

VORLESUNG 13

Vorlesung
Humboldt-Universität zu Berlin
Institut für Physik

Biologische Physik

Die Dynamik biologischer Prozesse im menschlichen Körper

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**Max Planck Institute
of Colloids and Interfaces**



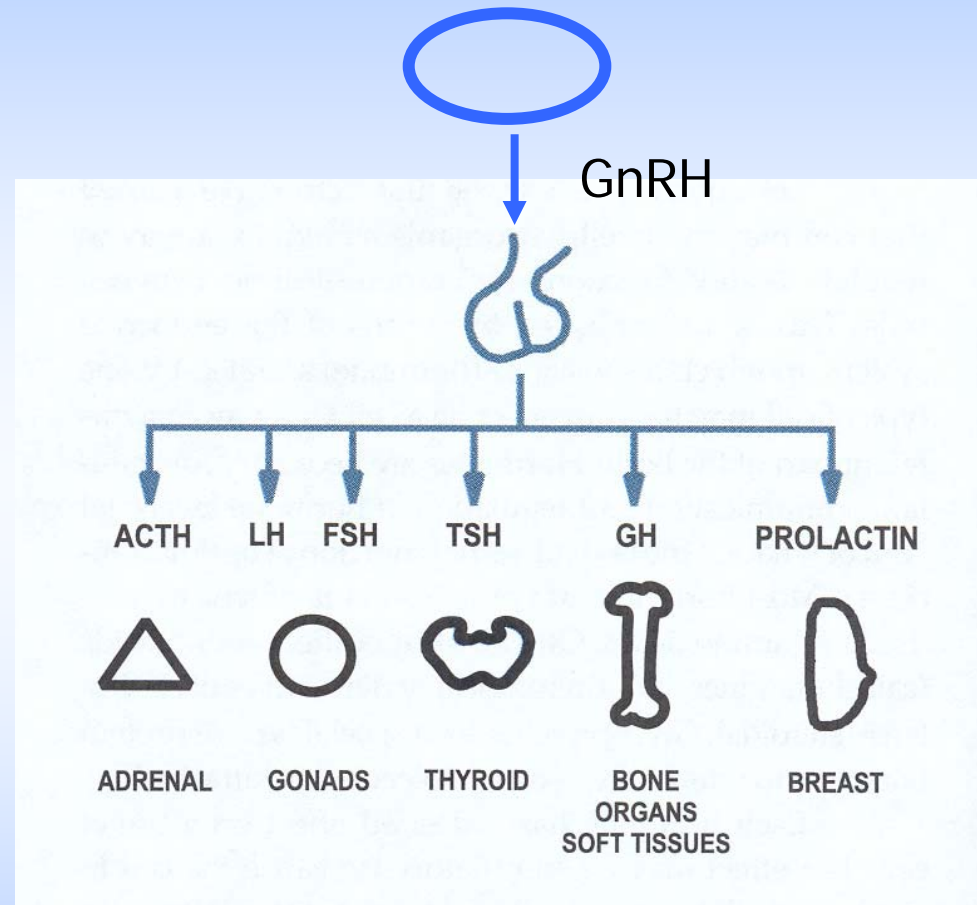
6 Endocrine system – hormone physiology

HYPOTHALAMUS

AND

PITUITARY

„master glands“:



GnRH: gonadotropin-releasing hormone – stimulates FSH and LH secretion

LH: luteinizing hormone – ovaries and testes

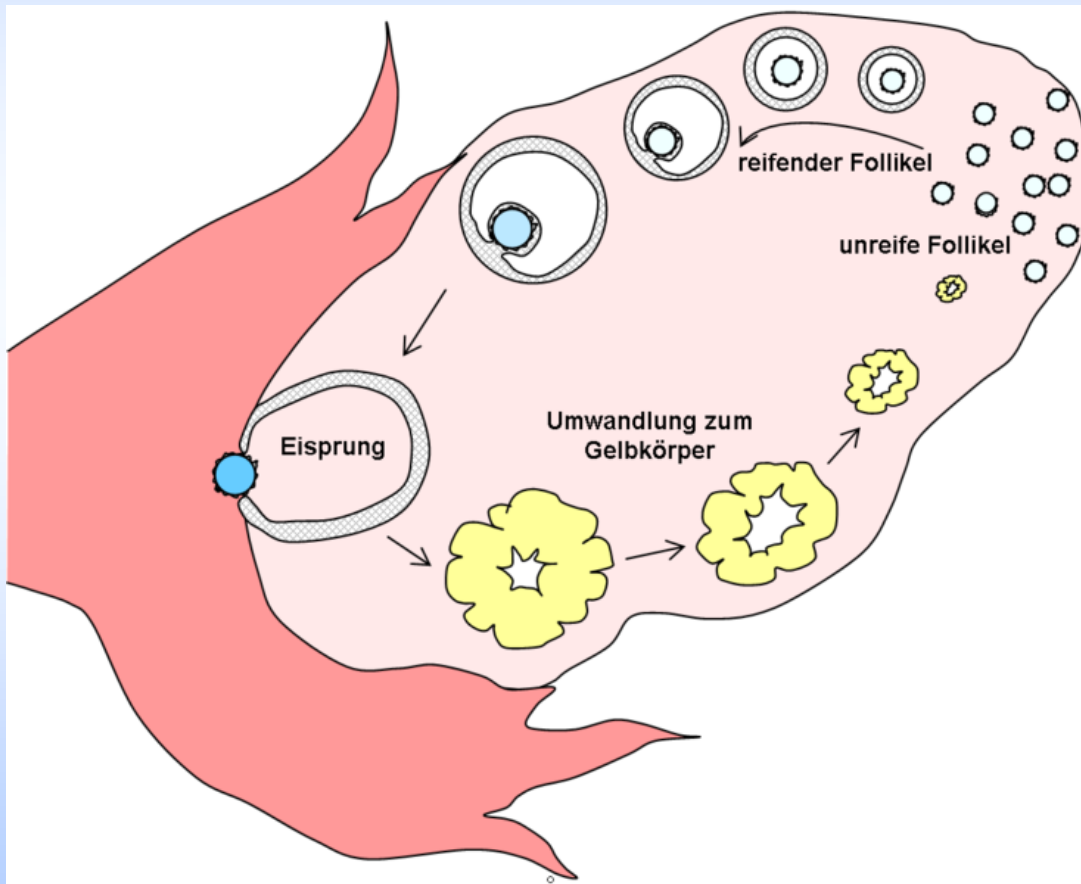
FSH: follicle-stimulating hormone – ovaries and testes





6.2 Ovulation

process in the menstrual cycle by which a mature ovarian follicle ruptures and discharges an ovum



in mammals the number of oocytes reaching full maturity is carefully controlled





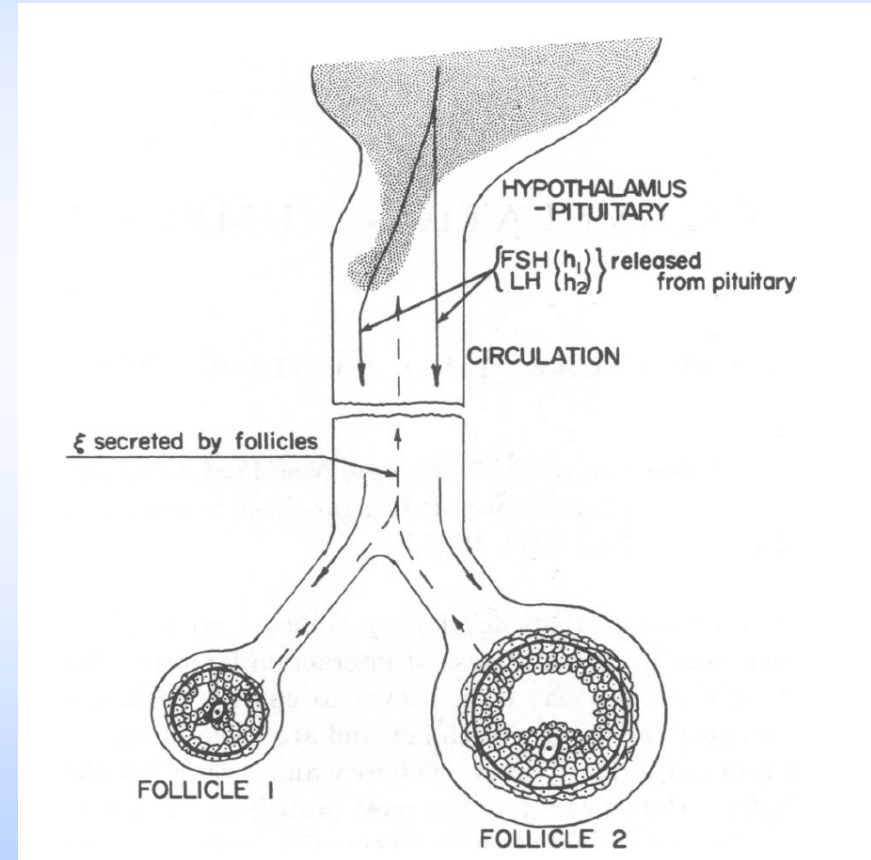
6.2 Ovulation

control of ovulation:

Lacker model:

three basic assumptions:

- 1) the rate at which follicles secrete estradiol is a marker of follicle maturity
- 2) the concentration of estradiol in the blood controls the release of FSH and LH from the pituitary
- 3) the concentrations of FSH and LH control the rate of follicle maturation, and at any given instant, the response of each follicle to FSH and LH is a function of the follicle's maturity





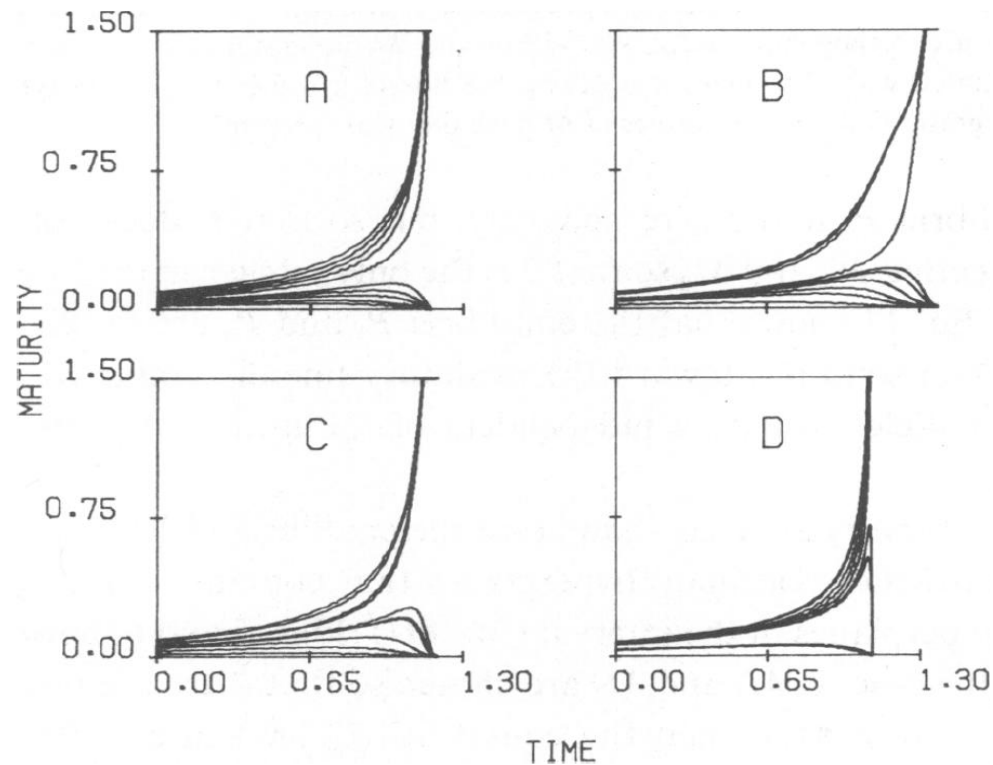
6.2 Ovulation

Lacker model:

$$\frac{d\xi_i}{dt} = f(\xi_i, \xi) = \xi_i [1 - (\xi - M_1 \xi_i)(\xi - M_2 \xi_i)]$$

$$\xi = \sum_{i=1}^N \xi_i$$

numerical
solutions:





6.2 Ovulation

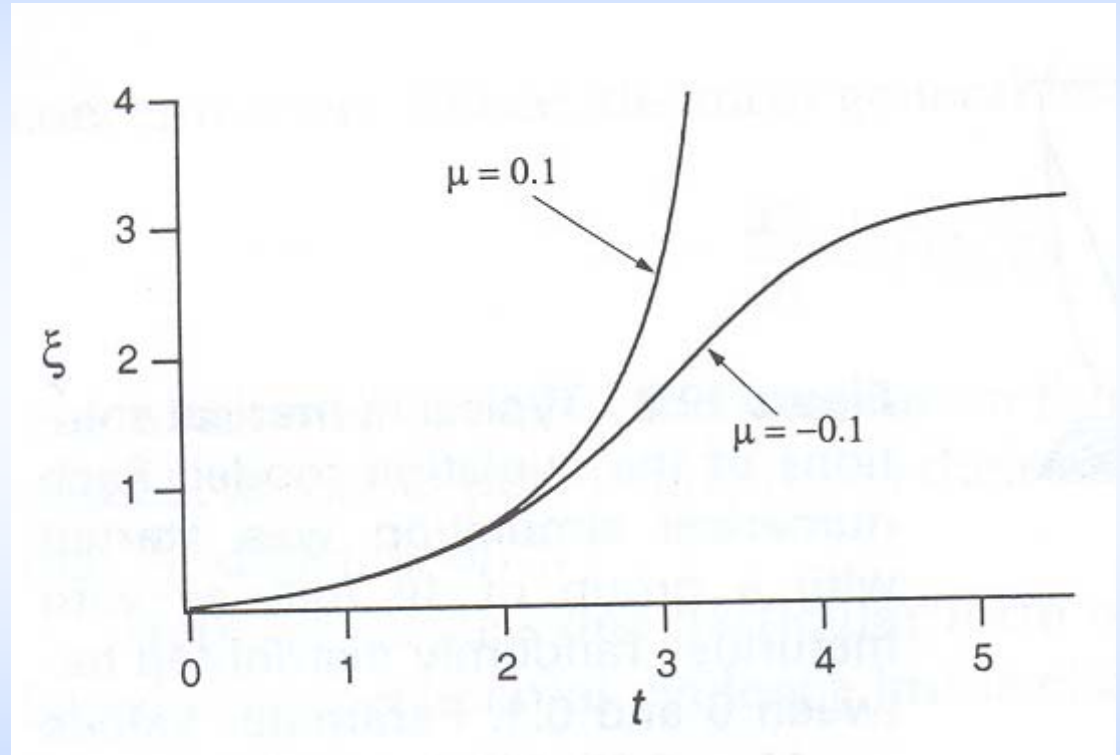
Lacker model:

symmetric solutions:

$$\frac{d\xi}{dt} = \xi + \mu\xi^3$$

solution:

$$\frac{\xi}{\xi_0} \sqrt{\frac{1 + \mu\xi_0^2}{1 + \mu\xi^2}} = e^t$$



$\mu > 0$ $\xi \rightarrow \infty$ *in finite time*

$\mu < 0$ $\xi \rightarrow \sqrt{-1/\mu}$ *for* $t \rightarrow \infty$

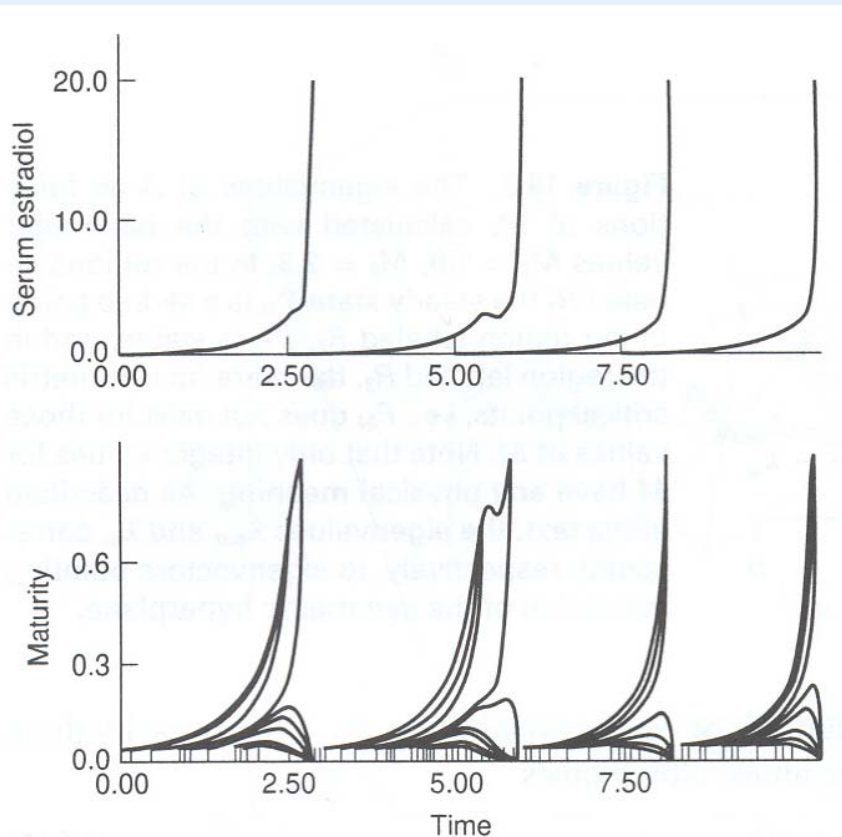




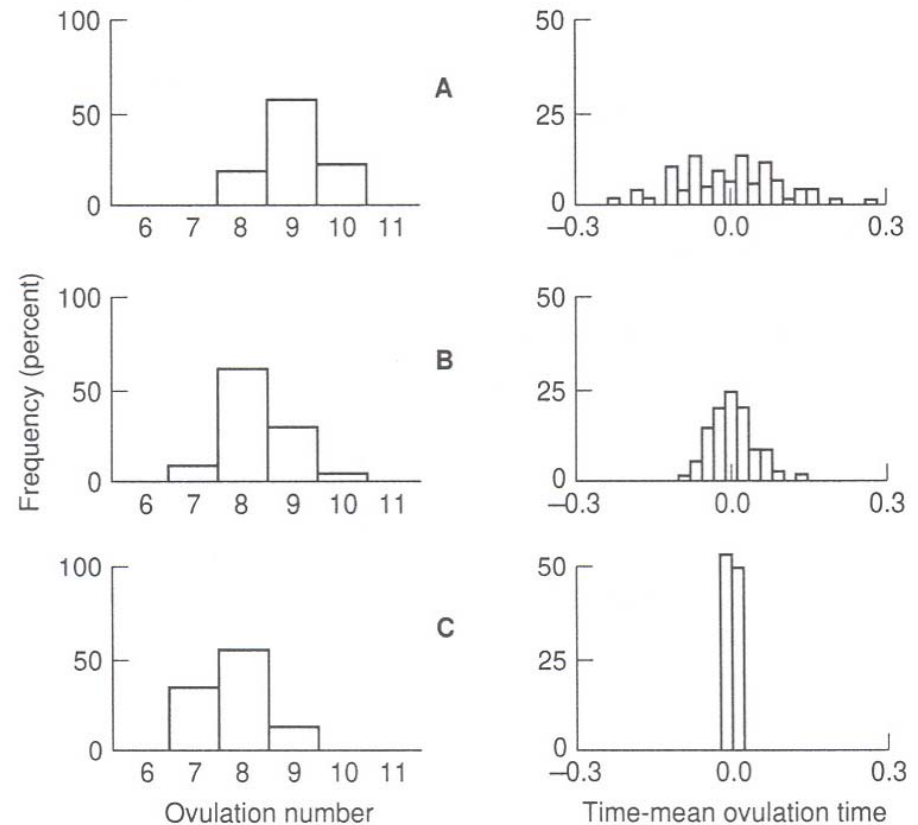
6.2 Ovulation

Lacker model:

follicles begin to develop
at random times:



effect of population size:



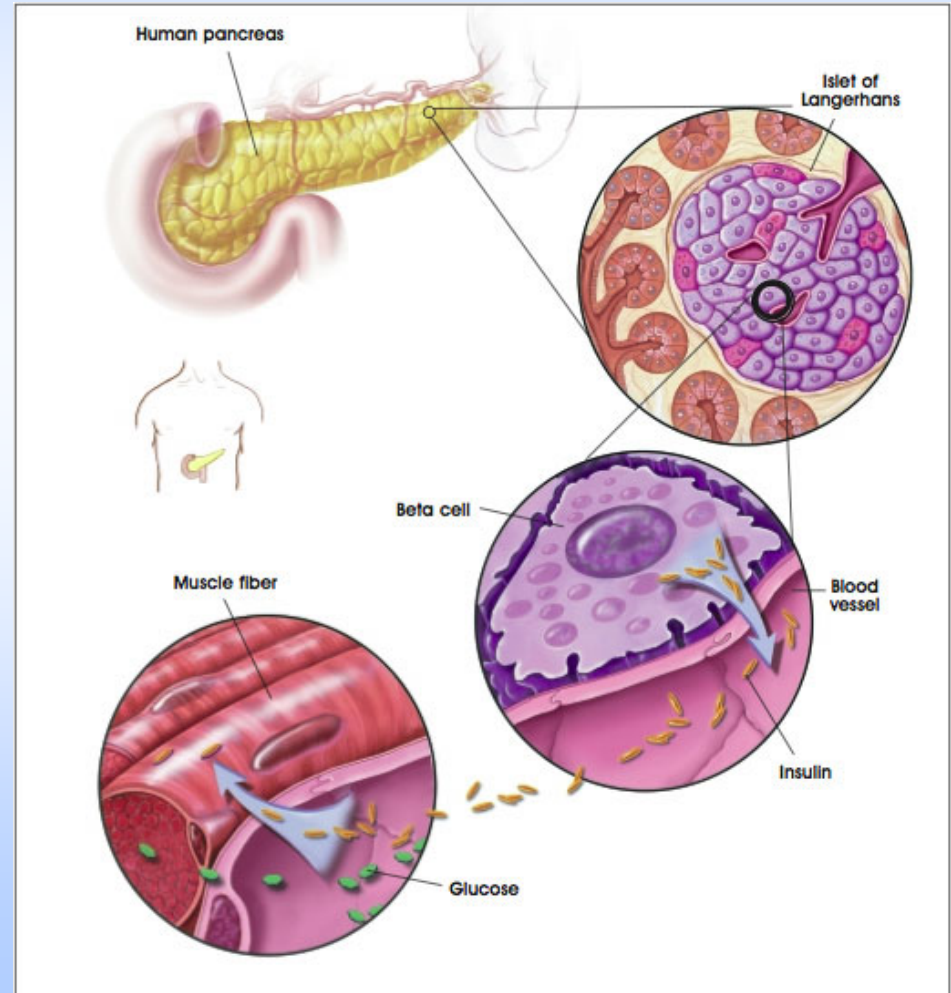
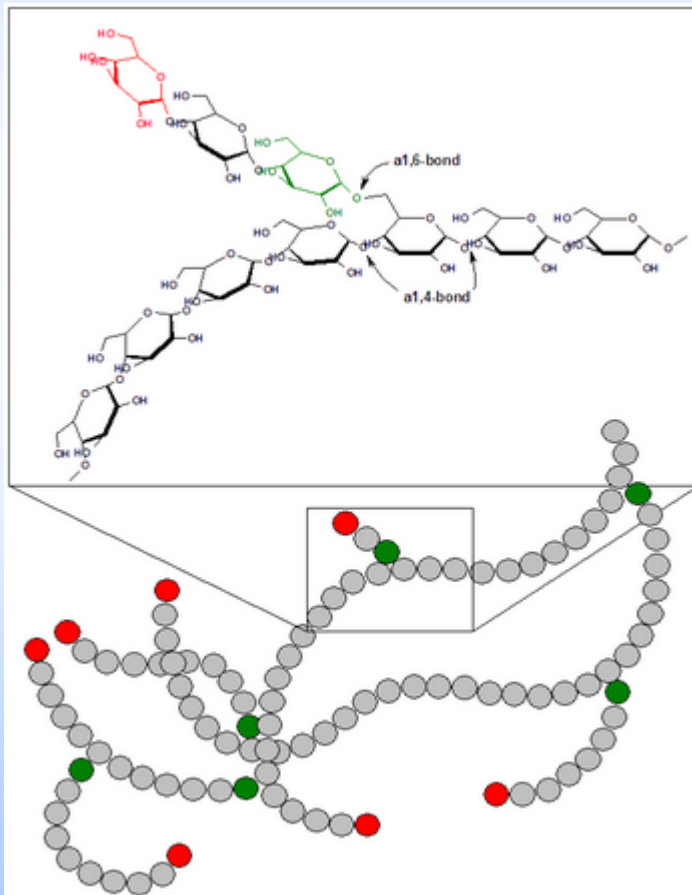


6.3 Glucose Metabolism

energy metabolism:

- anabolic (building) – glycogen, fatty acid
- catabolic (breakdown) – back to glucose

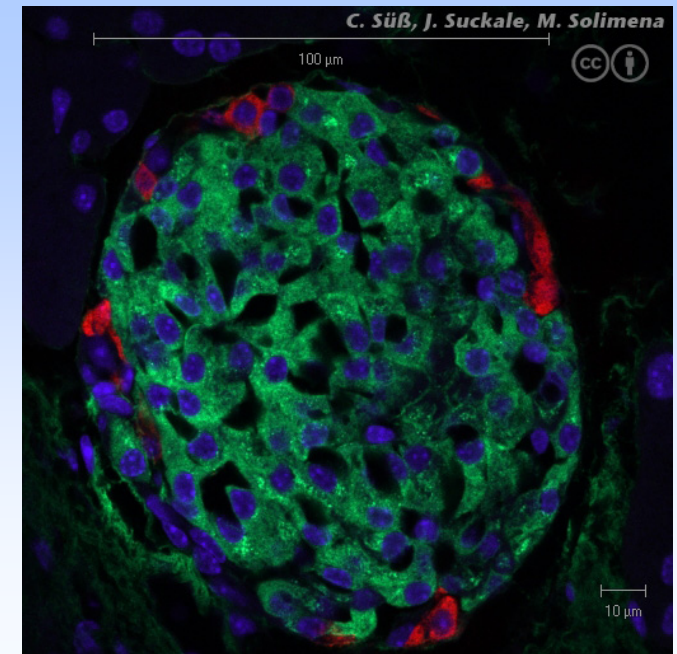
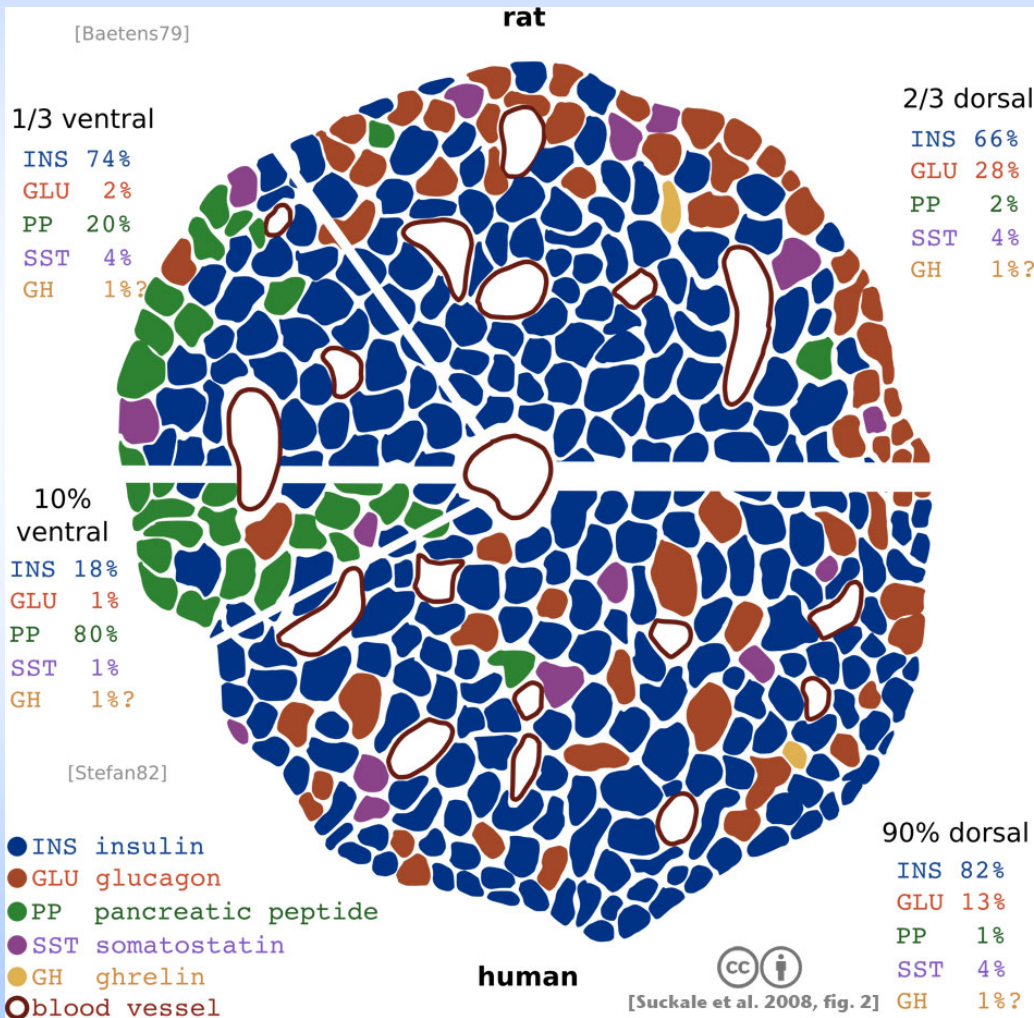
glycogen:





6.3 Glucose Metabolism

islets of Langerhans:



α cells: secrete **glucagon**
 β cells: secrete **insulin**
 δ cells: secrete **somatostatin**

a high concentration of glucose in the bloodstream stimulates the production of insulin, which in turn induces storage of excess nutrient





6.3 Glucose Metabolism

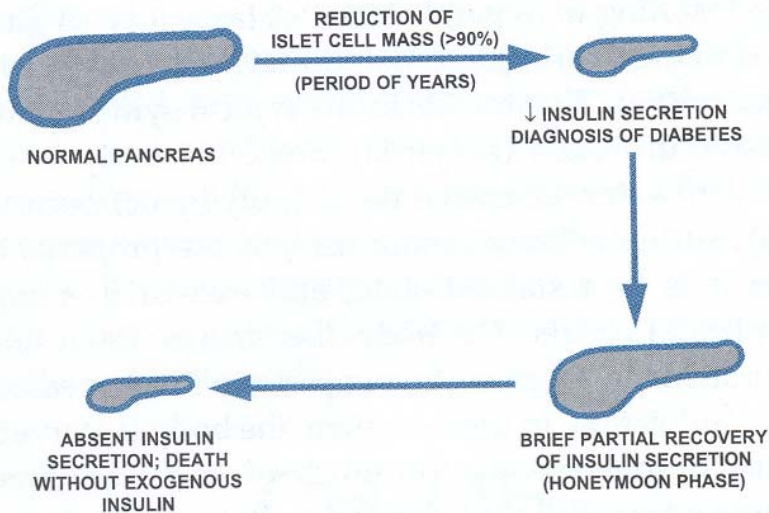
disorders: **DIABETES MELLITUS**

TYPE 1 DIABETES

TYPE 2 DIABETES

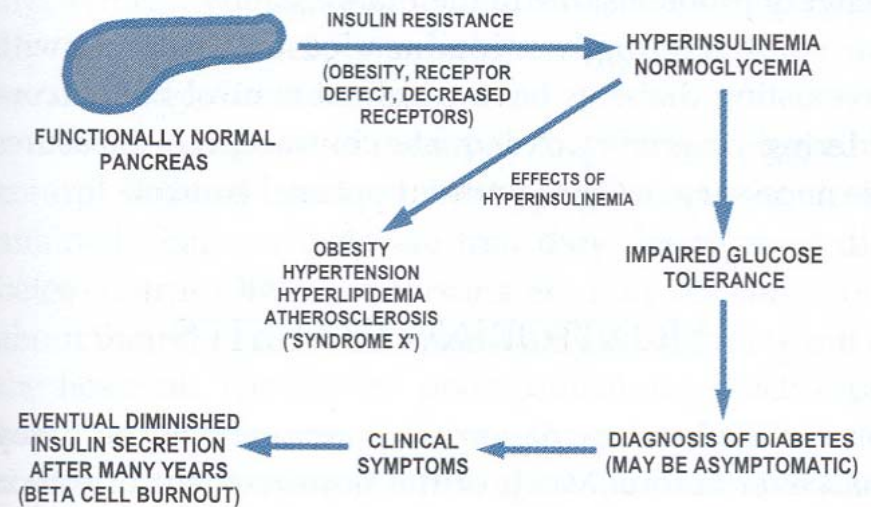
TYPE 1 (INSULIN-DEPENDENT) DIABETES

PATHOGENESIS: DESTRUCTION OF PANCREAS
IMMUNOLOGIC: MOST COMMON CAUSE (ANTI-ISLET CELL ANTIBODIES)



TYPE 2 (NON-INSULIN DEPENDENT) DIABETES

PATHOGENESIS: INEFFECTIVE USE OF ENDOGENOUS INSULIN
EVENTUAL DECREASE OF BETA CELL MASS OVER YEARS

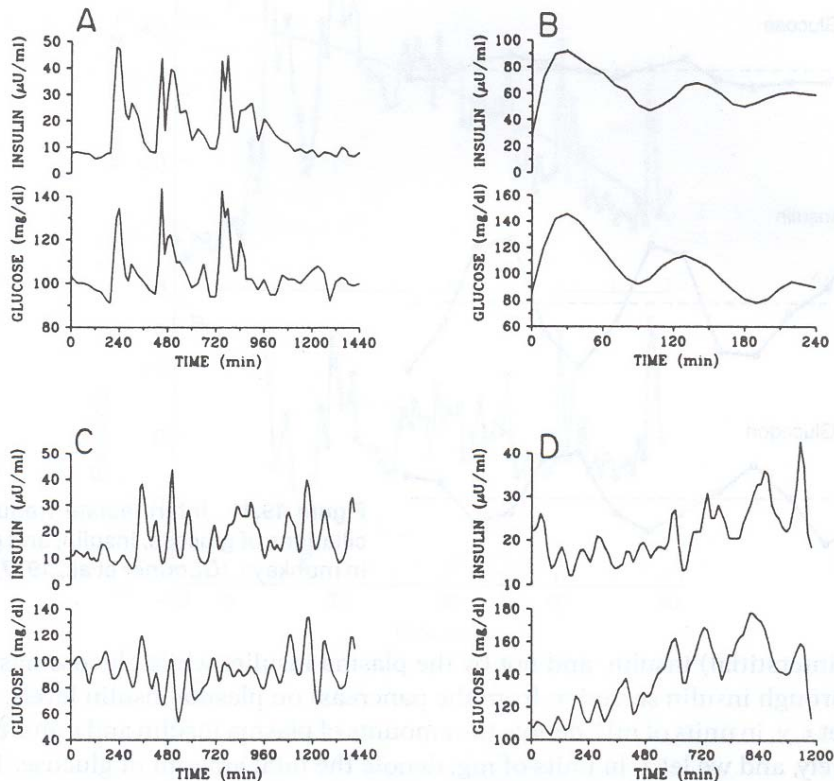




6.3 Glucose Metabolism

OBSERVATIONS:

ultradian oscillations:



- 1) oscillations occur during constant glucose infusion and are not dependent on periodic nutrient absorption from the gut; however, damped oscillations occur after a single stimulus such as a meal
- 2) glucose and insulin concentrations are highly correlated, with the glucose peak occurring about 10-20 minutes earlier than that of insulin
- 3) the amplitude of the oscillations is an increasing function of glucose concentration, while the frequency is not
- 4) the oscillations do not appear to depend on glucagon

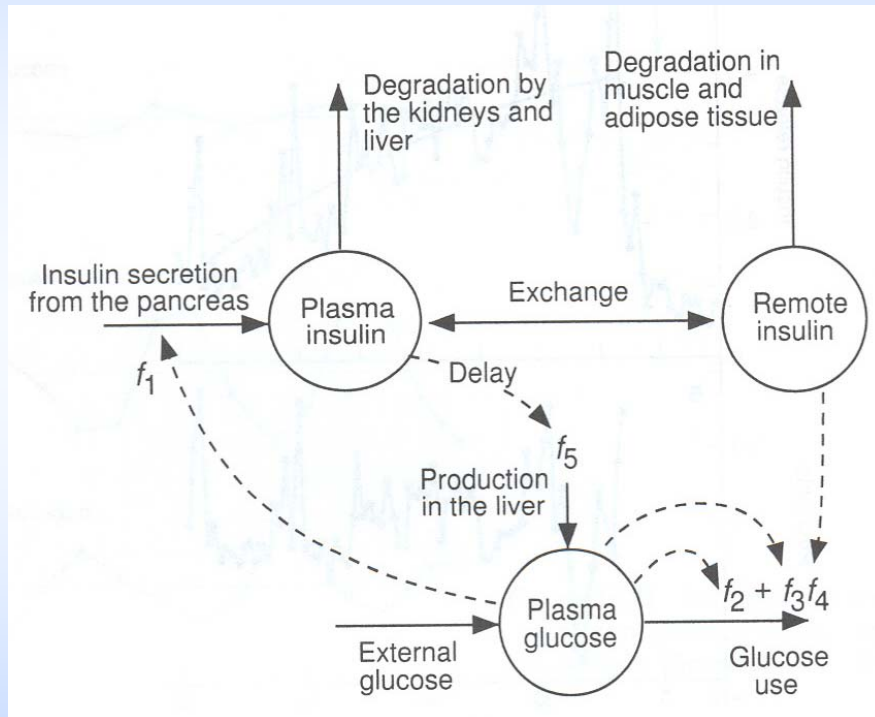




6.3 Glucose Metabolism

MODEL:

ultradian oscillations:



$$\frac{dx}{dt} = f_1(z) - \left(\frac{x}{V_1} - \frac{y}{V_2} \right) E - \frac{x}{t_1}$$

$$\frac{dy}{dt} = \left(\frac{x}{V_1} - \frac{y}{V_2} \right) E - \frac{y}{t_2}$$

$$\frac{dz}{dt} = f_5(h_3) + I - f_2(z) - f_3(z) f_4(z)$$

three-stage linear filter:

$$t_3 \frac{dh_1}{dt} = x - h_1$$

$$t_3 \frac{dh_2}{dt} = h_1 - h_2$$

$$t_3 \frac{dh_3}{dt} = h_2 - h_3$$

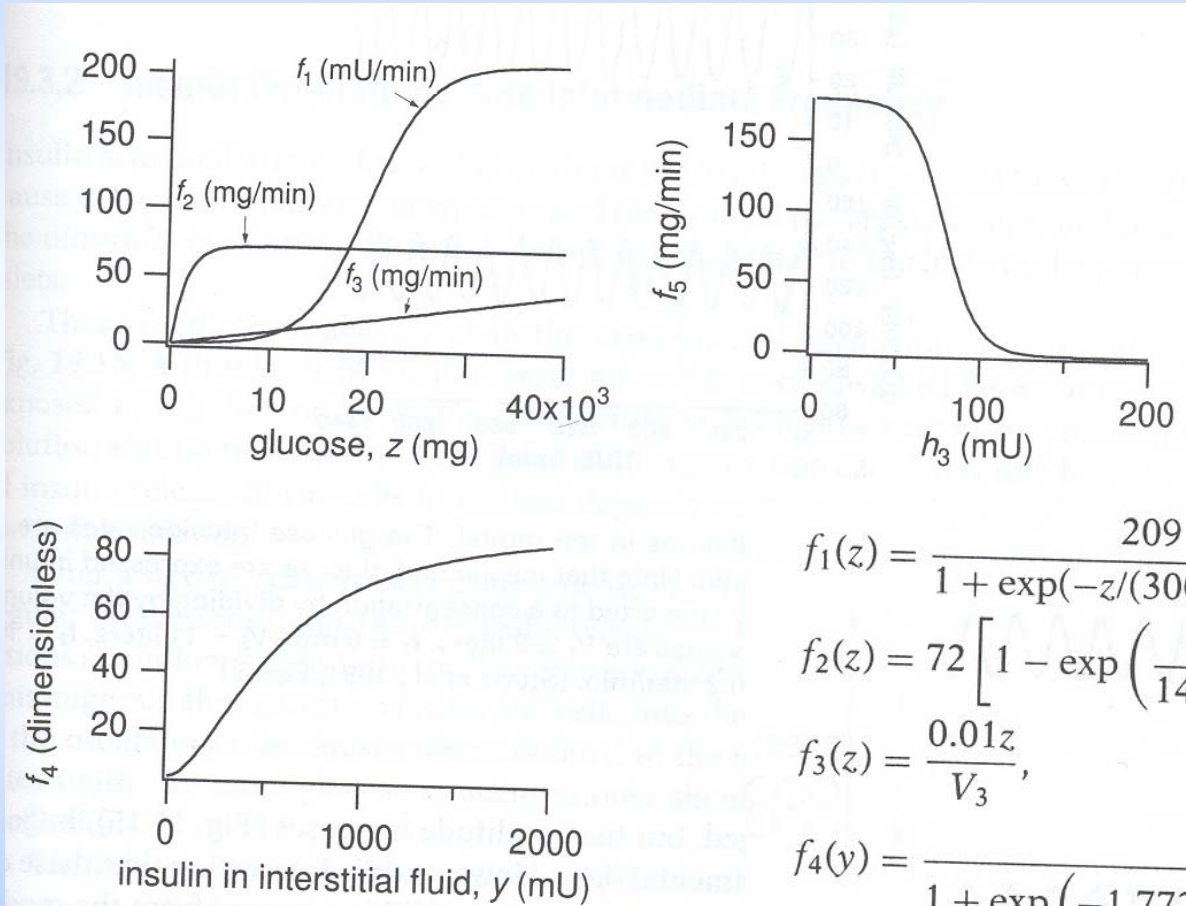




6.3 Glucose Metabolism

ultradian oscillations:

MODEL FUNCTIONS:



$$f_1(z) = \frac{209}{1 + \exp(-z/(300V_3) + 6.6)},$$

$$f_2(z) = 72 \left[1 - \exp\left(\frac{-z}{144V_3}\right) \right],$$

$$f_3(z) = \frac{0.01z}{V_3},$$

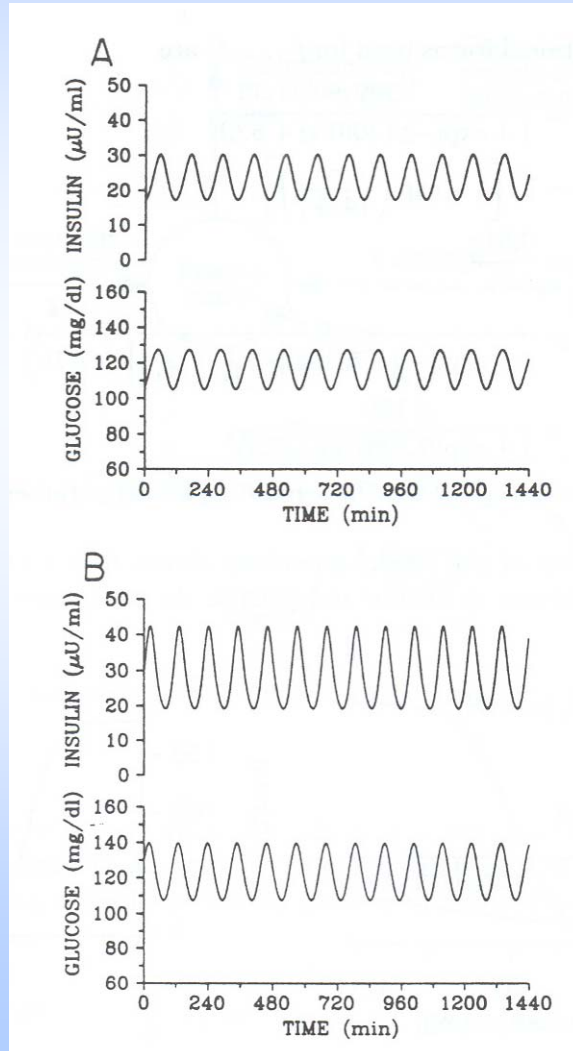
$$f_4(y) = \frac{90}{1 + \exp\left(-1.772 \log \left\{ y \left[\frac{1}{V_2} + \frac{1}{Et_2} \right] \right\} + 7.76 \right)} + 4,$$

$$f_5(h_3) = \frac{180}{1 + \exp(0.29h_3/V_1 - 7.5)},$$



6.3 Glucose Metabolism

ultradian oscillations:



MODEL RESULTS:

oscillations disappear:

- if the compartment of remote insulin is removed from the model
- if the delay caused by the three-stage filter is either too large or too small



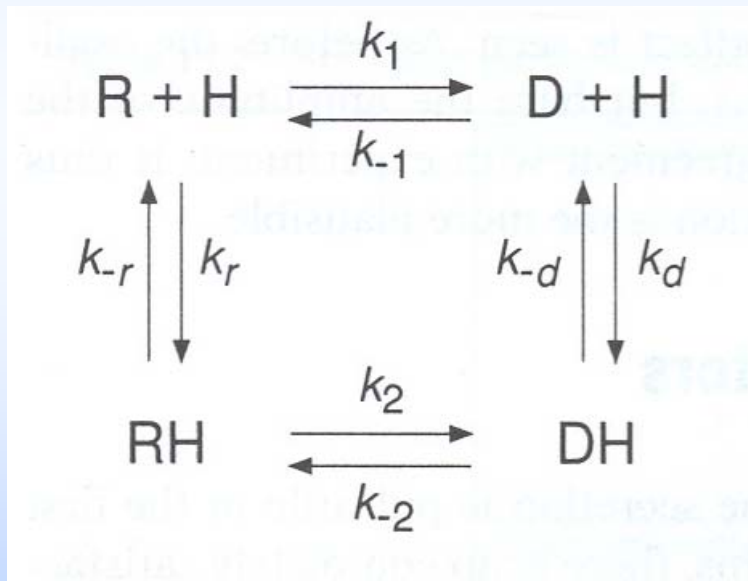


6.4 Adaptation of Hormone Receptors

exact adaptation:

receptor responds to a time-varying input,
but does not response to a constant hormone stimulus

hormone
concentration
 $H(t)$



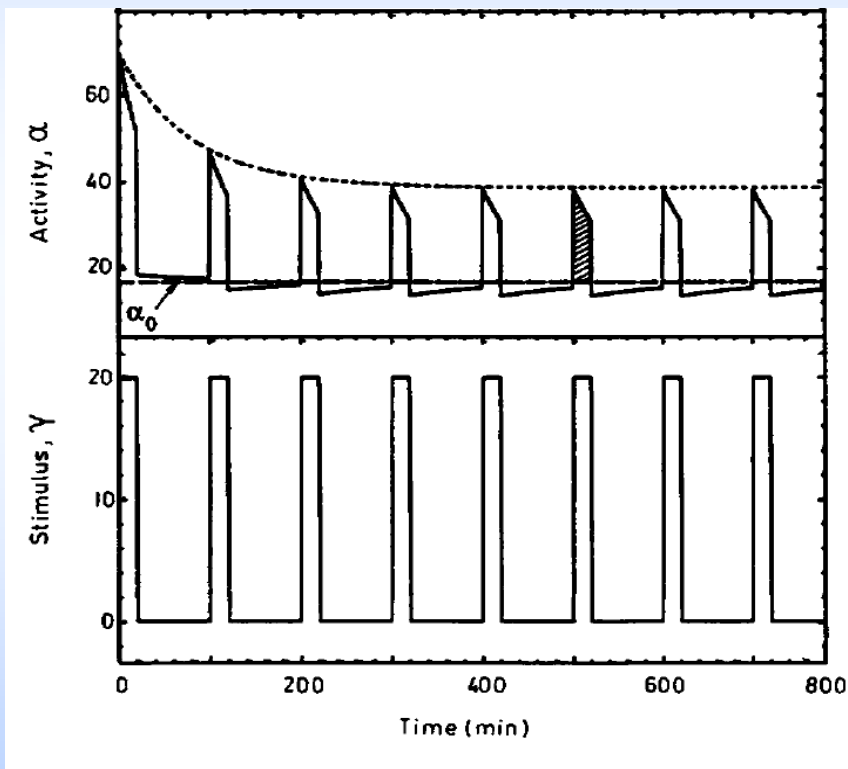
activity
 $A(t)$
+ cell response



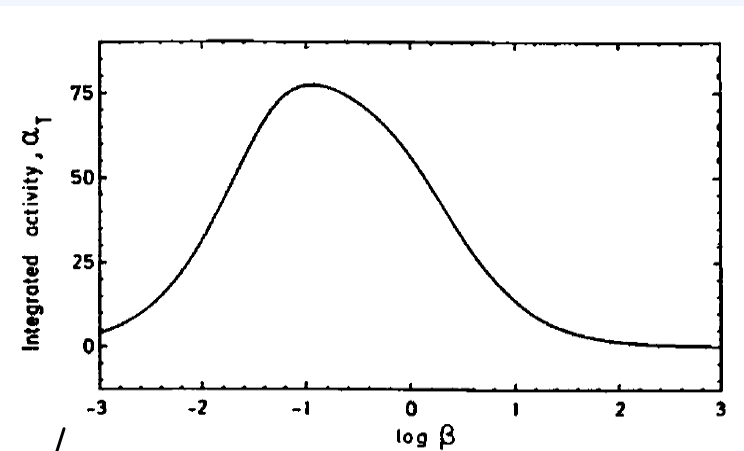
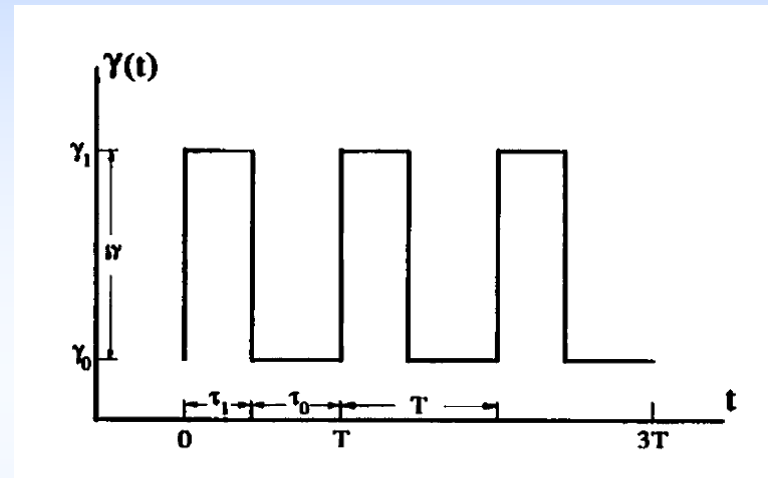


6.4 Adaptation of Hormone Receptors

activity curve generated by a periodic square-wave stimulus:



stimulus yielding
maximum responsiveness



$$\beta = \tau_1 / \tau_0$$

