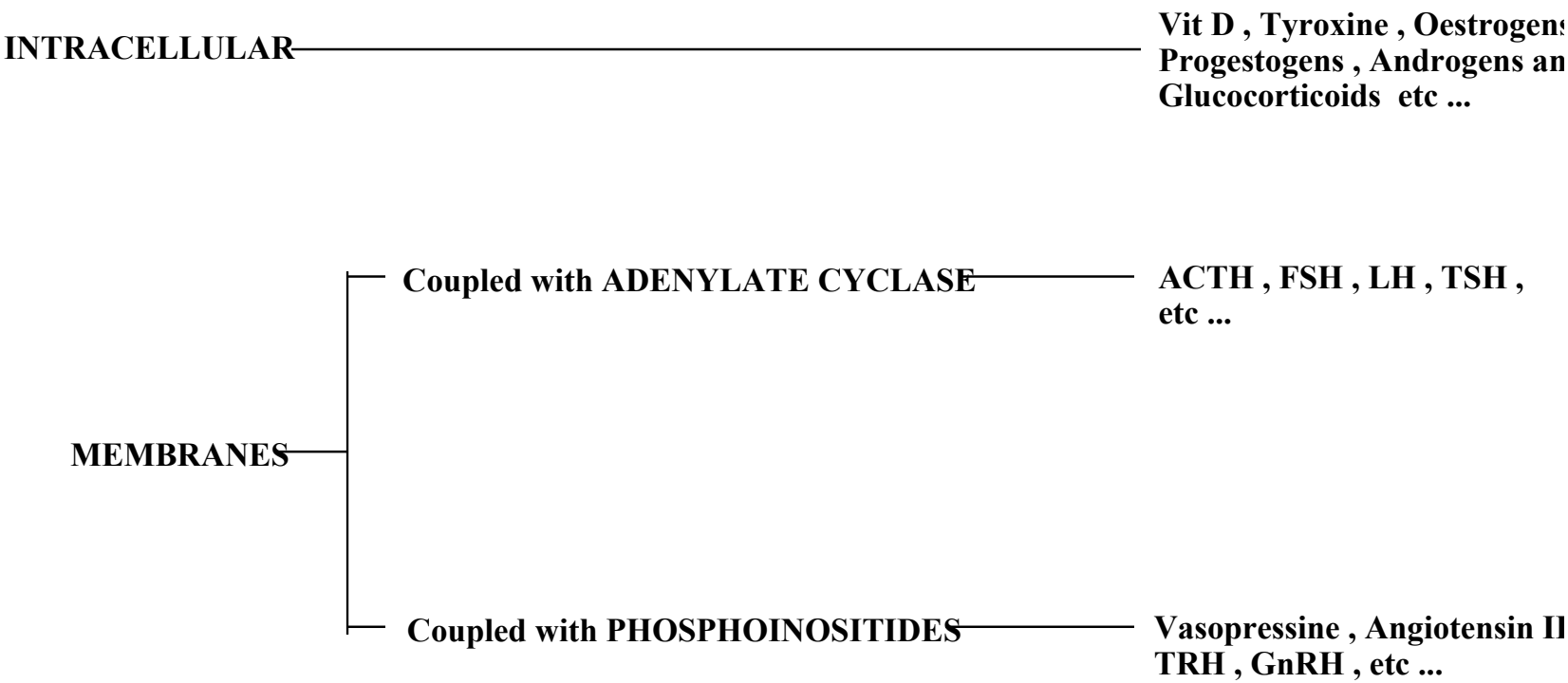
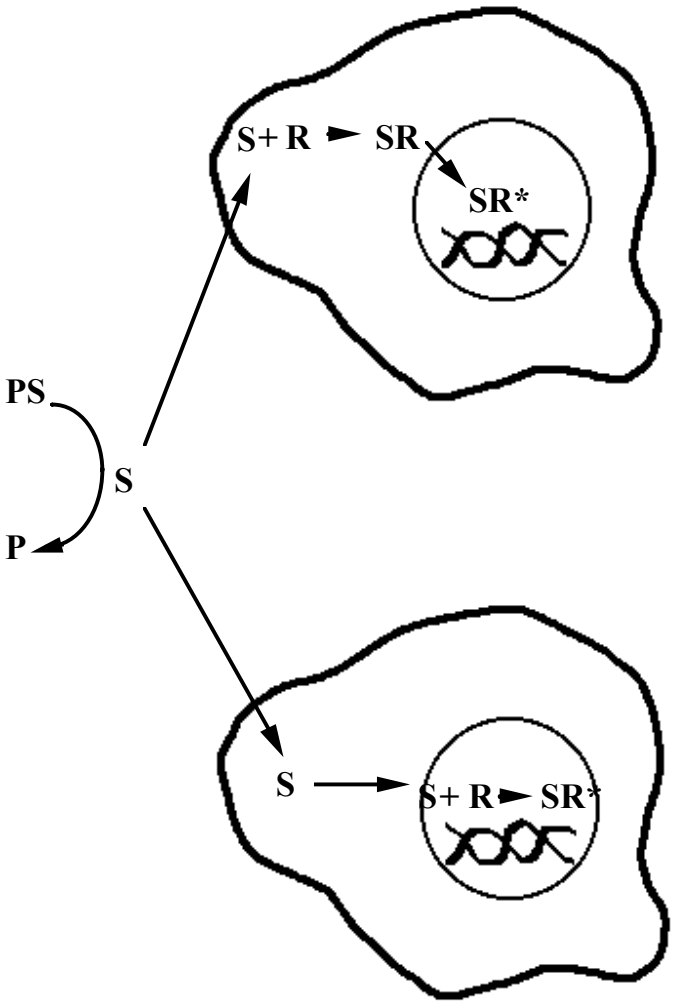
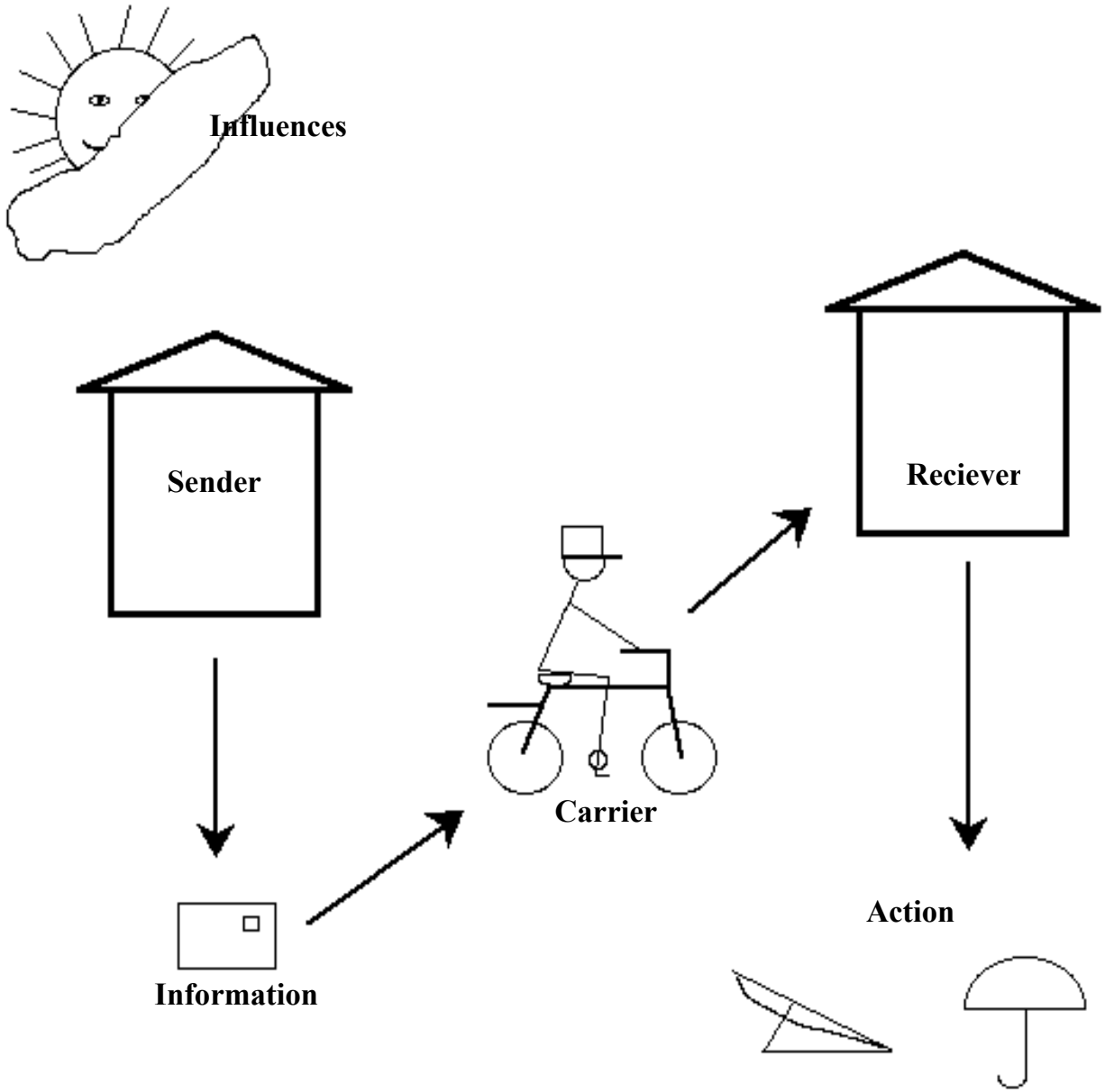
RECEPTOR TYPE AND SECOND MESSANGERS



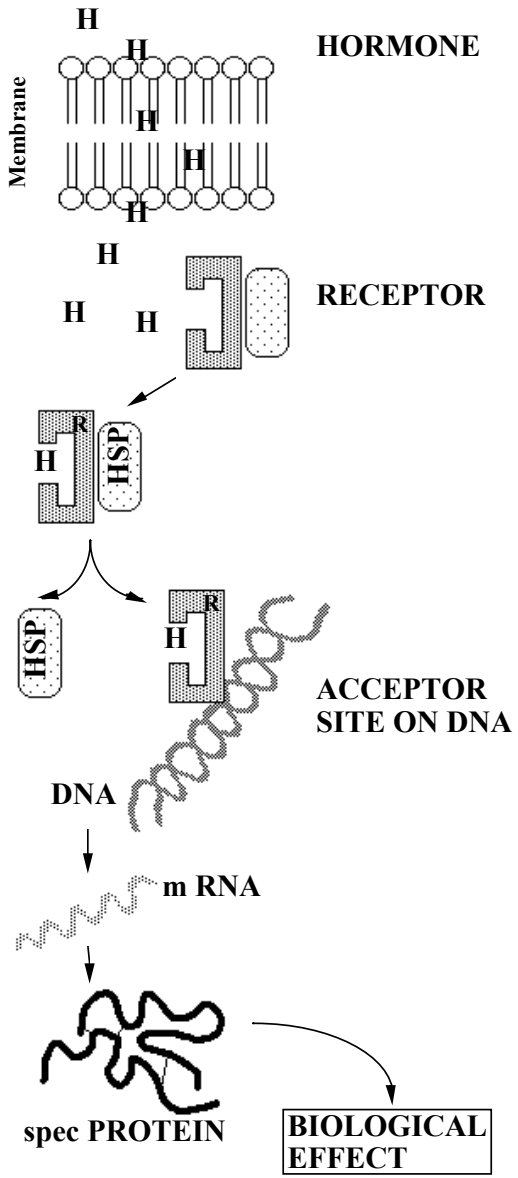
CYTOPLASMIC AND/OR NUCLEAR RECEPTORS



Genetically engineered receptors with a HRE from the Glucocorticoid receptor and a hormone binding domain from the Oestradiol receptor induce Glucocorticoid-like activities !


Influences
Sender
Reciever
Carrier
Information
Action

INTRACELLULAR RECEPTORS



Hormones diffuse "freely" through the plasma membrane.

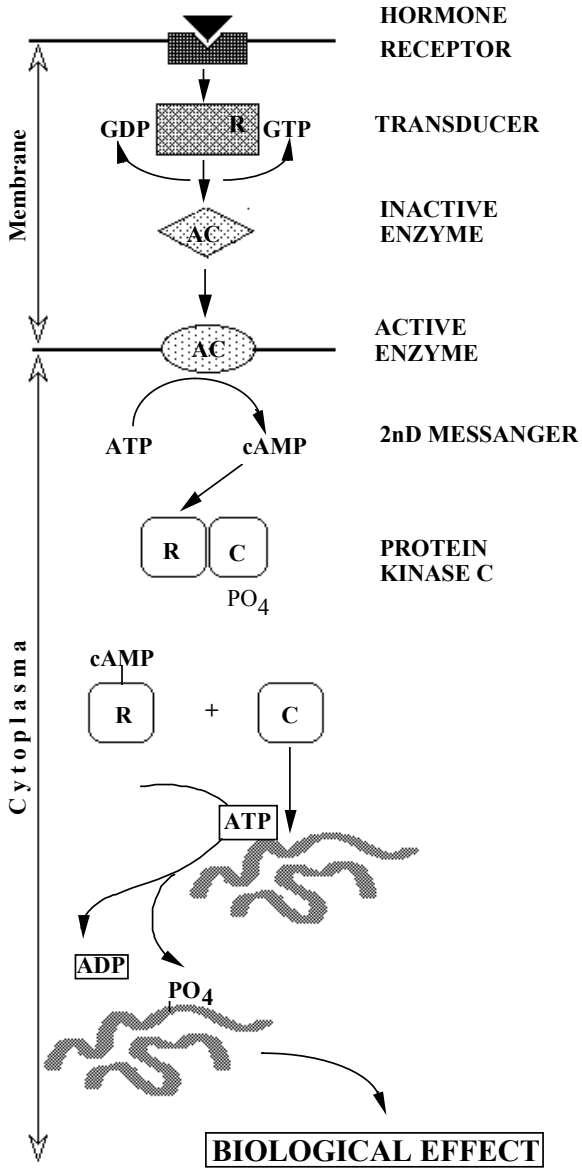
Hormones bind to the nuclear receptor and dissociate the Heat-Shock Protein (HSP).

The Steroid-receptor complex binds to DNA through its Hormone Regulatory Element domain. This initiates the lecture of one gene and the sythesis of a specific mRNA.

The specific mRNA migrates to the ribosomes where it initiates the sythesis of a specific protein.

The specific protein initiates the biological response.

MEMBRANE RECEPTOR COUPLED TO ADENYLATE CYCLASE



HORMONE RECEPTOR

The hormone binds to the acceptor site and favors bindig of GTP to N protein

TRANSDUCER

GTP-NProt complex activates adenylate cyclase (AC).

INACTIVE ENZYME

Activated AC migrates to the membrane surface towards the inner side of the cell.

ACTIVE ENZYME

Activated AC transforms ATP into cAMP.

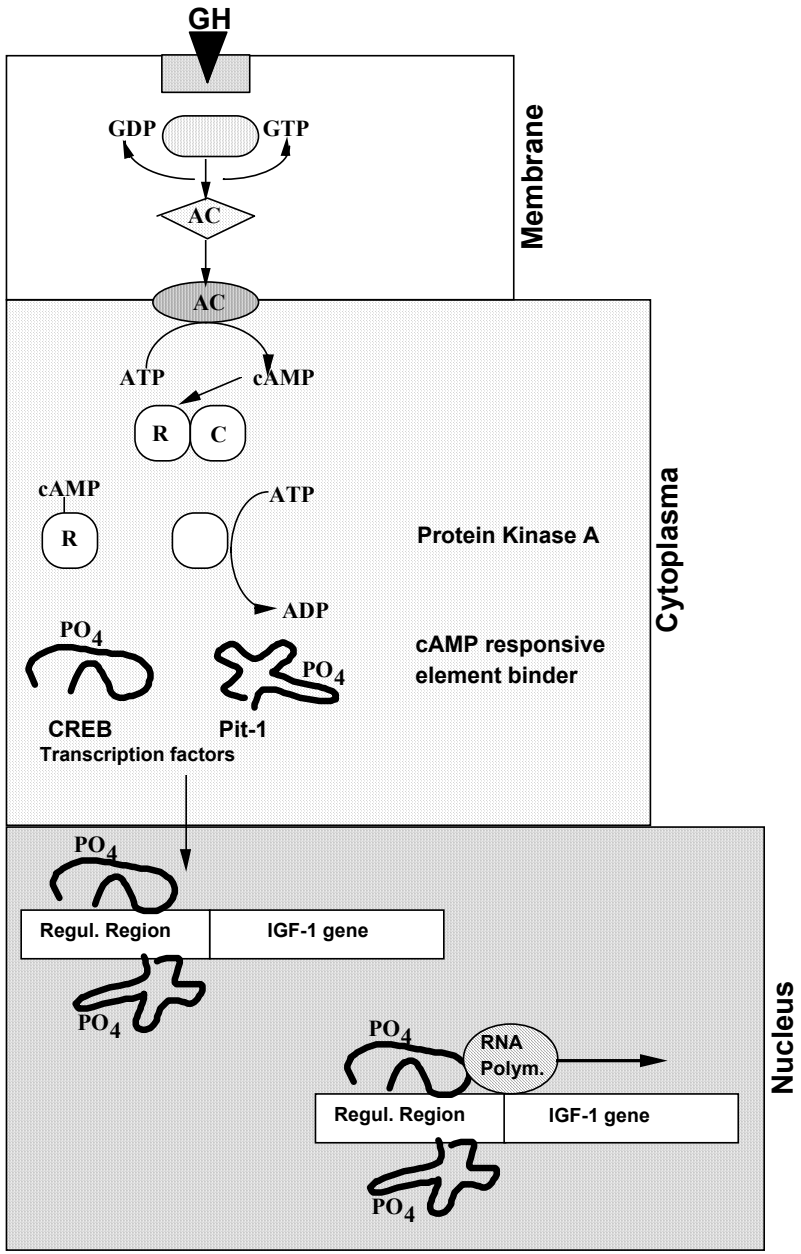
2nD MESSANGER

PROTEIN KINASE C

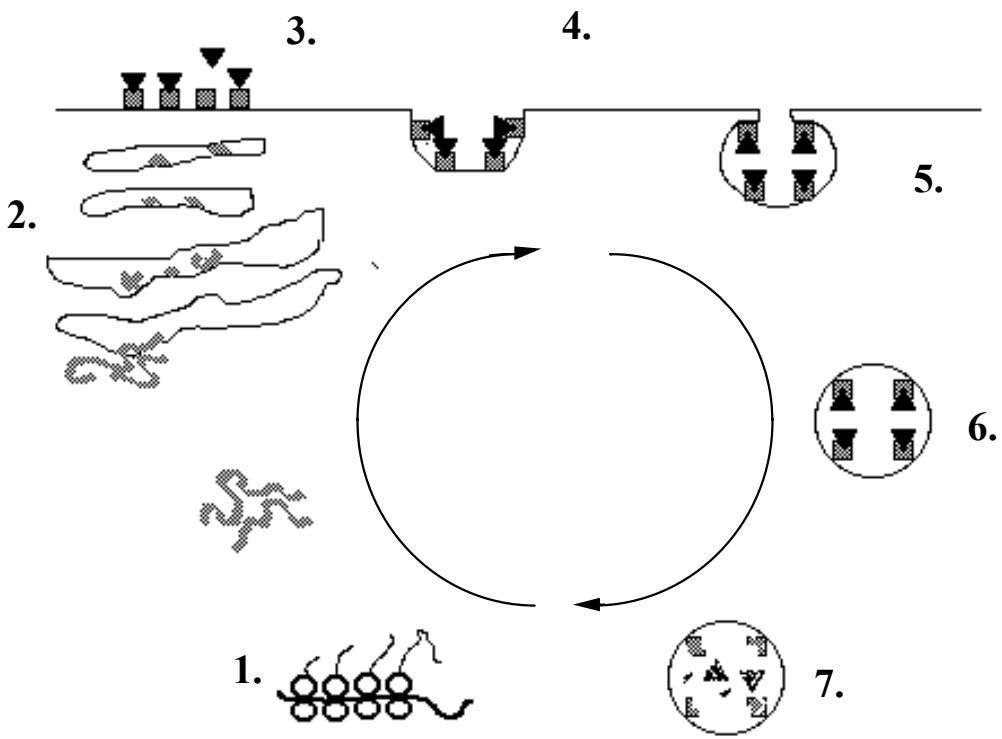
cAMP activates Protein kinase C by binding to its Regulatory unit (R). The Catalytic unit (C) is liberated.

The catalytic unit phosphorylates proteins or enzymes which become active.

The phosphorylated proteins or enzymes become activated and start the biological effect.


GH
GDP
GTP
AC
Membrane
AC
ATP
cAMP
R
C
cAMP
R
ATP
ADP
Protein Kinase A
cAMP responsive
element binder
PO4
PO4
CREB
Pit-1
Transcription factors
Cytoplasma
PO4
Regul. Region
IGF-1 gene
PO4
PO4
RNA
Polym.
Regul. Region
IGF-1 gene
PO4
Nucleus

THE RECEPTOR CYCLE

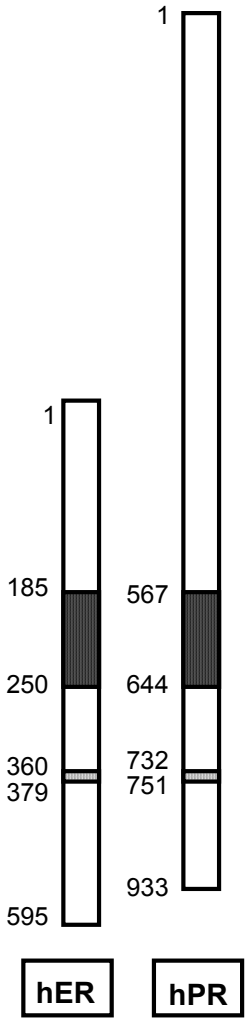


1. Synthesis of receptor proteins in the ribosomes
2. Processing of receptor proteins in the endoplasmic reticulum and transport of receptors through the Golgi to the plasma membrane.
3. Binding of the hormone to the membrane receptor.
4. Start of internalization through the formation of Coated Pits .
5. Invagination of plasma membrane portion rich in saturated receptors.
6. Formation of Coated Vesicles
7. Degradation of receptors and hormones and liberation of amino acids ready to be reused for protein synthesis.

REGULATION OF RECEPTORS

E_2	↗ PR	↗ ER
P	↘ P R	
FSH	↗ FSH R	↗ LH R
GnRH puls	↗ GnRH R	
GnRH bolus	↘ GnRH R	

STEROID RECEPTOR STRUCTURE



<u>Androgenes,Progestogenes,Oestrogens, Glucocorticoid,vitamin D and Tyroxine receptors have a similar structure. They are all cytosoluble dimers.</u>

They have a 60-80 % homologous DNA binding domain (Zinc finger) also called Hormone Responsive Element (HRE). This domain contains 8 cysteins and positively charged amino acids

They have a less homologous hormone binding domain (250 aa) in the C terminal region which contains hydrophobic amino acids.

hER 2x68 kDa hPR 2x110 kDa

Hormones are produced by Endocrine Glands and secreted into the circulation. They thus come into contact with all cells of the body. Only <u>TARGET CELLS</u> respond to the hormone. These cells have specific <u>RECEPTORS</u> for the hormone.

WHAT IS THE DISTRIBUTION OF RADIOACTIVE OESTRADIOL WHEN INJECTED IN A RAT ?