

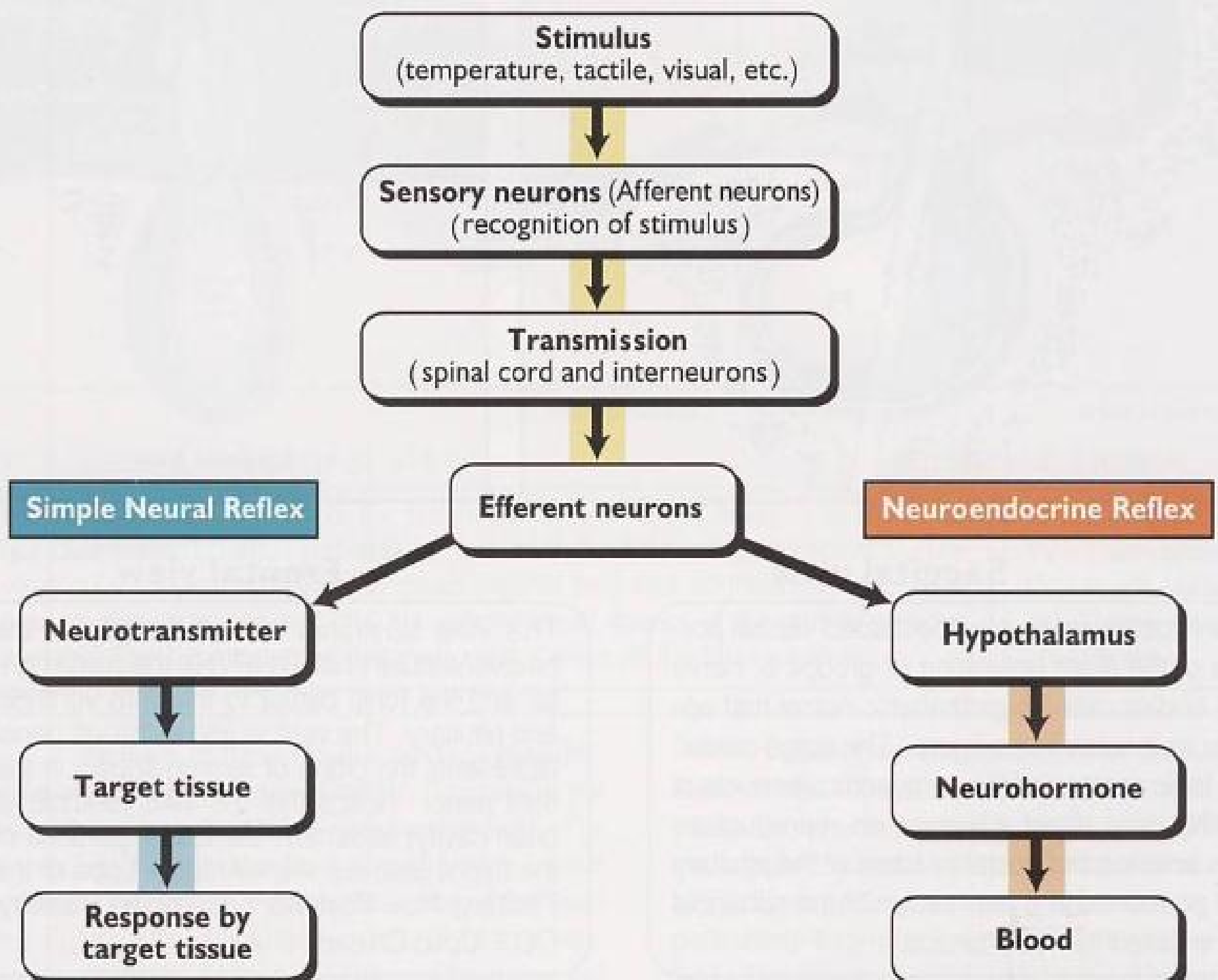
Neuro-Endocrine Regulation of Reproduction

Introduction

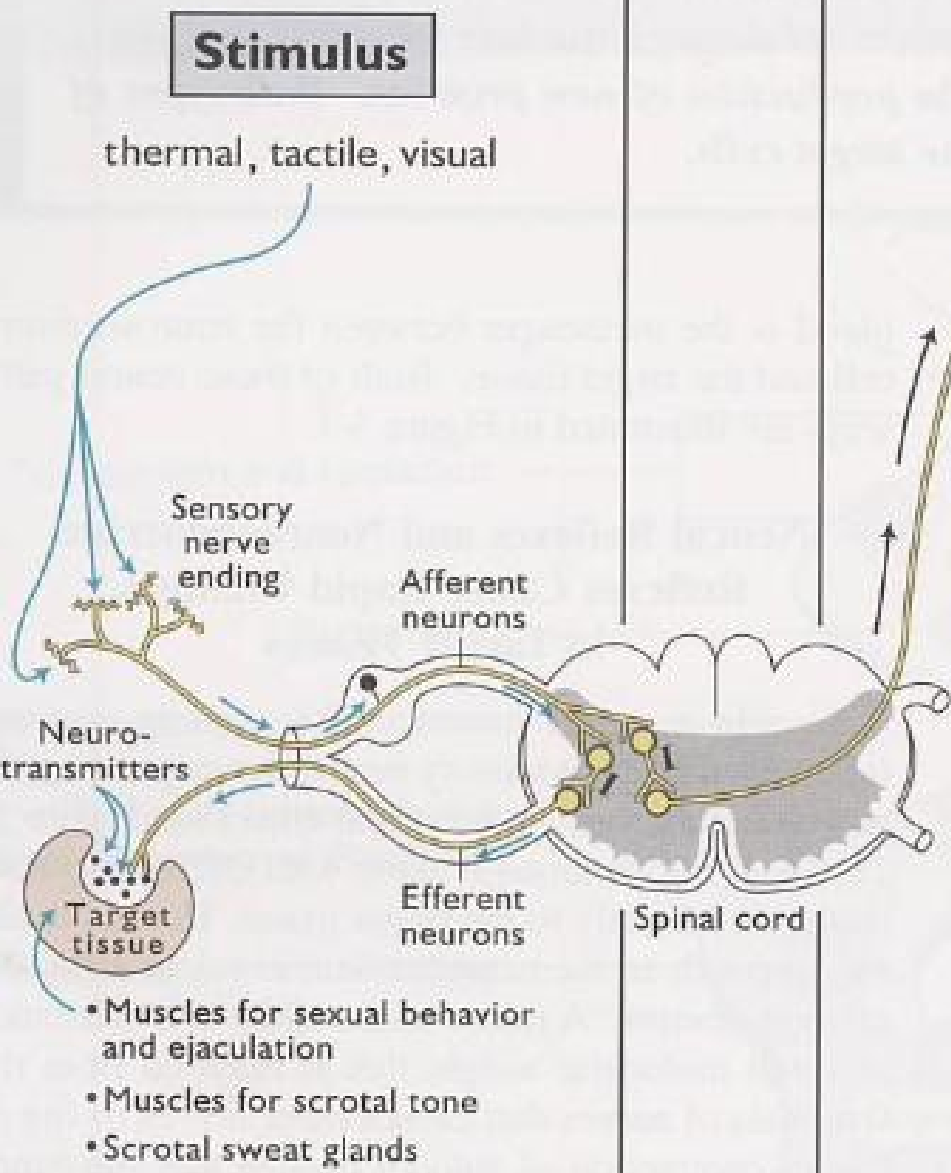
- Reproduction is controlled by complex interplay between **Nervous and Endocrine System - Neuro-Endocrine control**
- The two systems constantly interact to ***Initiate, Coordinate & Regulate*** all reproductive functions
- NS rapid response (seconds)
- ES slower response (minutes – hours)
- **Neuro-Endocrine control** of reproduction involves biochemical interaction between **Hypothalamus – Pituitary – Gonads - Genital Tract**

Neural control

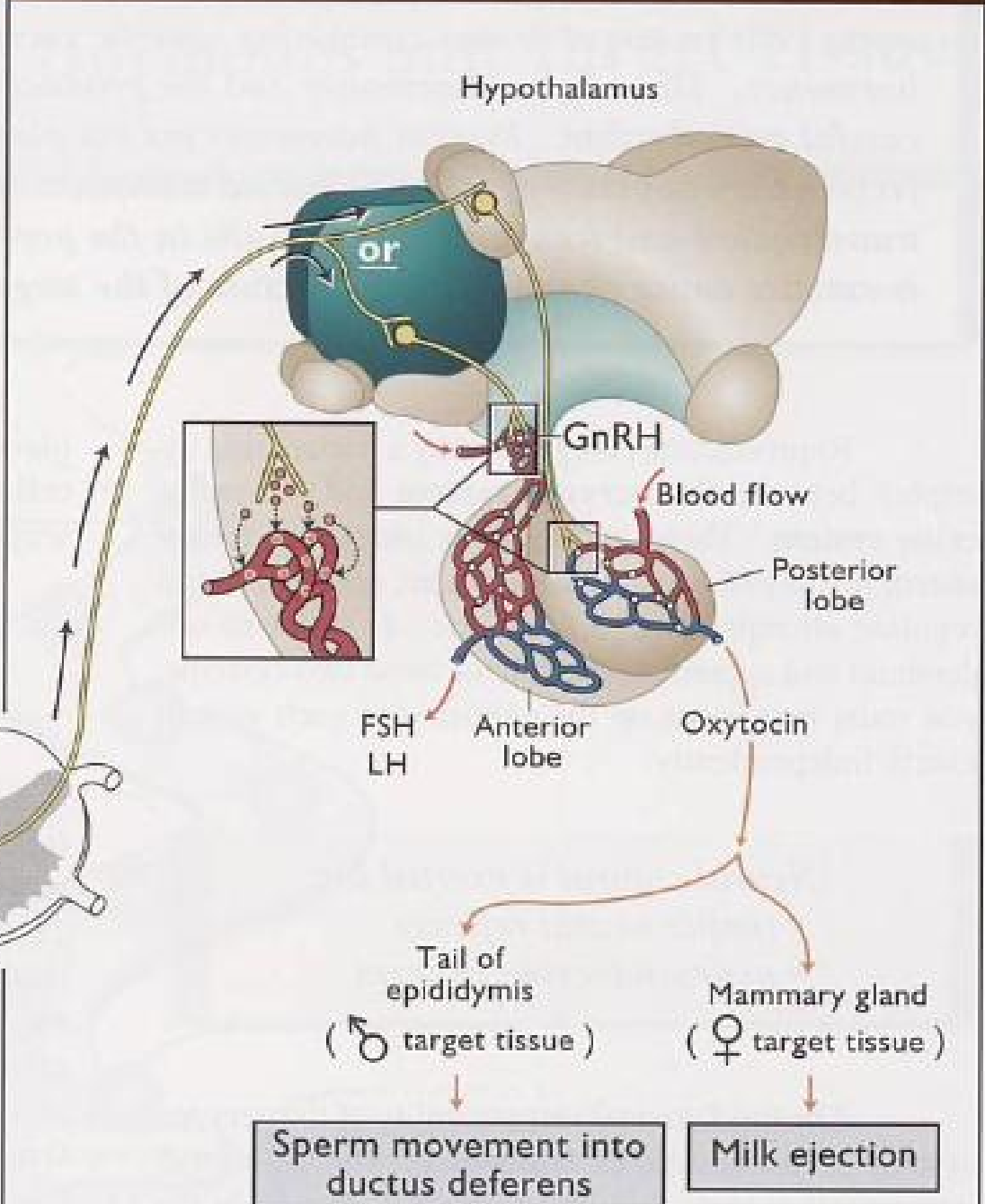
- NS translate external stimuli to nervous signal that bring **rapid** change in reproductive organs/tissue
- **Nervous control of reproduction**
 - └ Simple neural reflex (NT)
 - └ Neuroendocrine reflex (Neurohormones)



Simple Neural Reflex



Neuroendocrine Reflex



Endocrine Control

- **Endocrine Glands** controls reproduction by secreting **Hormones**
- **Endocrine Glands**: A ductless gland - Secretes substances (hormones) into blood or lymph **Vs Exocrine glands**
- Hormones; A substance produced by **endocrine glands** and released in to the blood stream to act on a remote **target tissue** and change its functional activity (protein synthesis)
- Hormones may get transported in circulation either freely or bound to carrier molecules
- Target tissues are tissues whose cells carry the

Cont ...

- Hormones are secreted into blood stream in minute quantities (nanogram to picogram)
- Hormones disappear from the body within a short time of their secretion because they get metabolized (Liver, Kidney, Lung) and excreted in urine/feces – short **Half Life**
- **Strength of hormonal action depends on;** pattern and duration of secretion, half life, and Hormonal potency
- **Hormonal potency** depends on receptor density and receptor-hormone affinity

Reproductive Hormones (RH)

- Reproductive Hormones are classified by their ***origin, primary mode of action, biochemical structure and Mechanism of Action***

1. Origin of RH

- ‖ **Hypothalamus**; GnRH, TRH, CRH, GH-RH, GH-IH,
- ‖ **Pituitary**; LH, FSH, STH, TSH, ACTH, hMG, Oxytocin
- ‖ **Gonads**: testosterone, DHT, estrogen, inhibin,

Cont ...

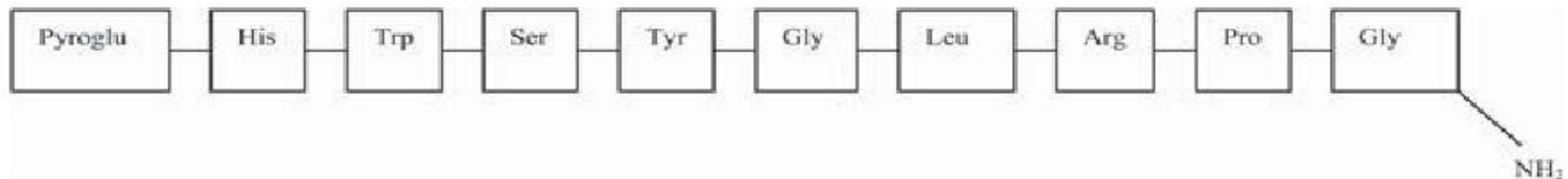
2. Mode of Action

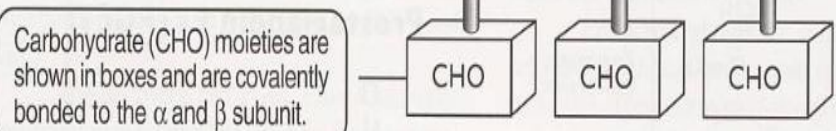
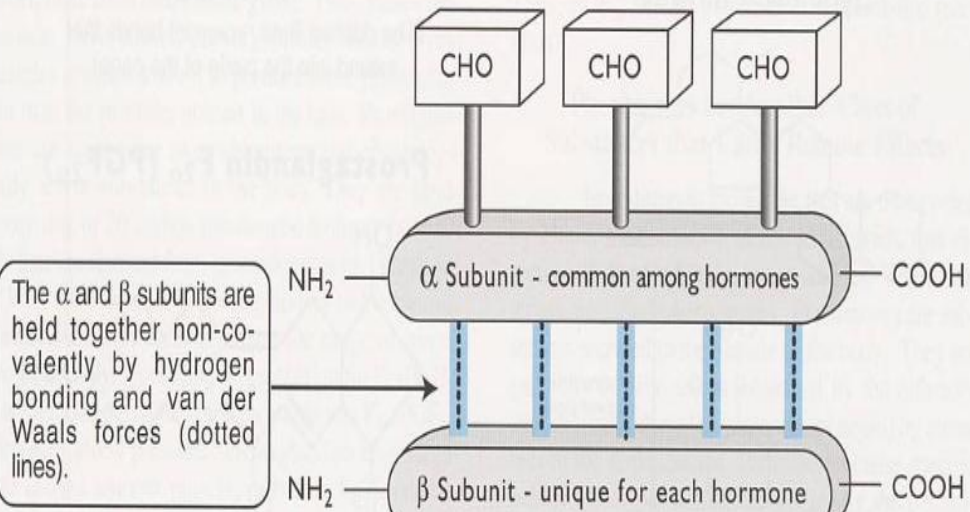
- **Primary Hormones of reproduction**
 - ┌ Stimulate secretion of other hormones
(**Releasing Hormones** - GnRH)
 - ┌ Stimulate Gonads (**Gonadotropins** - FSH/LH)
 - ┌ Sexual Promoters (Sex Steroids -Androgens)
- drive all reproductive functions
- **Secondary Hormones of Reproduction;**
Eg. Thyroxine, Adrenal Corticoids, GH - affect reproduction indirectly by maintaining homeostasis and sometimes more directly

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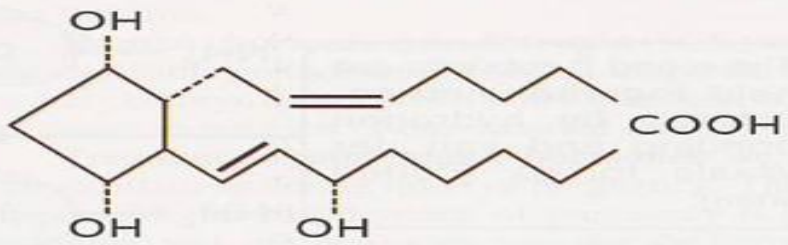
3. Biochemical Composition of RH - **affects artificial use ?**

- 1 **Polypeptides**; few aa Eg. GnRH
- 1 **Glycopeptides**; polypeptides with CHO moieties variable weight Eg. FSH, LH, TSH, ACTH, GH, Inhibin
- 1 **Steroids**; Testosterone & DHT
- 1 **Fatty acid**; Prostaglandins (PGF 2a and PGE2)
- 1 **Modified AA**; Melatonin from Pinal Gland

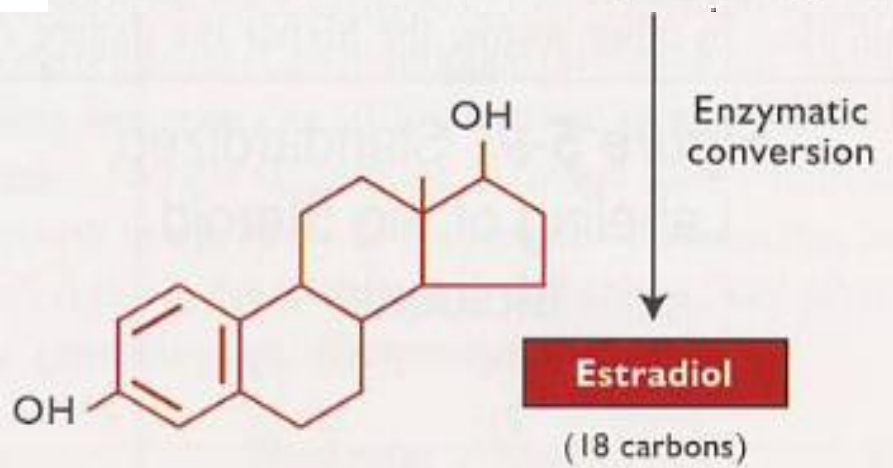
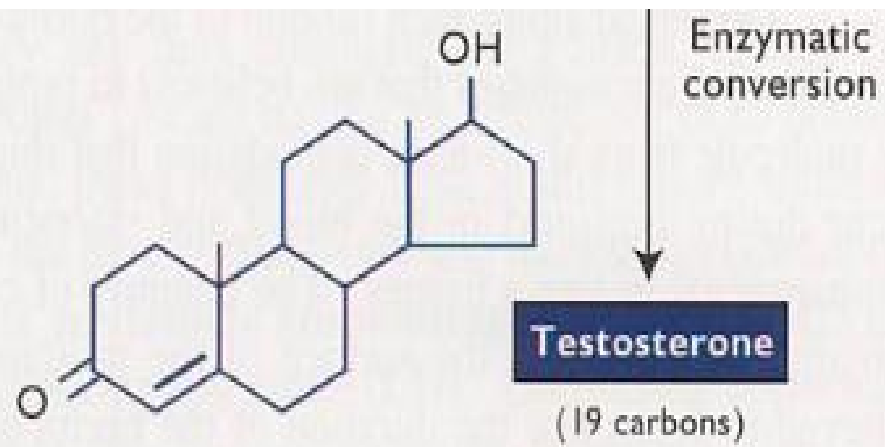
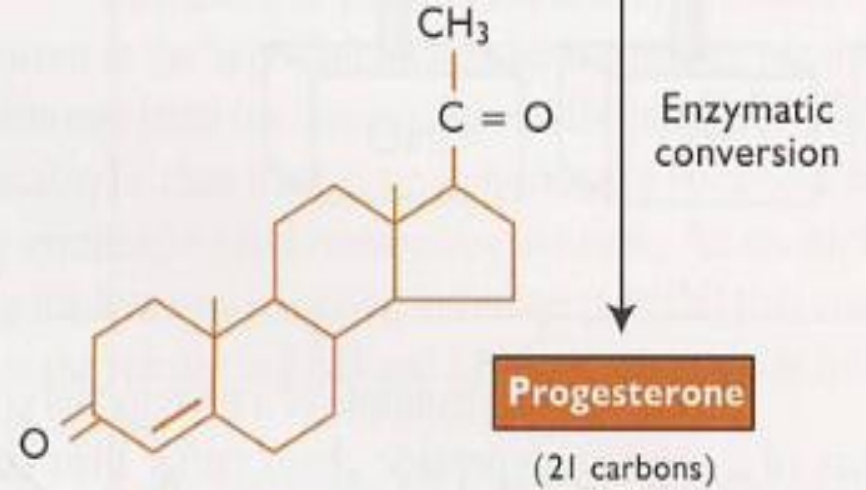
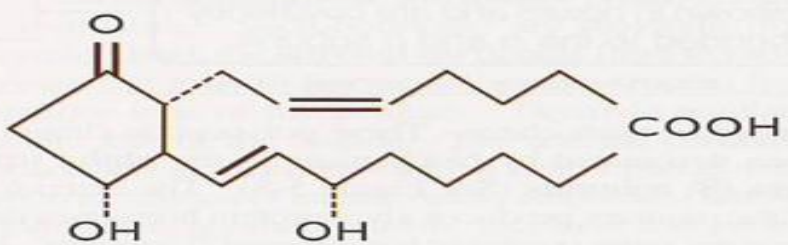




Prostaglandin F₂ α (PGF₂ α)



Prostaglandin E₂ (PGE₂)



Chemical Structure of Hormones

Molecular size of hormones that regulate

reproduction	Hormone	Molecular Weight
	FSH	30,000 to 37,000
	LH	26,000 to 32,000
	Prolactin	23,000 to 25,000
	HCG	37,700
	eCG	28,000
	Inhibin	>10,000
	Relaxin	6,500
	ACTH	4,500
	Oxytocin	1,007
	GnRH	1,200
	Estradiol	300
	Testosterone	300
	Progesterone	300
	PGF	300

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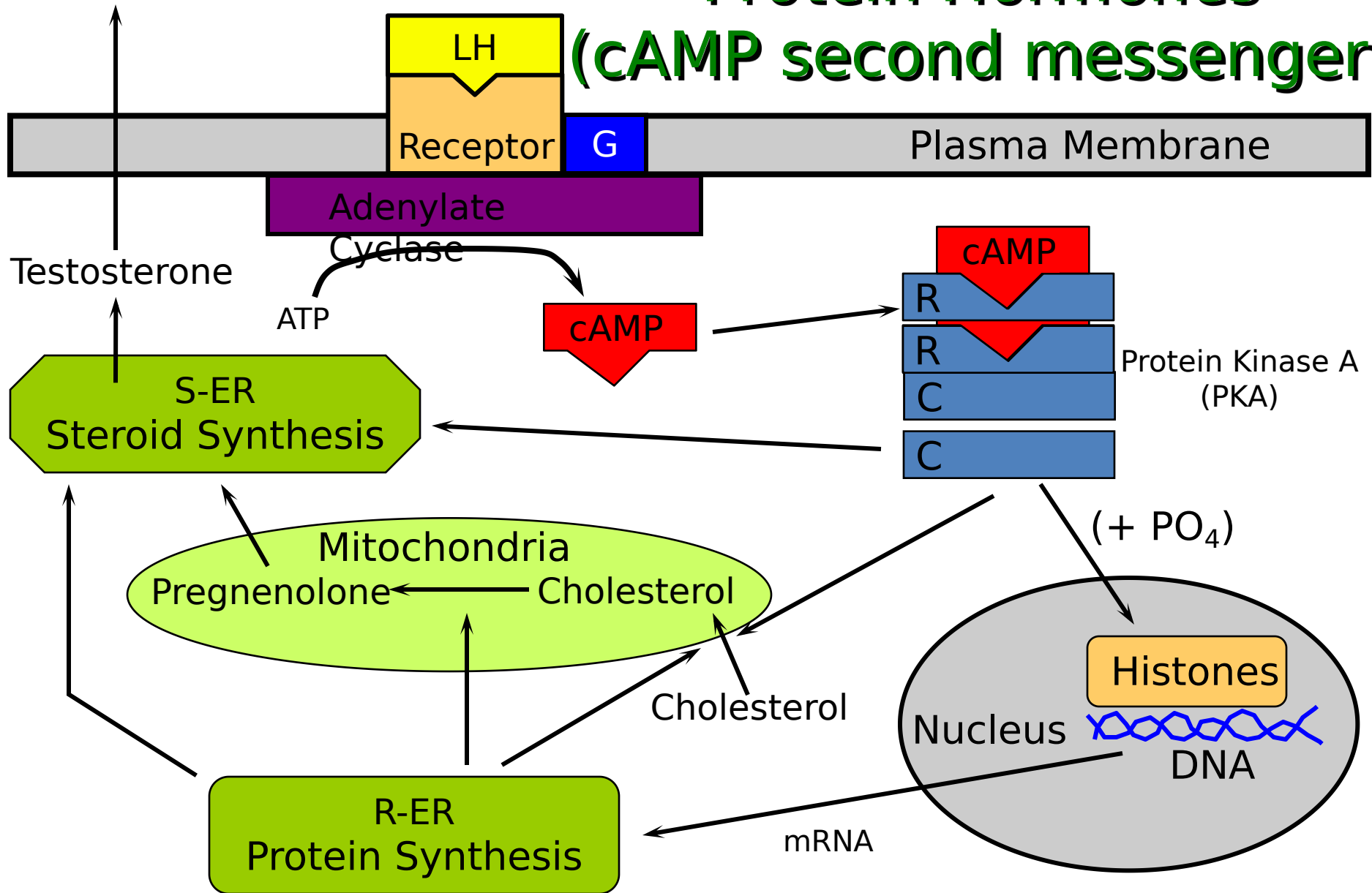
4. Mechanism of Action

- Depends on the biochemical composition of hormones
- └ Proteins hormones use cell **membrane bound receptors** to attach target cells and stimulation involves a **Second Messenger** (cAMP or Calcium)
- └ Steroid Hormones diffuse through cell membrane and attach to **nuclear receptors** to stimulate target cells

Mechanism of Hormone Action

Protein Hormones

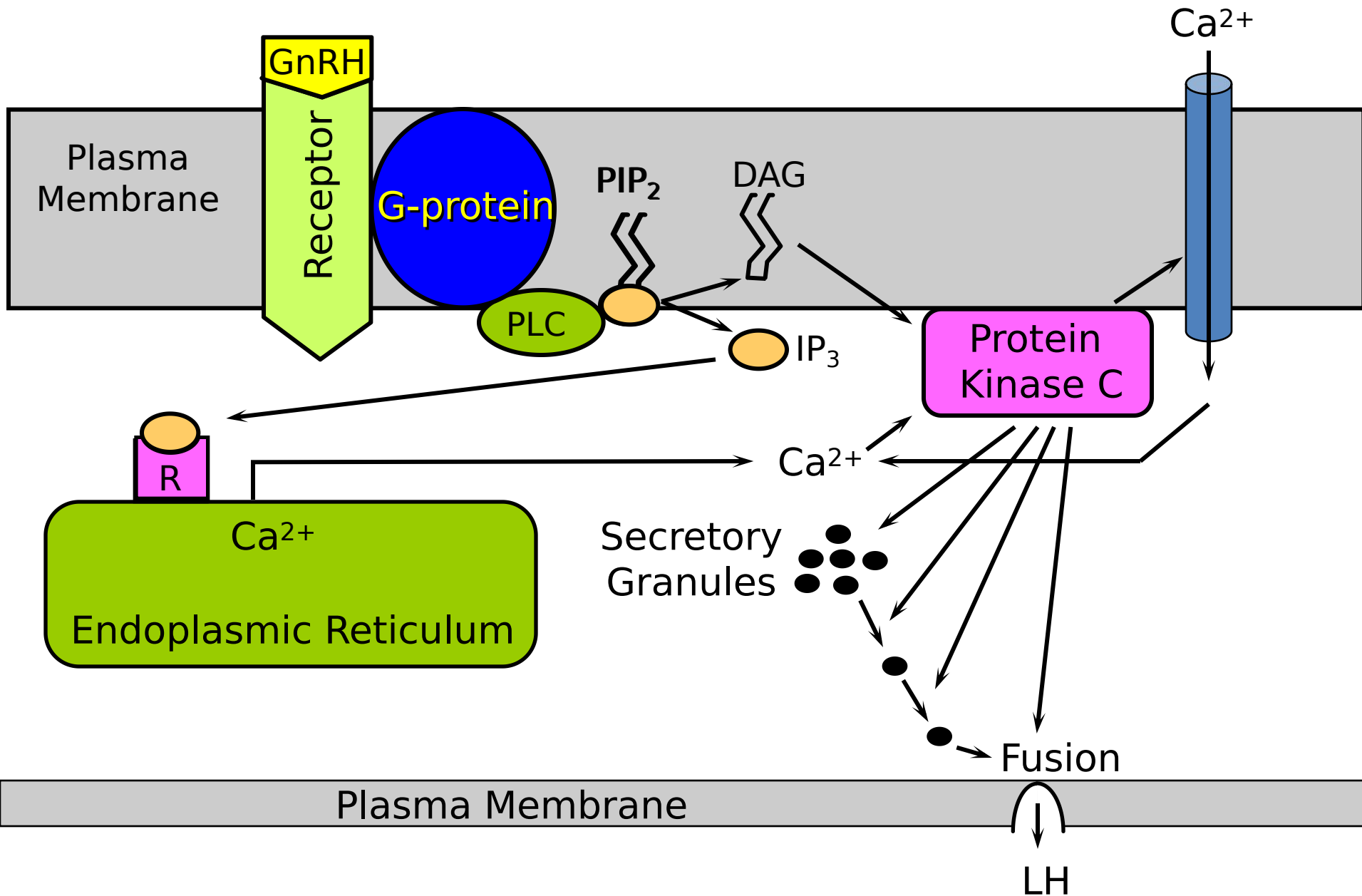
(cAMP second messenger)



cAMP Second Messenger Hormones

- Anterior Pituitary Hormones
 - LH, FSH, Prolactin
 - STH, ACTH, TSH
- Placental Hormones
 - hCG, eCG

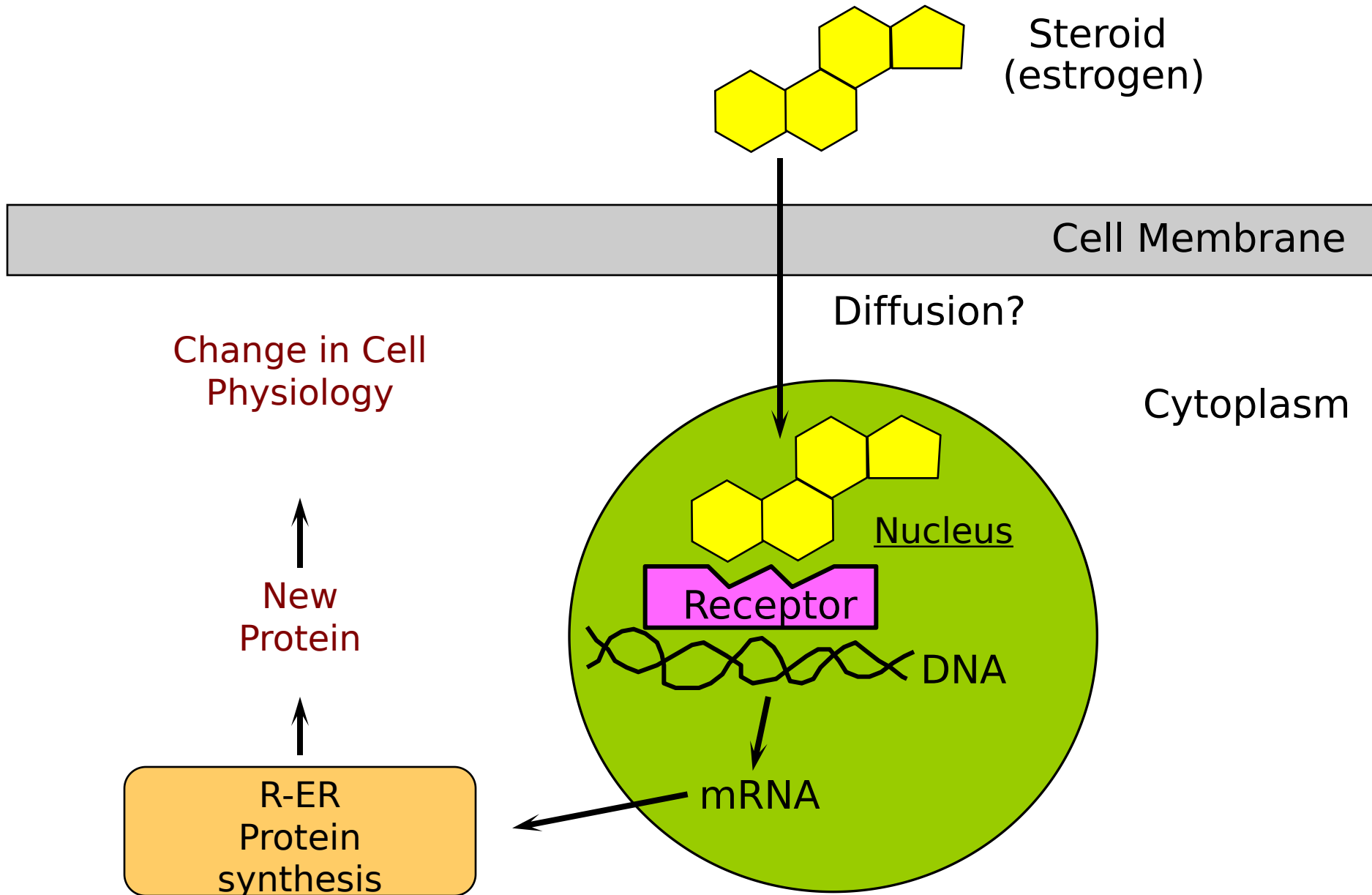
Protein Hormones (Ca^{2+} Second Messenger)

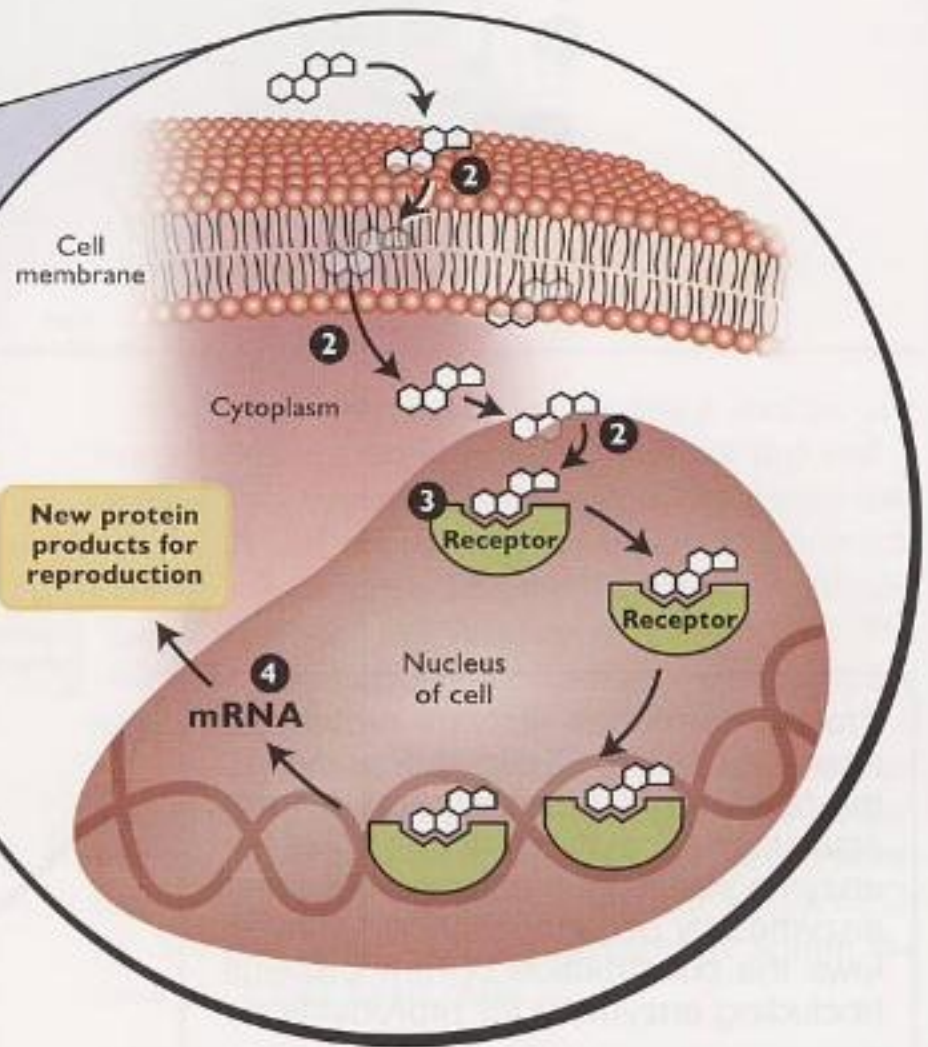
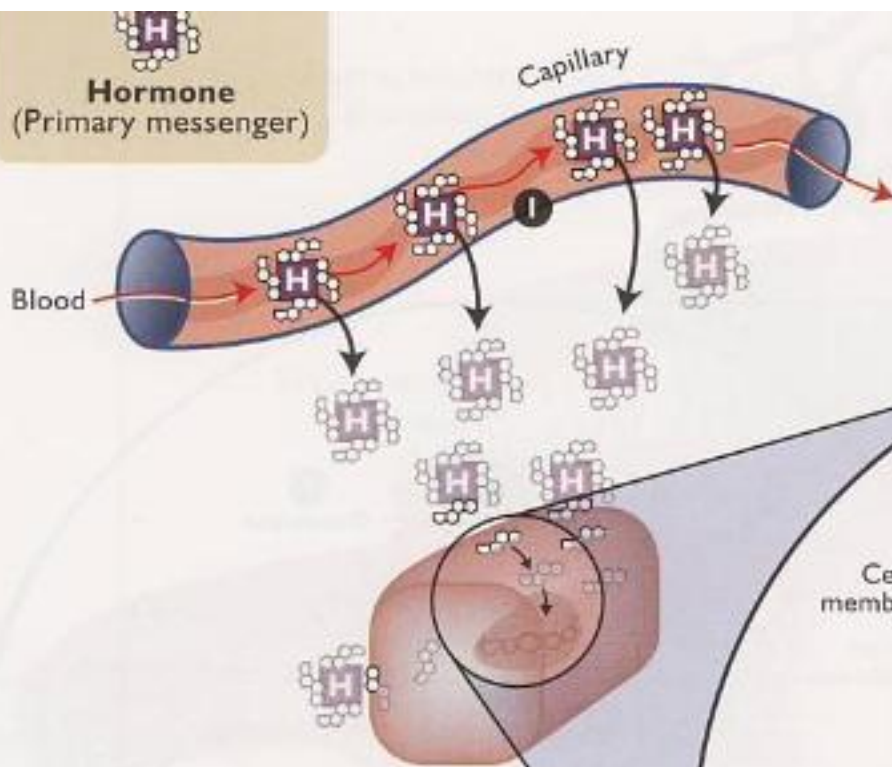


Calcium Second Messenger Hormones

- GnRH
 - triggers release of LH in anterior pituitary
- Oxytocin
 - triggers contractions of smooth muscle
- PGF₂
 - triggers apoptosis of cell
 - inhibition of progesterone synthesis

Steroid Hormone Action





Steroids diffuse through the plasma membrane, cytoplasm and nuclear membrane of the target cell. They bind to nuclear receptors that trigger mRNA production and eventually synthesis of new proteins including enzymes.

Steroid Hormone Mechanism

- Estradiol
- Testosterone, Dihydrotestosterone
- Cortisol

Cont ...

- **Pheromones**; substances secreted to the outside of the body to modulate sexual behavior
- Volatile in nature and Detected by **Olfactory system** of same species
- Pheromones affect the behavior and physiology of an animal including onset of puberty, detection female in heat

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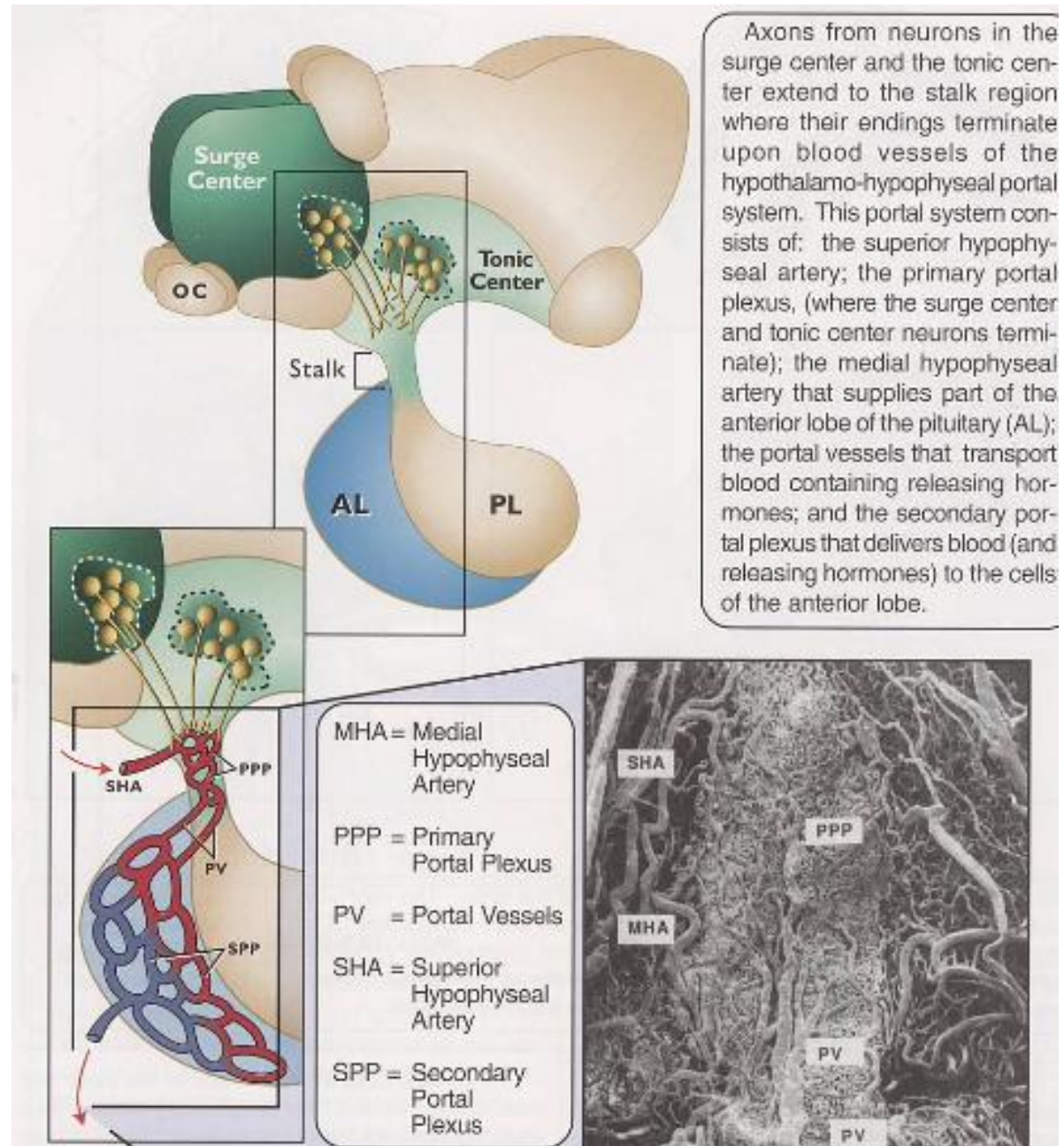
Hypothalamus is neural control center of reproductive hormones (1^{ry} or 2^{ry})

- The hypothalamus is stimulated by higher brain centers (external stimuli) to work in a stimulatory or inhibitory manner (by releasing several hormone-specific releasing/inhibiting factors = neurohormones).
- Hypothalamic **Releasing/Inhibiting Hormones** – control secretion of **tropic hormones from anterior pituitary**
- **Indirectly Controls:** appetite, thirst, body temperature, vasomotor activity, emotion, use of body nutrient reserves, activity of intestine, sleep, **sexual behavior and reproduction**

Releasing Hormones of the Hypothalamus

- Gonadotropin releasing hormone (GnRH)
 - » LH, FSH release
- Thyrotrophin releasing hormone (TRH)
 - » TSH and Prolactin release
- Corticotrophin releasing hormone (CRH)
 - » ACTH release
- Growth hormone releasing hormone (GH-RH)
- Somatostatin (Growth Hormone Inhibiting Hormone)

Hypothalamic
Neurons
communicate
with the Anterior
lobe of Pituitary
Gland through a
**Hypothalamo-
Hypophyseal
Portal System**
(specialized
capillary
network)



Preoptic
nuclei cell

**GnRH
Nuclei**

Superior
hypophyseal
artery

**Cells of
Anterior
Pituitary**

- LH
- FSH
- Prolactin
- STH
- TSH
- ACTH

Capillary
plexus

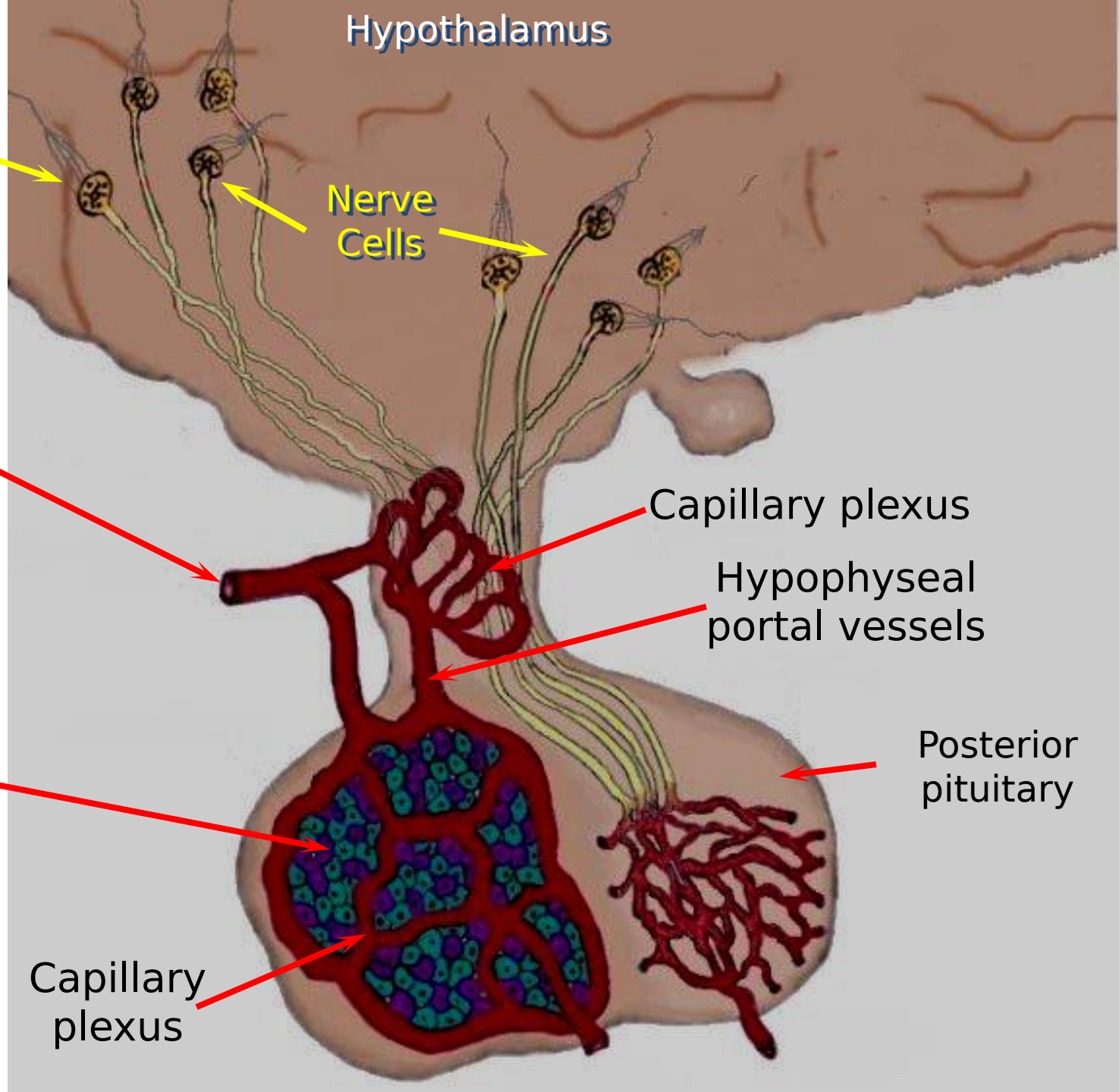
Hypothalamus

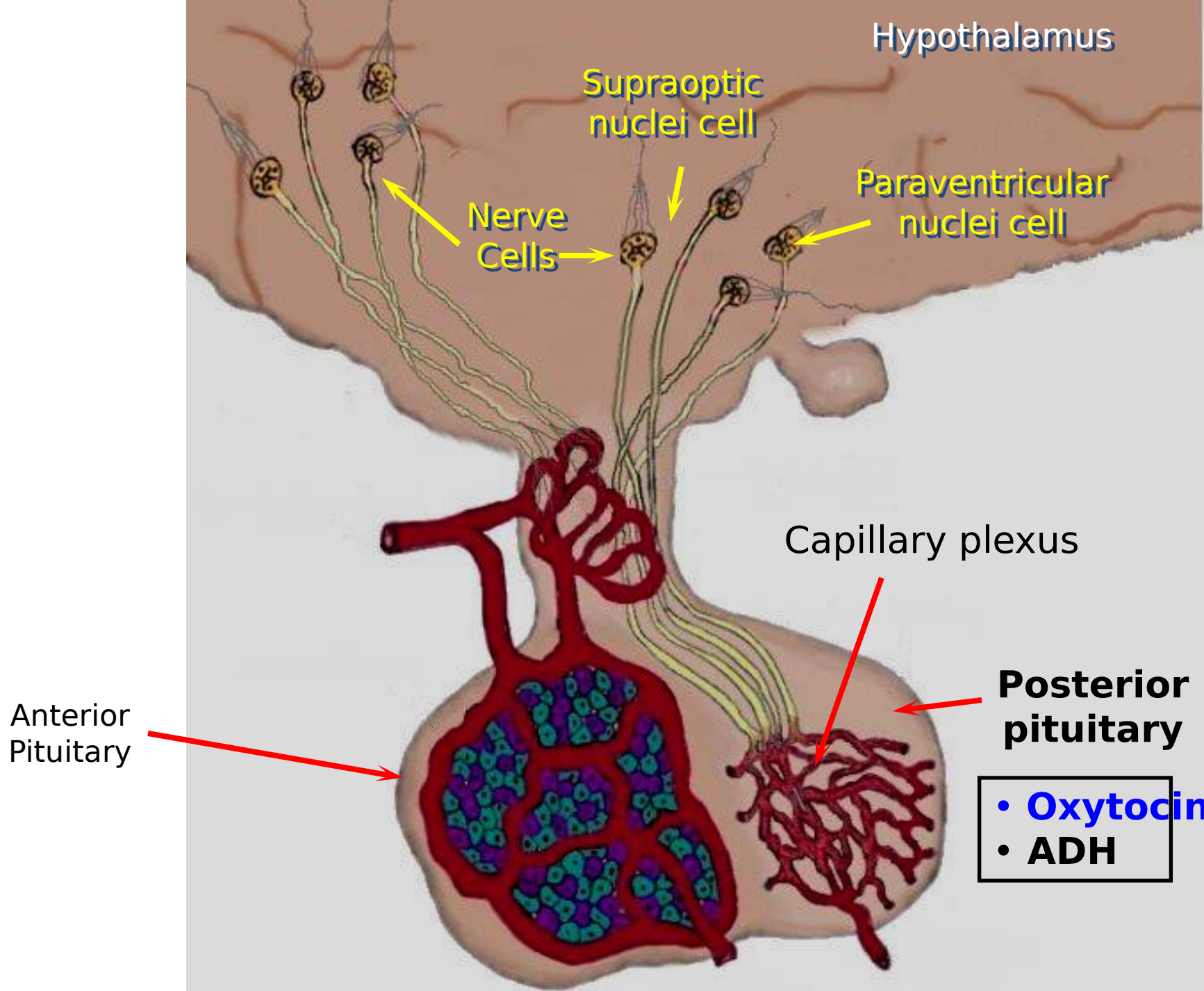
Nerve
Cells

Capillary plexus

Hypophyseal
portal vessels

Posterior
pituitary

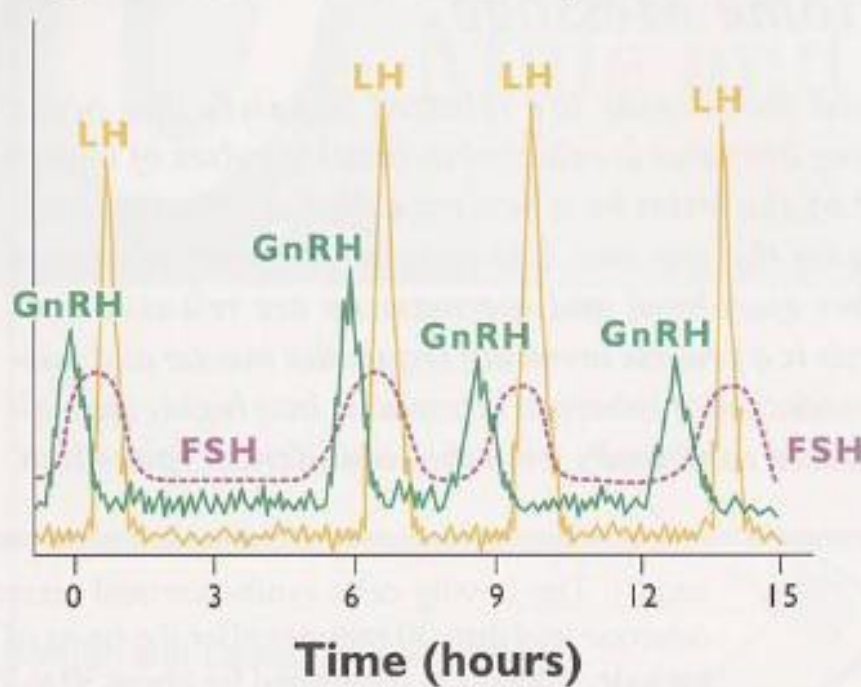




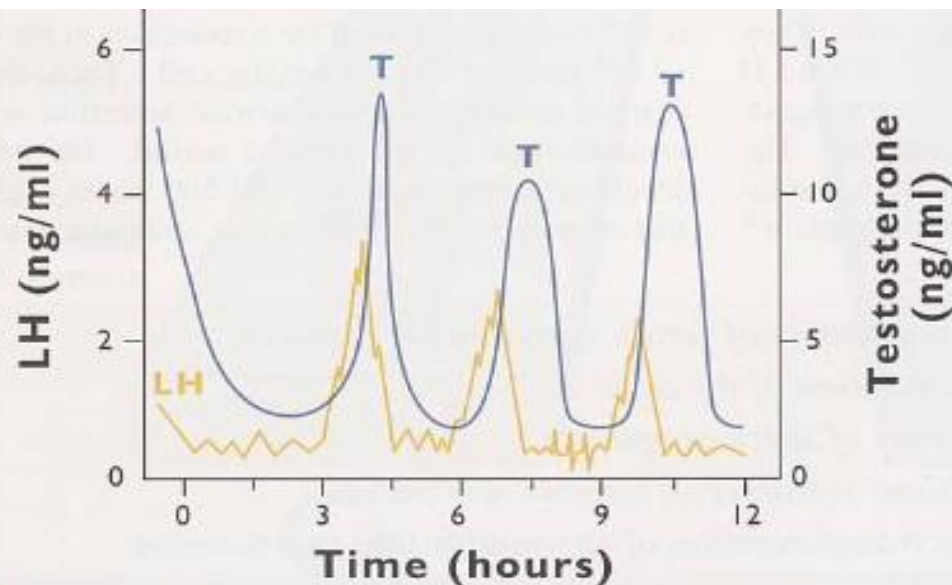
Endocrine Control of Male Reproduction

- Male reproductive physiology is under the primary endocrine control of the pituitary gonadotrophins,
- LH and FSH
- Secretion of gonadotrophins is controlled by hypothalamic gonadotrophin-releasing hormone (GnRH).
- LH – Leyding/Interstitial Cells – Steroidogenesis
- FSH – Sertolic Cells – androgen binding peptide (ABP), Estrogen, DHT, Estrogen Spermatogenesis, Inhibin
- NFB Control of Gonadotropins
LH – Hypothalamic GnRH
FSH – Testosterone, DHT, Estrogen & Inhibin on A. Pituitary
- Episodic GnRH relase – pulsatile LH & Testosterone secretion

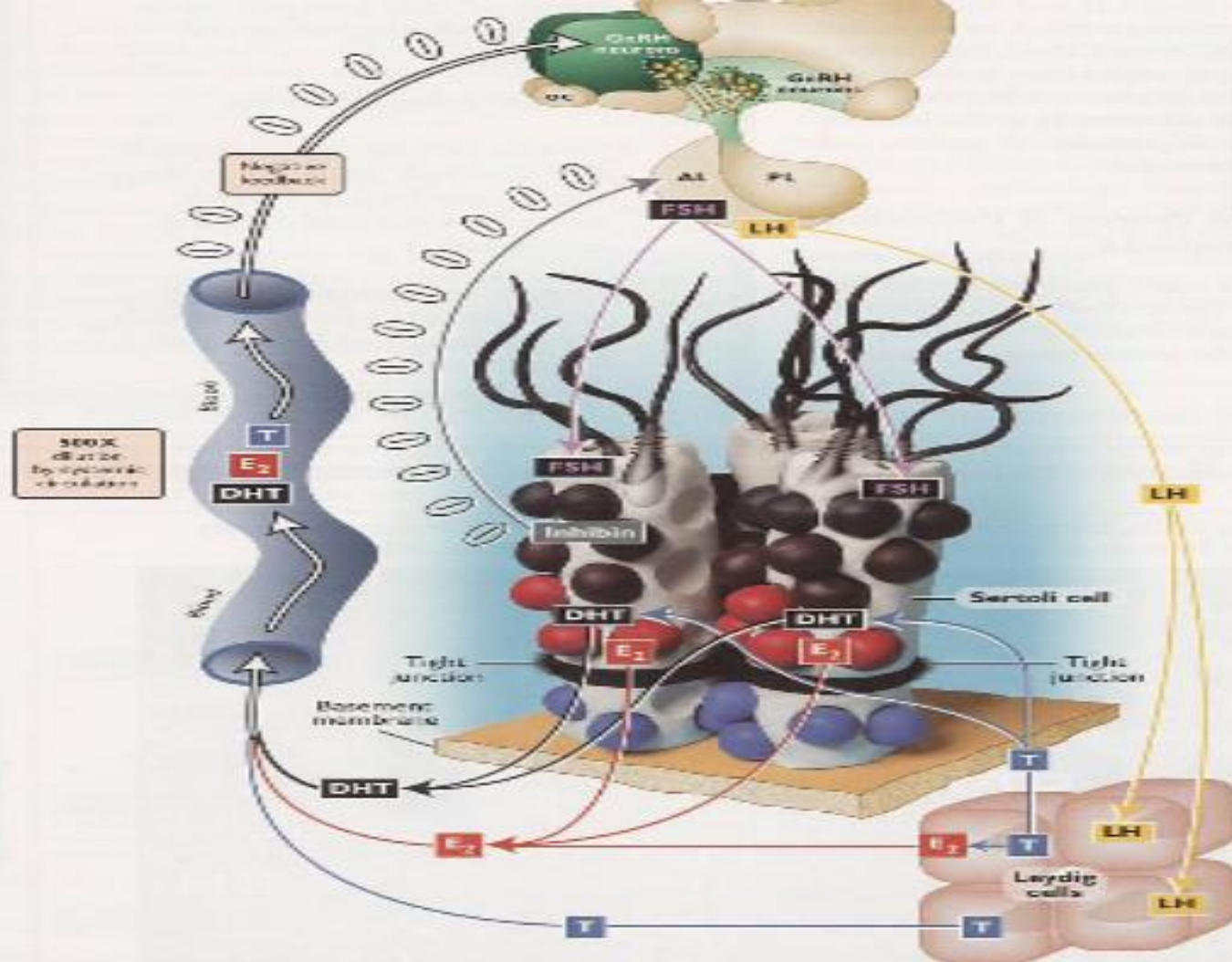
Relative blood hormone concentrations



GnRH causes the release of LH and FSH. Episodes of all three hormones occur between 4 and 8 times in 24 hours. The lower FSH profile, when compared to LH, is due to inhibin secretion by Sertoli cells. Also, the greater duration of the FSH episode is probably due to its longer half-life (100 min) when compared to LH (30 min).



LH is elevated for a period of 0.5 to 1.25 hours, while the subsequent testosterone (T) episode lasts for 0.5 to 1.5 hours.



Blue spheres = spermatogonia; Red spheres = primary spermatocytes; Brown spheres = secondary spermatocytes; Black spheres = spermatozoa

Testosterone (T) produced by the Leydig cells is transported into the Sertoli cells where it is converted to dihydrotestosterone (DHT) and also estrogen (E₂). Testosterone and E₂ are transported by the blood to the hypothalamus where they exert a negative feedback on the GnRH neurons.

LH binds to receptors in the interstitial cells of Leydig and FSH binds to Sertoli cells. Leydig cells produce testosterone that is transported to the adjacent vasculature and the Sertoli cells where T is converted to DHT.