Drug Receptors

by the end of this lecture you should be able to

- identify the receptor superfamilies
- describe how drugs interact with enzymes and carrier molecules, ion channels and DNA
- identify drugs which work in non-specific ways
- know the clinical relevance of this

What would you do?

treating animals

- work out wht is wrong with the animal
- work out what you want the drug to do
- decide on class of drugs
- look up which drug

problems?

- infection
- pain
- tissue overgrowth
- lameness

molecular targets for drugs

- receptors
- ion channels
- enzymes
- carrier molecules
- DNA
- non specific

non specific targets

- osmotic diuretics
- radioactive iodine

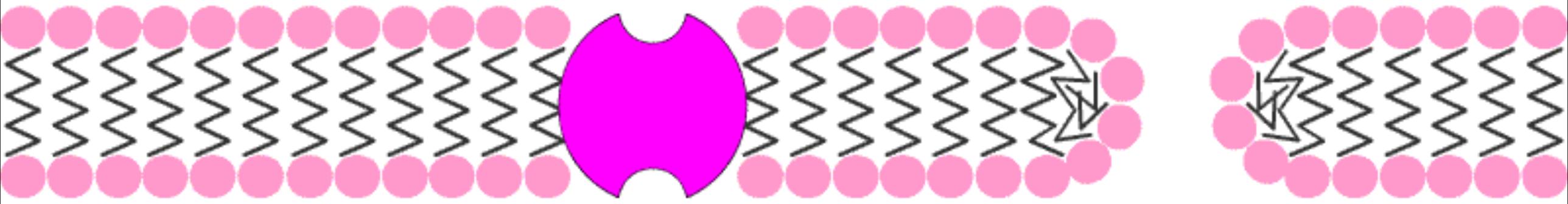
DNA

- many antibiotics
  - bacterial DNA
  - mammalian DNA
- anticancer drugs

carrier molecules

- transport small molecules into or out of cells
  - many antidepressants
  - ivermectin

drug



diffusion across
lipid membranes

carrier mediated
transport

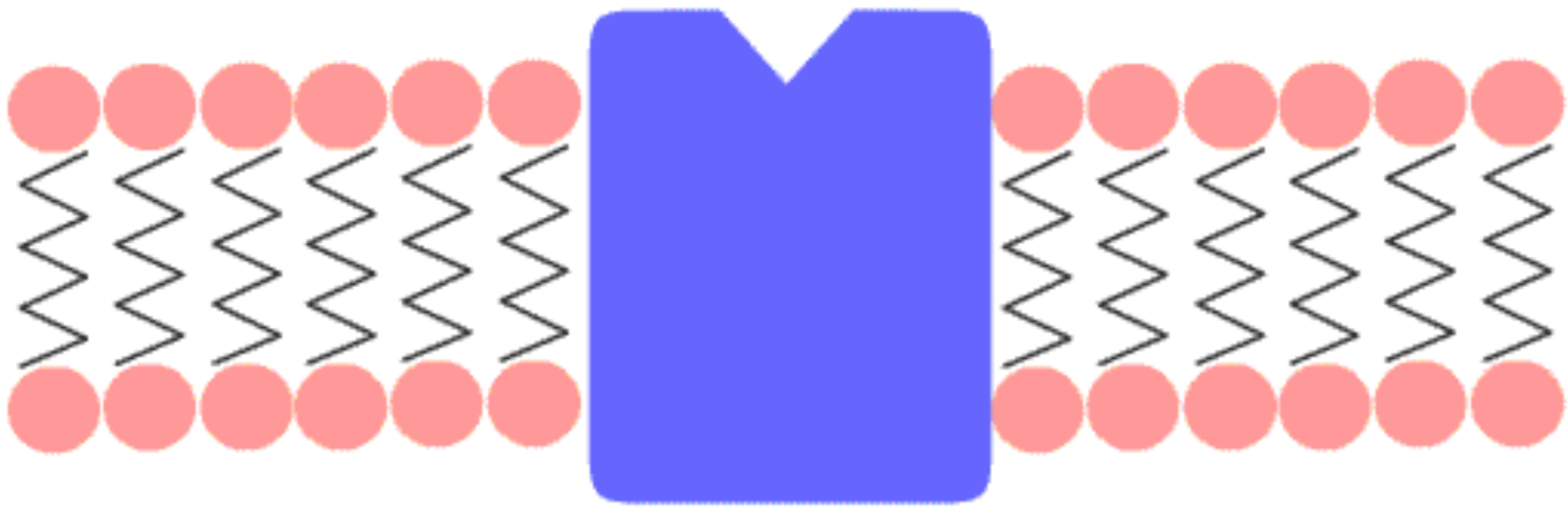
diffusion through
aqueous channel

enzymes

- compete with substrate
- false substrate
- prodrugs

RUN

substrate



enzymes

- most antibiotics
- organophosphate insecticides
- aspirin type drugs

ion channels

- most drugs block rather than open channels
- do not confuse with ionotropic receptors!!

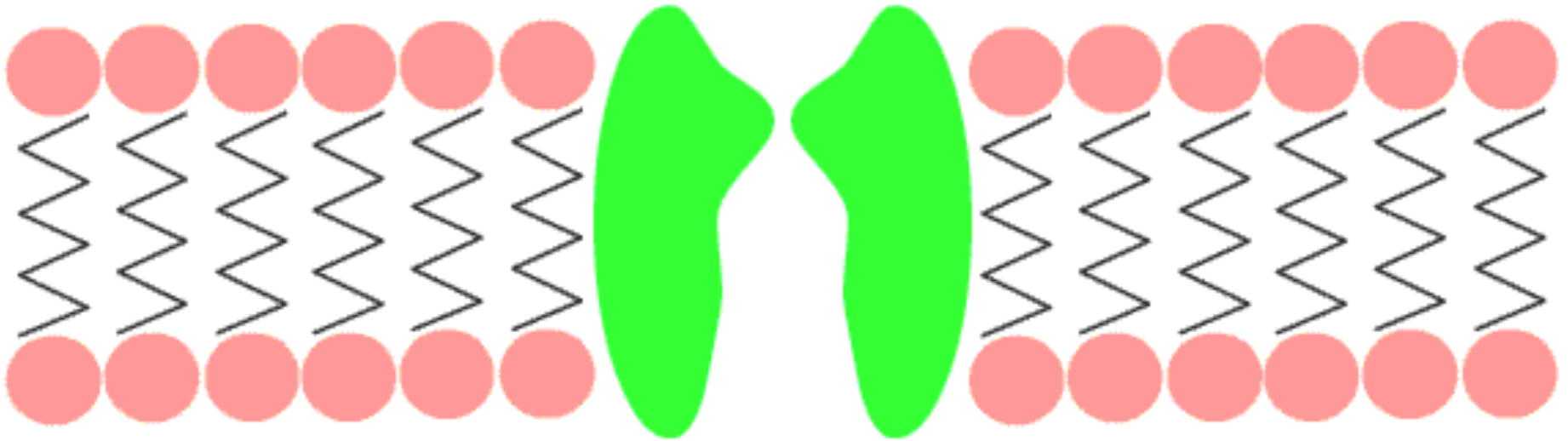
ketamine

RUN

Na^+

Na^+

Na^+

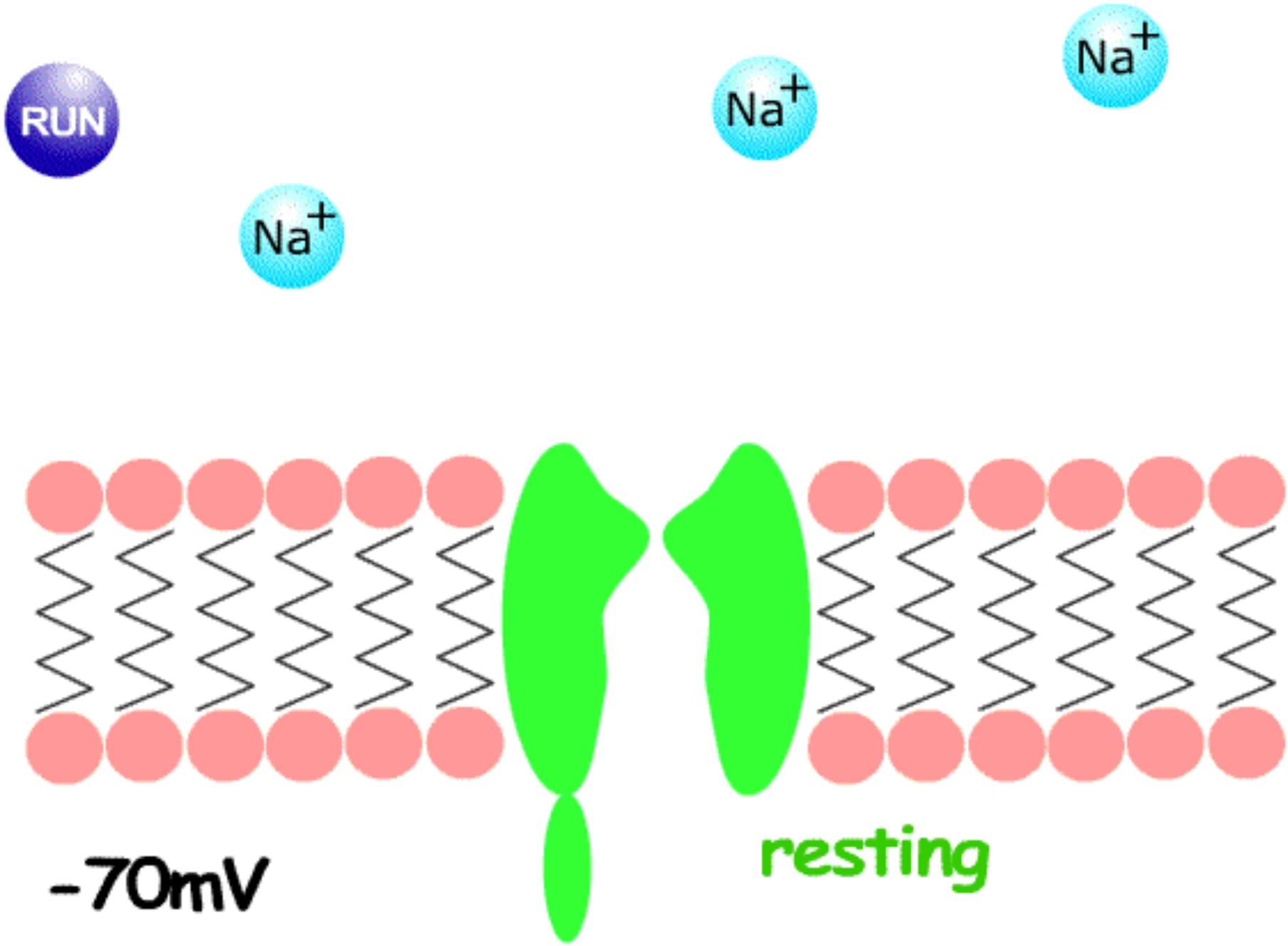


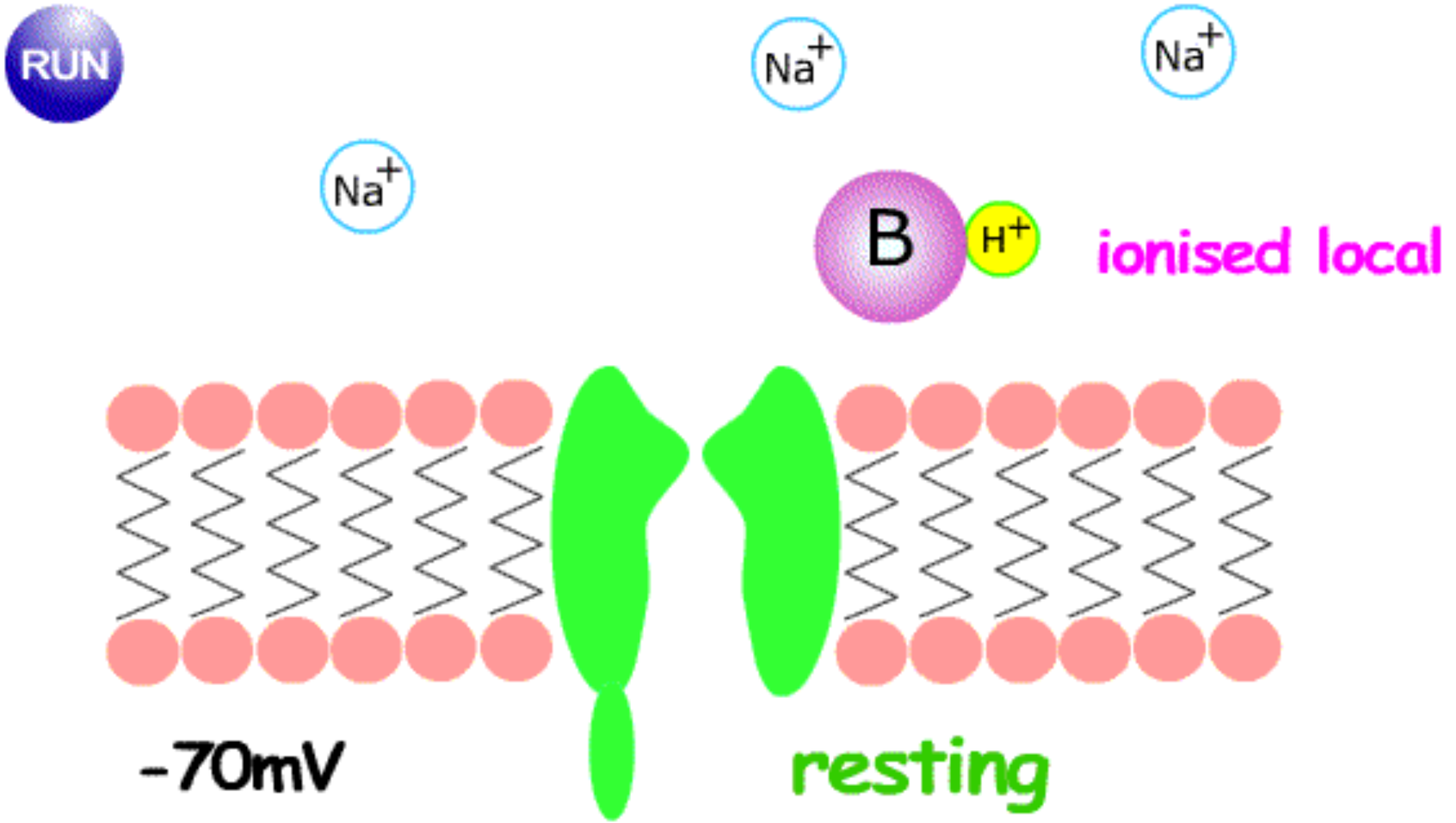
-70mV

ion channel

ion channels

- ketamine
- local anaesthetics


RUN
Na+
Na+
Na+
-70mV
resting


RUN
Na+
Na+
Na+
B
H+
ionised local
-70mV
resting

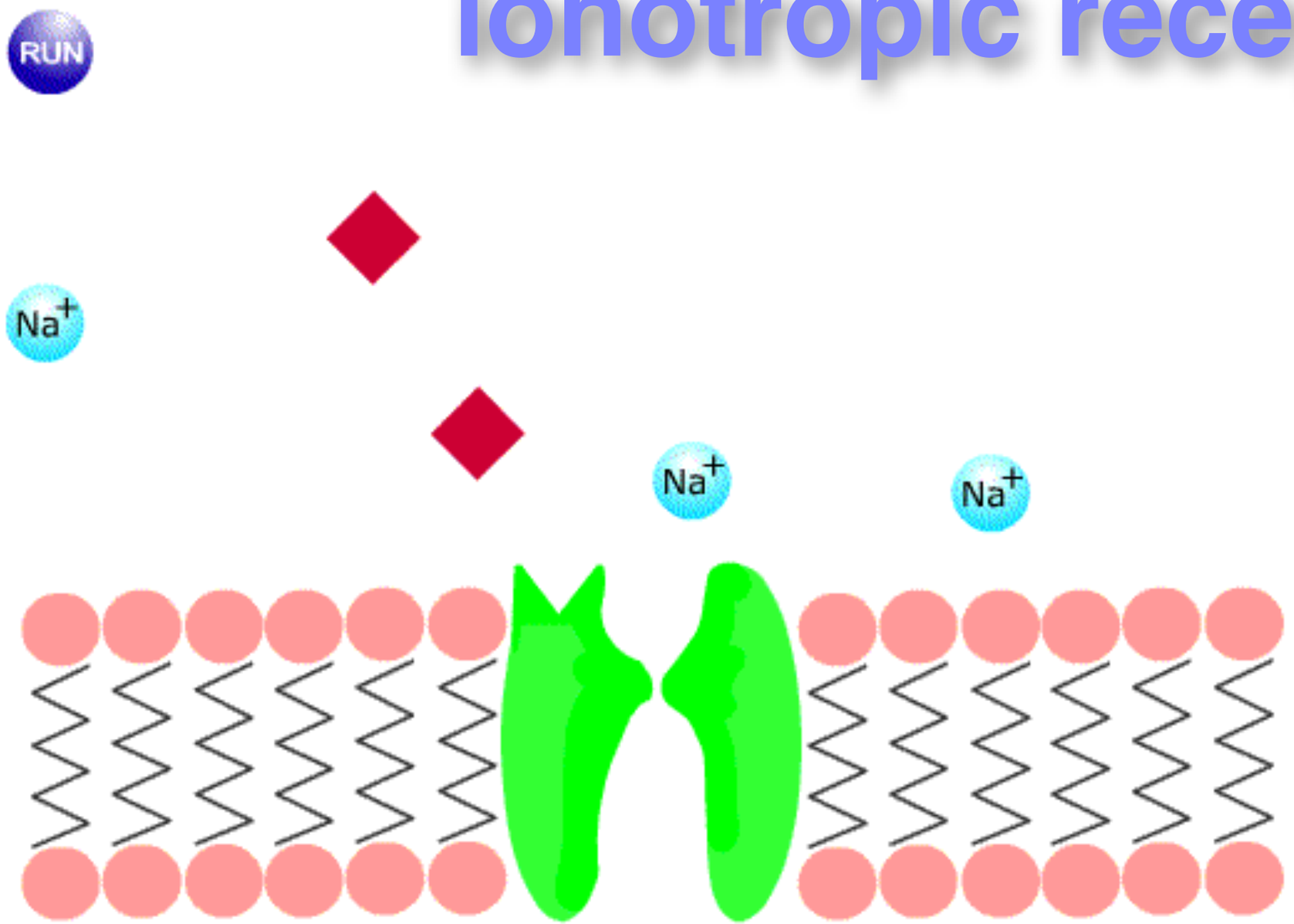
receptor

- a protein molecule (or group) which binds to specific ligands and then does something
- ligand ~ key, receptor ~ lock

receptors

- ionotropic receptors
- metabotropic (G protein coupled) receptors
- tyrosine kinase coupled receptors
- nuclear receptors

ionotropic receptor



ionotropic receptors

- milliseconds
  - nicotinic ACh receptors
  - AMPA receptors
  - GABA receptors

drug

RUN

Na^+

Na^+

Na^+

Na^+

receptor

G protein

target

GTP

metabotropic receptor

Metabotropic receptors

- 7 trans membrane regions
- At least 4 different G protein α subunits

Metabotropic receptors

- Seconds to minutes
  - opioid receptors - morphine
  - adrenergic receptors - xylazine
  - muscarinic ACh receptors - atropine

drug

receptor

P

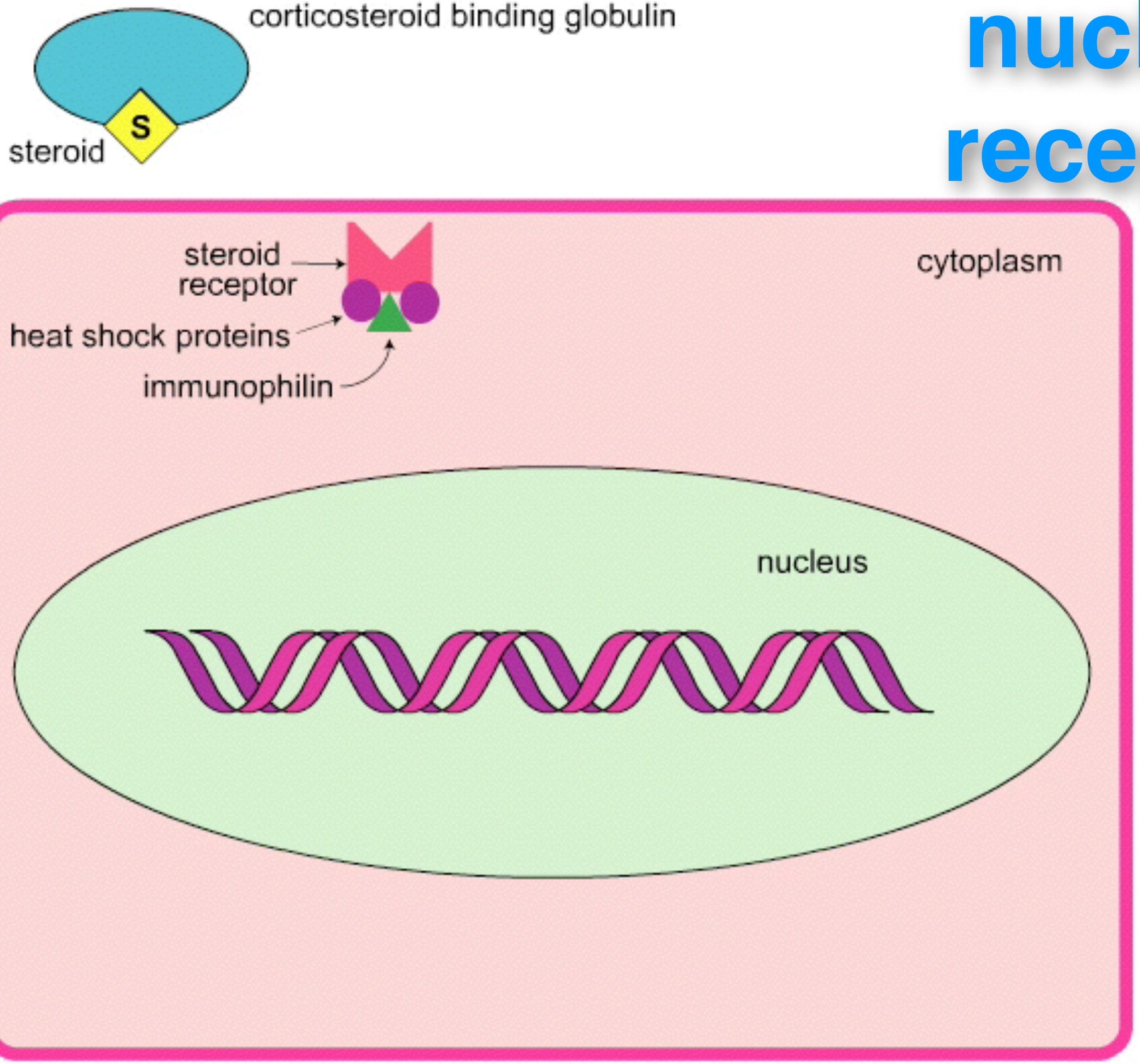
P

tyrosine kinase coupled R

tyrosine kinase coupled receptors

- minutes to hours
- many hormones
  - insulin
  - thyroid hormone

nuclear receptor



nuclear receptors

- hours - days
  - corticosteroids
  - oestrogen

receptor complexity

- drugs can act at more than one receptor
- more than one drug can act at one receptor
- activation of more than one receptor may be necessary for effect
- receptor numbers change according to use & disease
  - "paradoxical pharmacology"
- may be different in different tissues

effects of disease

- autoantibodies to receptors
- mutations in genes for receptors
- changes in ligand secretion

Second messengers

- lots of different systems
- can get complicated!!

receptor subtypes

- adrenergic receptors
  - α receptors
    - α1 receptors
    - α2
      - α2A
      - α2B
      - α2C
      - α2D
  - β receptors
    - β1
    - β2
    - β3

specificity

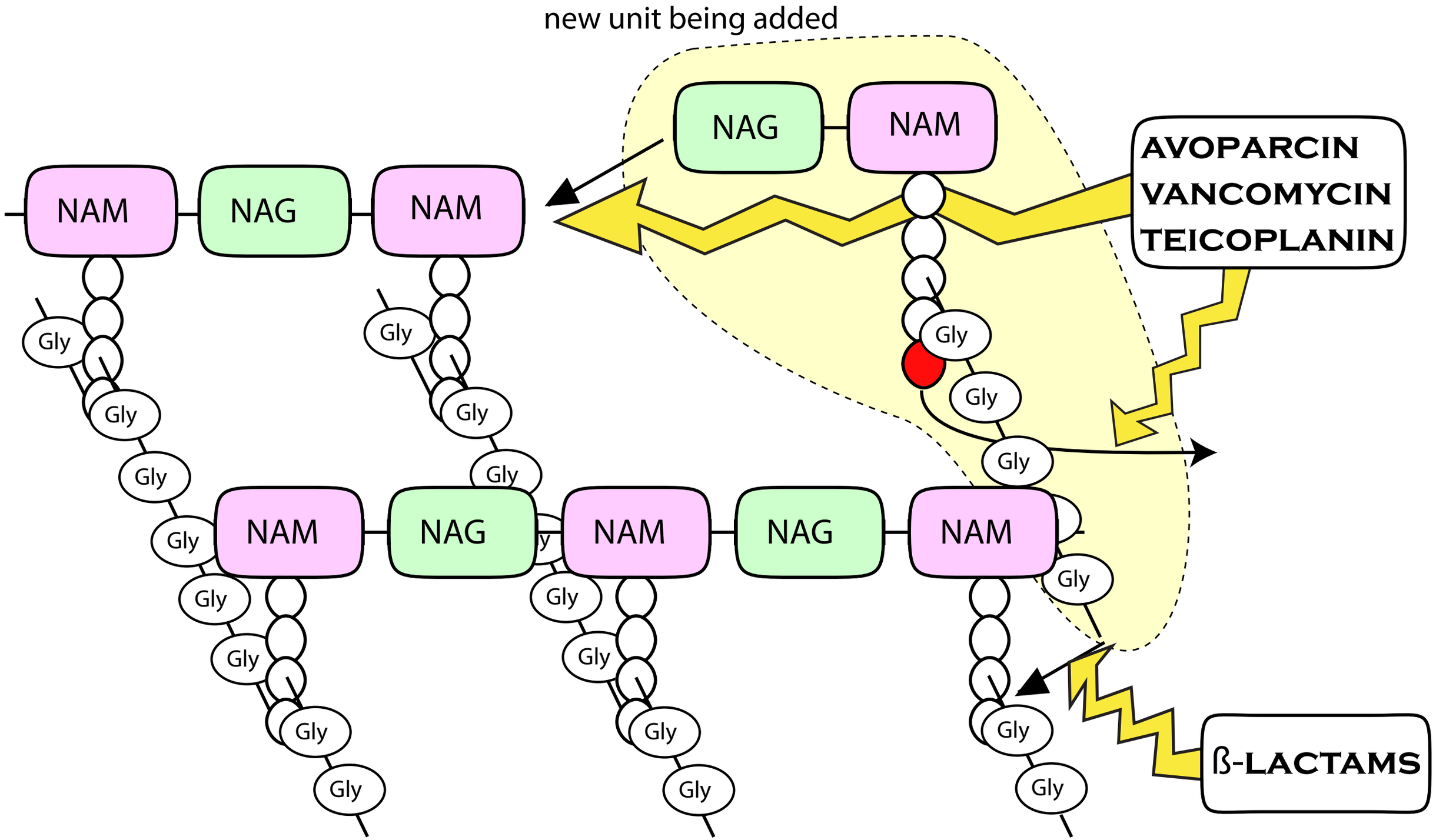
- physical barriers
- receptors in tissue
- receptor subtypes
- receptor collaboration / helpers

studying receptors

- binding experiments
- sequencing receptors
- cloning receptors
- transfection & patch clamping

What does penicillin do?

- how does it kill the bacteria without killing the sheep?


new unit being added
NAG
NAM
AVOPARCIN
VANCOMYCIN
TEICOPLANIN
NAM
NAG
NAM
NAM
NAG
NAM
Gly
ß-LACTAMS

Drug action

- Drugs can produce effects by binding to receptors, enzymes and carrier molecules; by blocking ion channels or by exerting a physical effect.
- There are four superfamilies of receptors: ionotropic, metabotropic, kinase coupled and nuclear.
- There may be several layers of reactions in the signal transduction system between drug binding and effect.
- Drug interactions at the site of action can be clinically important (more next lecture!)