1, \mathcal{D} \neq 0$: synthetic gene oscillator demonstrates CR

$\Rightarrow$ there is some optimal noise for which a genetic unit displays most ordered dynamics.

$\boxed{\text{Synthetic gene relaxation oscillator:}}$

model for a network of $i = 1 \ldots N$ cells

$$\frac{du_i}{dt} = \alpha_1 f(v_1) - u_i + \alpha_3 h(w_i)$$

$$\frac{dv_i}{dt} = \alpha_2 g(u_i) - v_i$$

$$\frac{dw_i}{dt} = \varepsilon\,(\alpha_4\, g(u_i) - w_i) + 2d\,(w_e - w_i) + \underbrace{\sqrt{2\mathcal{D}}\,\xi_i(t)}_{\text{noise}}$$

$$\frac{dw_e}{dt} = \frac{d_e}{N} \sum_{i=1}^{N} (w_i - w_e)$$

Cellular fate controlled by external signal

$N=1, \ \mathcal{D} \neq 0$

$$\frac{du}{dt} = \alpha_1 f(v) - u + \alpha_3 h(w) + \underbrace{C \cos(\omega_{ex} t)}_{\text{external periodic signal}}$$

The frequency of the genetic unit ω_0 shifts towards the frequency of the external signal ω_{ex} $\Rightarrow$ external signal regulates the frequency of protein production/expression.

$N=2, \ \mathcal{D}=0$

two coupled genetic oscillators, no noise

- high multistability
- more complex determ. bif. diagram

$N=2, \ \mathcal{D} \neq 0$

two coupled units with noise

- stochastic phenomenological bifurcations

$N=500, \ \mathcal{D} \neq 0$: the same type of stoch. bif. as for $N=1$, $N=2$.

Interpretation : the cells are initially identical and produce protein with one constant concentration ($\mathcal{D}=0$, stable focus) in the presence of noise new intervals of protein production occur $\Rightarrow$ different protein concentrations are possible $\Rightarrow$ different cellular functionality $\Rightarrow$ differentiation of cells into various types

4. Synchronization in the presence of noise

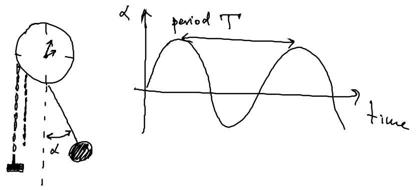
4.1 What is sync? Classical example of a pendulum clock.

Sync is an adjustment of rhythms of oscillating objects due to their weak interaction

* What is an oscillating object?
* What do we understand by the notion "rhythm"?
* What is an interaction of oscillating systems?
* What is an adjustment of rhythms?

We consider a classical example of a pendulum clock

Self-sustained oscillator



Mechanism: potential energy of the lifted weight (or compressed spring, or electrical battery) → → oscillating motion of the pendulum.

1) Takes energy from the source and maintains steady oscillation of the pendulum

2) The exact form of the oscillatory motion is entirely determined by internal parameters of the clock and does not depend on I.C.

These two features are typical for self-sustained oscillators.

Properties

1) internal source of energy; mathematically, an oscillator is described by autonomous (without explicit time dependence) dynamical system

2) the form is defined by the param. of the system and does not depend on I.C.

3) the oscillation is stable to (at least rather small) perturbations: Being disturbed, the oscillation soon returns into its original shape

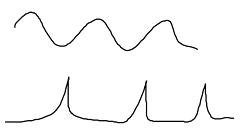
Examples: clock, lasers, pacemakers of human hearts, electronic circuits.

$\Rightarrow$ they can be synchronized!

<u>Period and frequency</u>

$f = \frac{1}{T}$

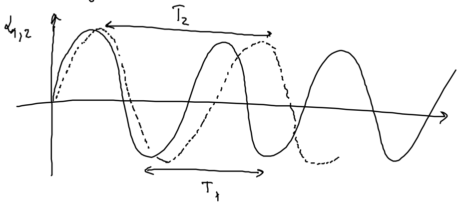
$\omega = 2\pi f = \frac{2\pi}{T}$



<u>Natural frequency</u> is the freq. of the autonomous (isolated) system

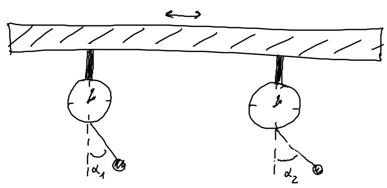
<u>Coupling of oscillating objects</u>

Pendulum clock: the clocks seem to be identical, but they are not.



Two similar pendulum clocks cannot be perfectly identical; due to a tiny parameter mismatch the have slightly diff. periods ($T_2 > T_1$).

Let us now consider two <u>weakly</u> interacting clocks: coupling through a common support. The beam is not rigid, but can vibrate <u>slightly</u>.



<u>Adjustment of rhythms</u>

Experiments show that even a weak interaction can synchronize two clocks. $\Rightarrow$ they start to oscillate with a common period $\rightarrow$ frequency locking.

What are the factors which define whether they sync or not?

1) <u>Coupling strength</u>

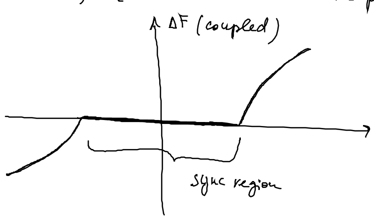
Pendulum clock: the ability of the beam to move $\Rightarrow$ if the beam is absolutely rigid $\Rightarrow$ no interaction $\Rightarrow$ coupling strength is zero

2) <u>Frequency detuning</u>

$\Delta f = f_1 - f_2$

$f_1, f_1 \rightarrow$ characterize free (uncoupled) oscillators

$F_1, F_2 \rightarrow$ obtained in the presence of coupling



Δf (uncoupled)

$\downarrow$ frequency detuning = frequency mismatch

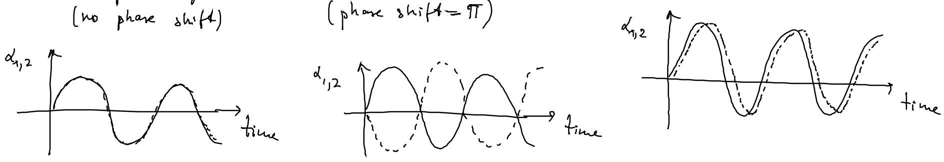
This curve is typical for interacting oscillators, independent of their nature (mechanical, electronic, chemical).

Synchronization

$\swarrow$ in-phase sync (no phase shift)

$\searrow$ anti-phase (phase shift $= \pi$)

$\rightarrow$ phase-lag (a fixed phase shift)



Synchronization

$\swarrow$ external (ω_1)

$\omega_1 \longrightarrow \boxed{\omega_2}$

$\searrow$ mutual sync (ω_3)

$\omega_1 \longleftrightarrow \omega_2$