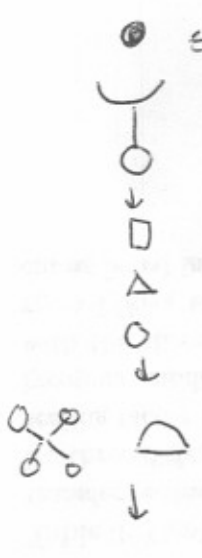
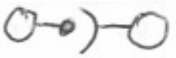
Cell signalling : a physicist's view

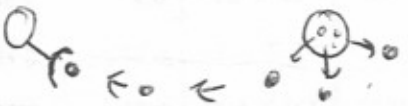


Intercell. Signaling

1 contact dep

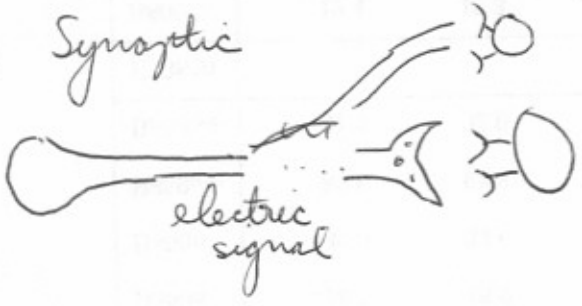


2 Paracrine



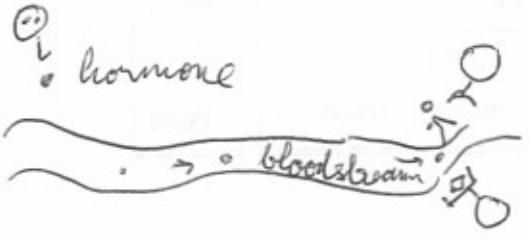
affects only cells in imm. neighborhood

3 Synoptic



specificity through wiring

4 Endocrine



specificity through target cells

Cells are programmed to respond to specific combinations of extracell signal mol.

→ survive

+ D, E → divide

+ F, G → differentiate

no g signals → die (apoptosis)

Molecule turnover rate determines response rate
(for shut-off and switch-on)

- half life, time until concentration falls ~~by~~ to half ~~of~~ if all synthesis were stopped

~~A~~ ~ < 10 min

Cells can modulate sensitivity to concentration

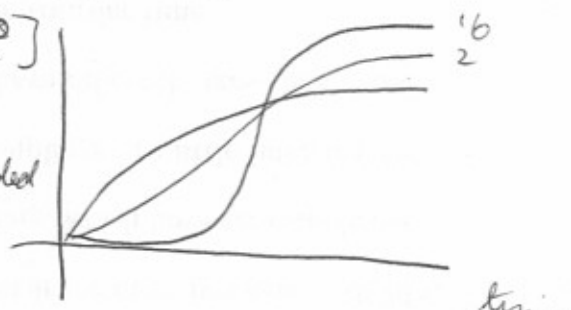
- number of receptors required for response

$$E + nS \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow{k_{cat}} E + P$$

$$v = k_{cat}[ES]$$

Michaelis Menten Kinetics

If more signalling molecules are needed steeper switch



Feedback

positive feedback → threshold responses
ultimate switch

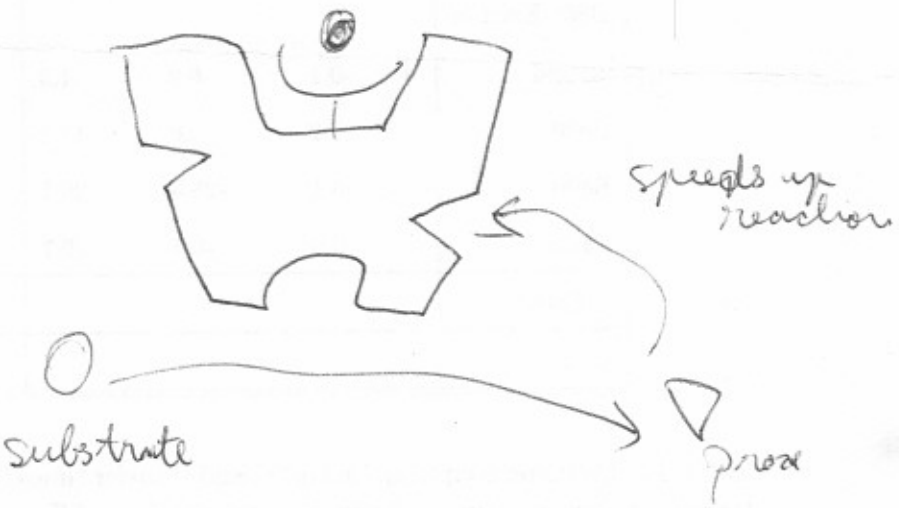
negative feedback → desensitization (adaptation)

receptor downregulation

receptor inactivation

inactivation of signalling protein

inhibitory protein



Cell-surface receptors

largest class: G-protein coupled receptors

ion channel linked

enzyme linked → protein kinases

→ Phosphorylization

Second messengers

adaptors

Nuclear receptors (hormone) enter nucleus, bind DNA

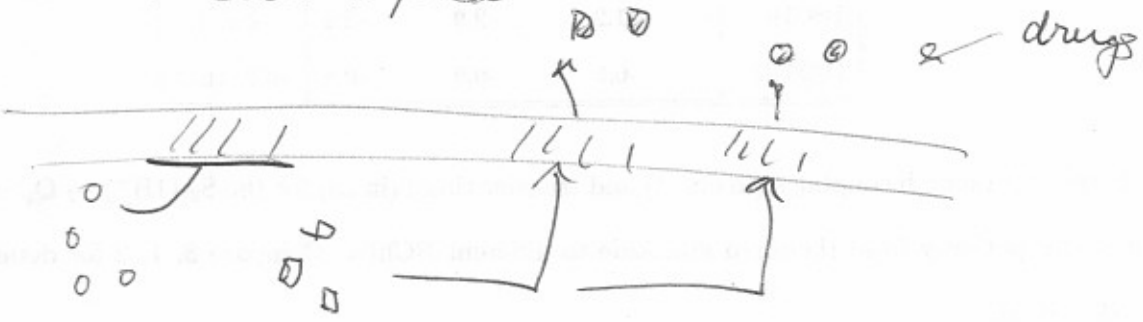
Steroid / thyroid hormones Vit D, retinoids

→ primary response proteins

→ shut-off primary response

(or)

activate sec. response



Immediate control

① Turnover - rate : life-time, production rate

Math: faster TO → faster response (shorter)

slower → longer-lasting response

chemistry: Water-solubility a major factor
< 10 min
h - d for insoluble

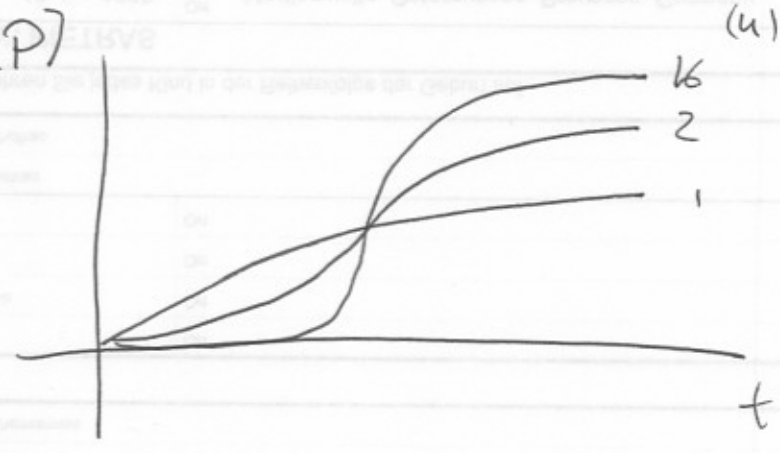
---

② # receptors required for response

$$E + nS \underset{k_-}{\overset{k_+}{\rightleftharpoons}} ES \xrightarrow{k_{cat}} E + P$$

$$v = k_{cat}[ES]$$

Michaelis-Menten kinetics



Signalling Proteins

Nitric Oxide NO

Signal from nerve cells to muscle cells

~~→ relaxes ←~~

→ activates cyclic GMP in cells
→ relaxes muscle cells

Viagra (keeps GMP levels high)

Nuclear Receptors Signals

Steroid hormones — cortisol / sex hormones / Vit D → Ca^{2+} metab.
Thyroid hormones — increase metabolic rate
retinoids — Vit A

→ activate nuclear receptors that bind directly to genes

insoluble in water
made soluble through carrier proteins

Chemistry ?

Signal transducers

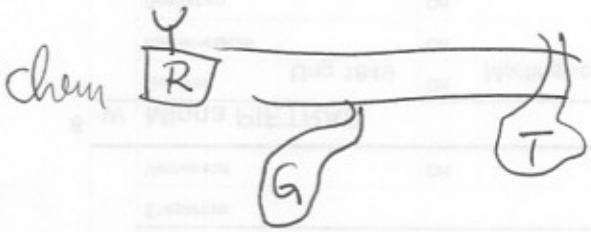
(cell-surface receptors : target of water-soluble proteins)

① Ion-channel-linked receptors

② G-protein linked receptors

Receptor-target IA mediated by membrane-associated shuttle protein

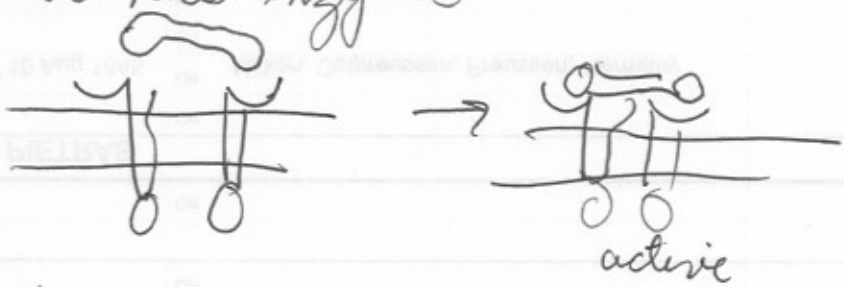
trimeric GTP binding prot (G-protein)



largest class

③ Enzyme-linked receptors

→ activates enzymes



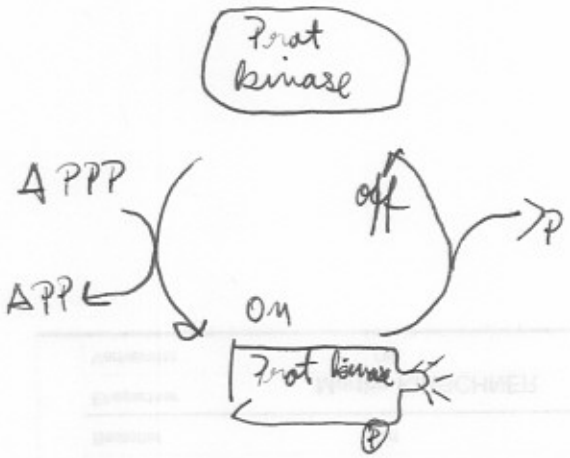
Protein kinases

→ cause phosphorilization

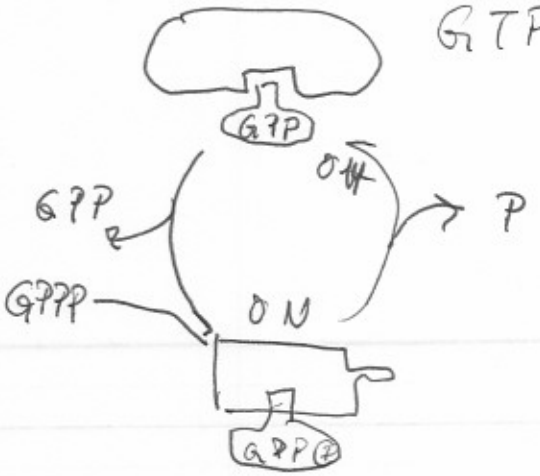
Switching usually involves phosphate

activation : P addition

de-activation : P removal



Phosphorylation cascade possible



GTP binding protein