Self-organized entrainment in a model for endocrine system

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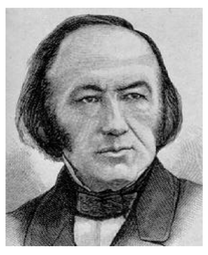
Introduction

Endocrine system



Claude Bernard stated that the endocrine system regulates the internal milieu of an animal.

The "internal secretions" were liberated by one part of the body, traveled via the bloodstream to distant targets cells.

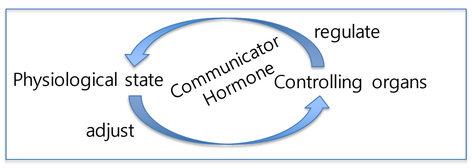
Claude Bernard (1813~1878): the father of endocrinology

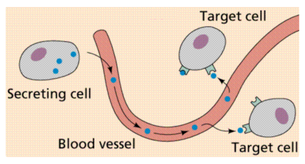
➢ The concept that hormones acting on distant target cells to maintain the stability of the internal milieu was a major advance in physiological understanding.

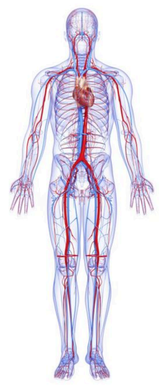
➢ The secretion of the hormone was evoked by a change in the milieu and the resulting action on the target cell restored the milieu to normal.

The desired return to the status quo results in the maintenance of **homeostasis**

A hormone is any member of a class of signaling molecules produced by glands in multicellular organisms that are transported by the circulatory system to target distant organs to regulate physiology and behavior - Wikipedia





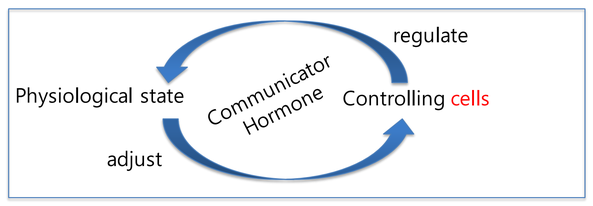


Long-range biochemical messenger: hormone

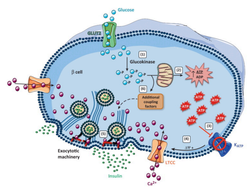
Pulsatile secretion of the hormones

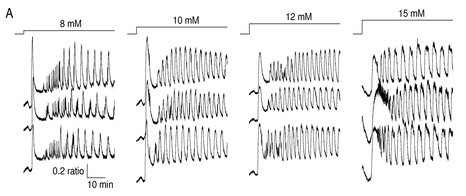
Living systems are rhythmic

Rhythms are composed by active/silent phase



Insulin secretion arising at pancreatic beta cells

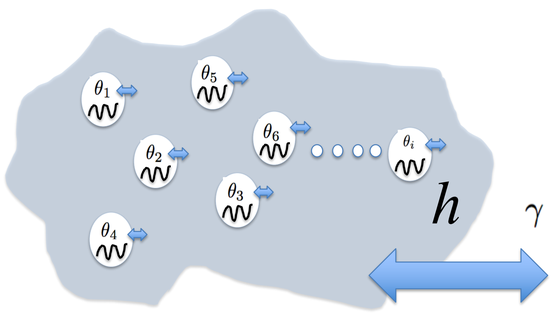




The hormones are secreted and affected at distinct location — Cooperativity
Secreting cells are extremely crowded — Stochasticity

System modeling

Active/silent phase described by phase modulation



Isolated active rotators

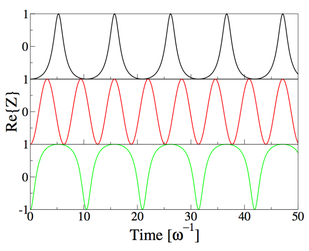
$$\dot{\theta}_n = \omega_0 - \mu(h)\cos\theta_n$$

$$\dot{h} = \gamma - \frac{1}{N}\sum_{n=1}^{N}\cos\theta_n$$

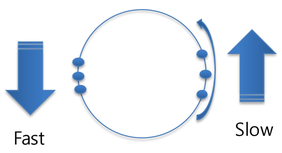
Negative feedback

Surrounding environment

$$\dot{\theta} = \omega_0 - \mu\cos\theta$$



$\left|\frac{\mu}{\omega_0}\right|$

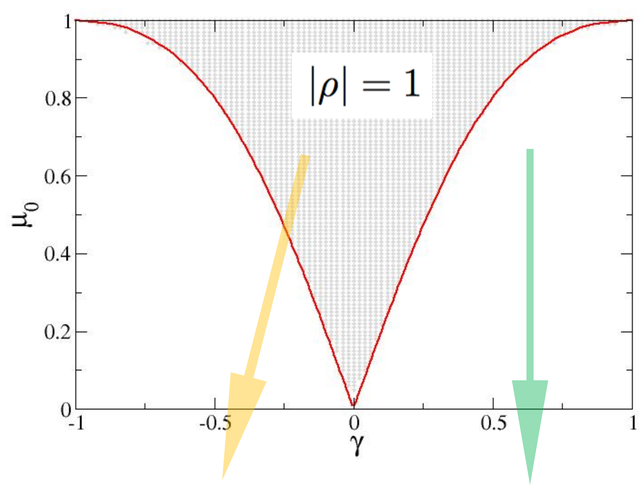


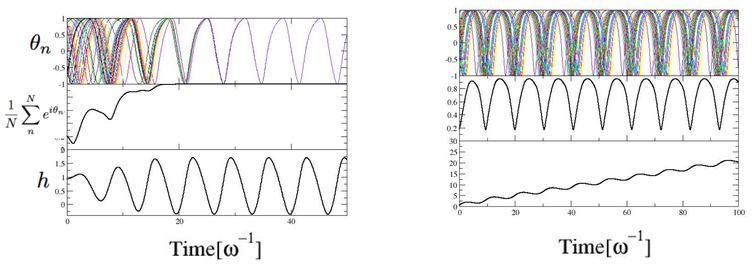
Self-sustained oscillation

Phase locked at $cos^{-1}\left|\frac{\omega_0}{\mu}\right|$

Self-organized entrainment

$$\mu(h) = \mu_0 \tanh h, \;\; N = 50 \qquad \rho = \frac{1}{N}\sum_{n}^{N} e^{i\theta_n}$$





Entrainment boundary

$$\dot{\theta}_i = \omega_0 - \mu(h)\cos\theta_i$$
$$\mu(h) = \mu_0 \tanh h$$

Ott-Antonsen ansatz
delta-function frequency distribution

$$\dot{\rho} - i\omega_0\rho + i\frac{\mu(h)}{2}(\rho^2 + 1) = 0$$

By substituting:

$$\rho(t) = X(t) + iY(t), \;\; \{X, Y\} \in \{\Re\}$$

$$\dot{X} = (\mu(h)X - \omega_0)Y$$
$$\dot{Y} = \omega_0 X - \frac{\mu(h)}{2}(X^2 - Y^2 + 1)$$
$$\dot{h} = \gamma - X$$

Linearized stability
condition: existence of fixed point

$$\gamma^{max} = \left|\frac{\omega_0}{\mu_0}\left(1 - \sqrt{1 - \frac{\mu_0^2}{\omega_0^2}}\right)\right|$$

Red solid line

➢ The entrainment is independent from choice of $\mu(h)$

Biomimetic analog controller

Biomimetics (bio-inspired system)

Named by Otto Schmitt in 1950s who explicitly mimicked nerve

Transfer of ideas and analogues from biology to technology
Not only mimicry morphology but also its functional mechanism

Provide an efficient way from nature

"Nature took millions of years to improve their own mechanisms ! "

Realization !

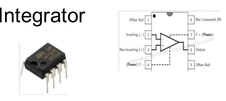
$$\dot{\theta}_n = \omega_0 - \mu(h)\cos\theta_n$$
$$\dot{h} = \gamma - \frac{1}{N}\sum_{n=1}^{N}\cos\theta_n$$

$$X \equiv \frac{1}{N}\sum_n cos\,\theta_n \qquad Y \equiv \frac{1}{N}\sum_n sin\,\theta_n$$

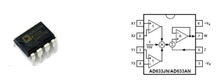
$$\dot{X} = (\mu(h)X - \omega_0)Y$$
$$\dot{Y} = \omega_0 X - \frac{\mu(h)}{2}(X^2 - Y^2 + 1)$$
$$\dot{h} = \gamma - X$$

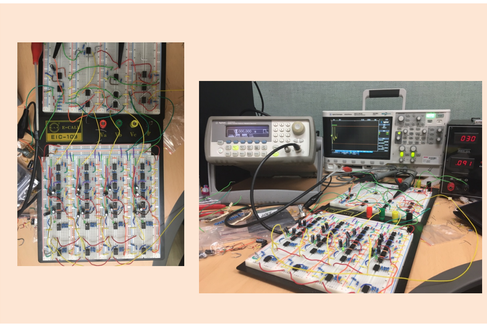
Operational Amplifier

Integrator



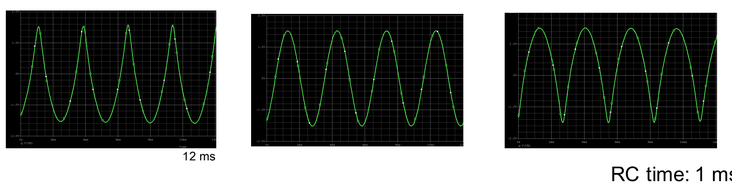
Multiplier : AD633





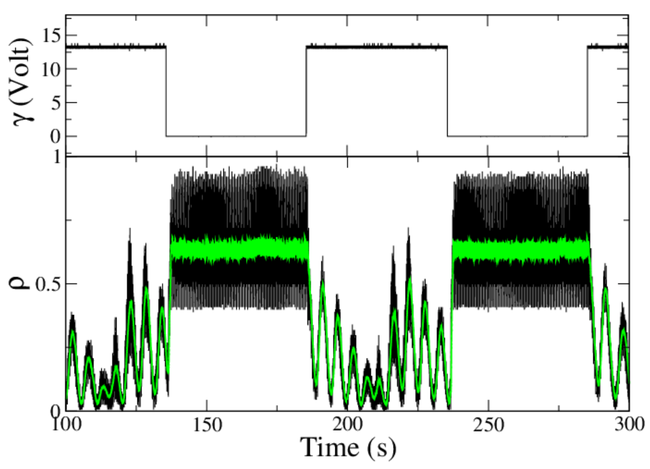
μ_0 =0.4 V | 0 V | -0.4 V

$cos\,\theta_n$



RC time: 1 ms

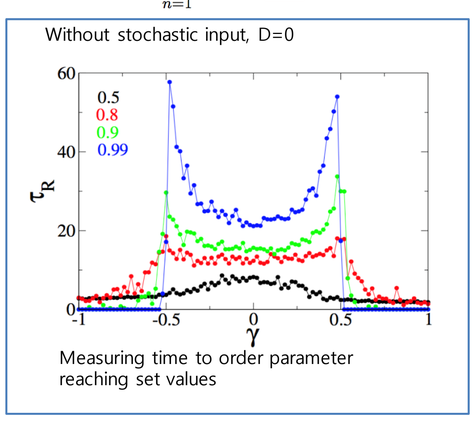
Measuring two distinct regime in biomimetic system



The entrainment robust against to considerable noise

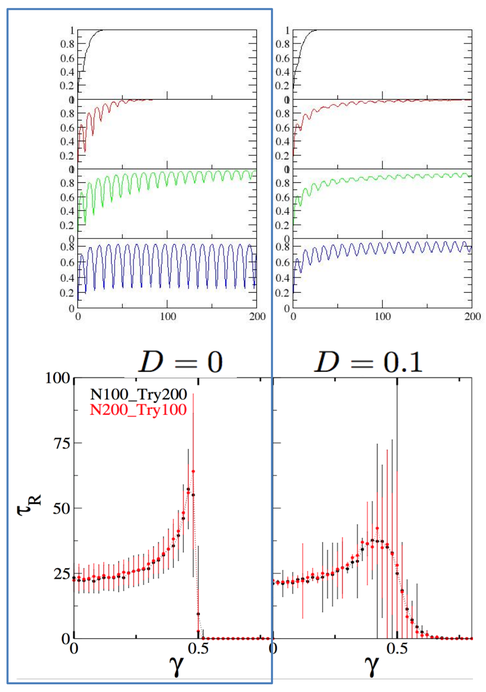
Plan of future work

$$\dot{\theta}_n = \omega_0 - \mu(h)\cos\theta_n \qquad \langle\zeta(t)\rangle = 0$$
$$\dot{h} = \gamma - \frac{1}{N}\sum_{n=1}^{N}\cos\theta_n + \zeta(t) \qquad \langle\zeta(t)\zeta(t')\rangle = D\delta(t - t')$$



Stochastic force to environment gives rise to wider γ

Stochastic input helps cooperativity ! ?



Conclusion

- ✓ We suggest simple mathematical model inspired by biological feedback
- ✓ We found 'self-organized entrainment' that the feedback via environment entrain phases of effectors to have synchronous responses
- ✓ Based on an analog circuit, the proposed entrainment successfully realized and demonstrated
- ✓ We believe that this phenomenon would be shed light on the possible way to explanation of 'cooperativity' arising at endorine system

Thank you very much for your attention