

A red mushroom with white spots, likely an Amanita muscaria, is growing in a field of dry grass. The mushroom has a bright red cap with numerous white, irregular spots. The background is a dense field of dry, yellowish-brown grass.

Drug Receptor Interactions

A red mushroom with white spots, resembling a fly agaric, is growing in a field of dry grass. The mushroom has a bright red cap with irregular white patches and a thick, white, slightly wrinkled stem. The background is a dense field of dry, yellowish-brown grass.

agonist

- **A drug which interacts with a specific receptor to produce a response**
 - **ie, it has efficacy**

efficacy

- The ability to produce a response after binding

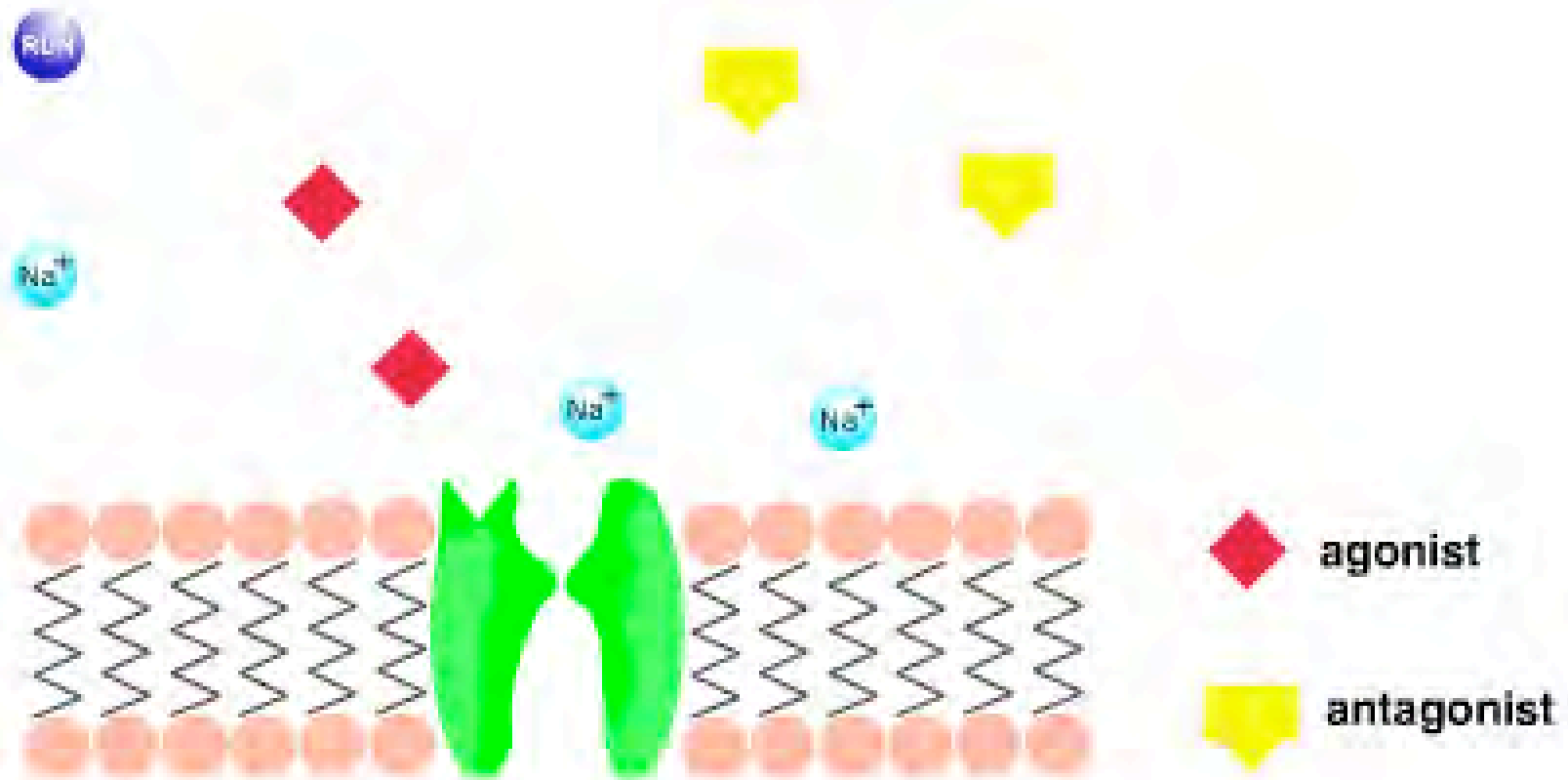


antagonist

A red mushroom with white spots is growing in a field of dry grass. The mushroom is the central focus of the image, and its color contrasts with the brownish-yellow grass. The text 'antagonist' is overlaid on the upper part of the mushroom.

- A drug which occupies a receptor stopping an agonist getting in
- it produces no effect on its own
 - ie, it has no efficacy

competitive antagonist

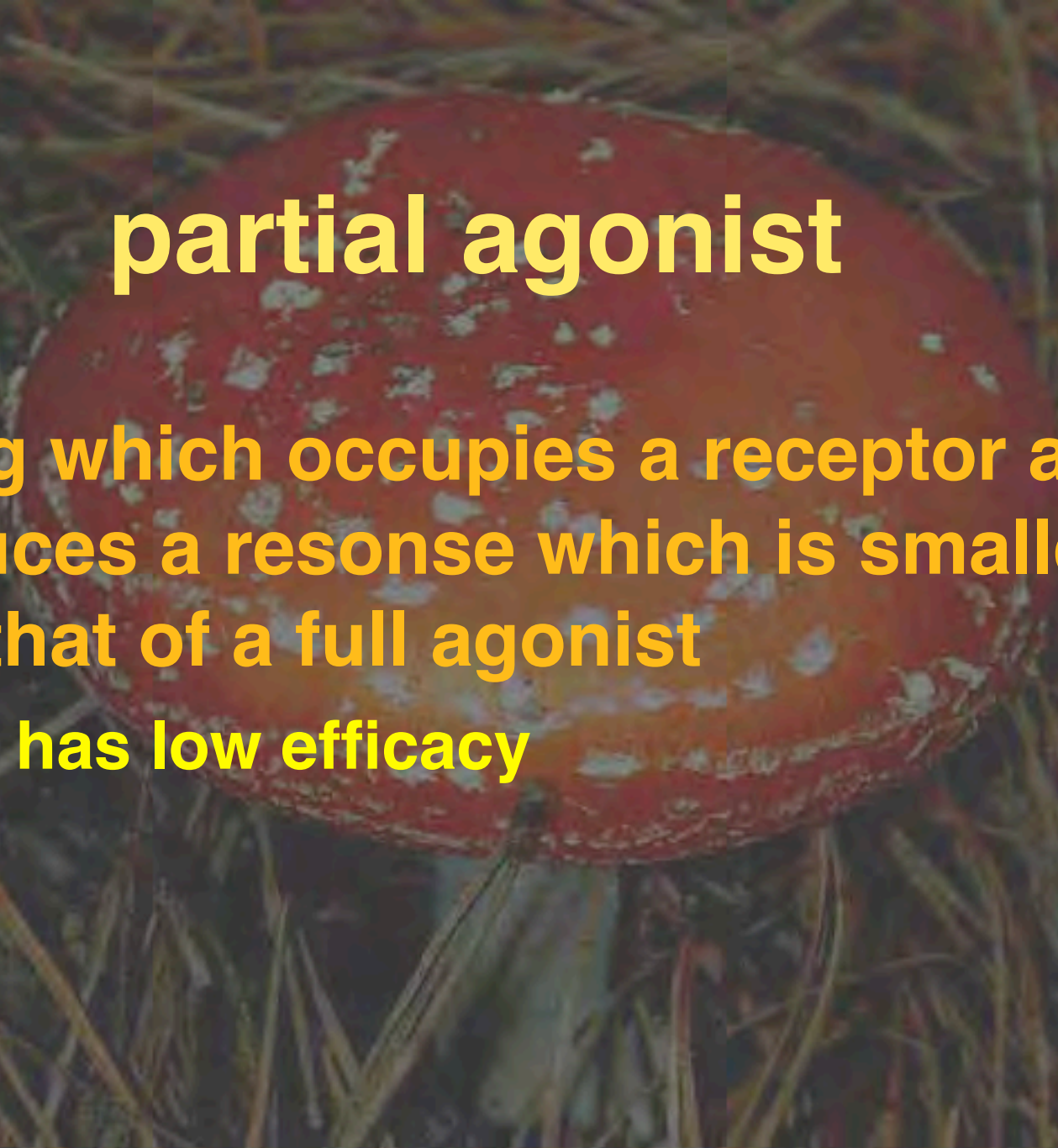


inverse agonist

- A drug which occupies a receptor to produce the opposite effect to an agonist
 - ie, it has negative efficacy
- it is also blocked by an antagonist
- constitutive activation required

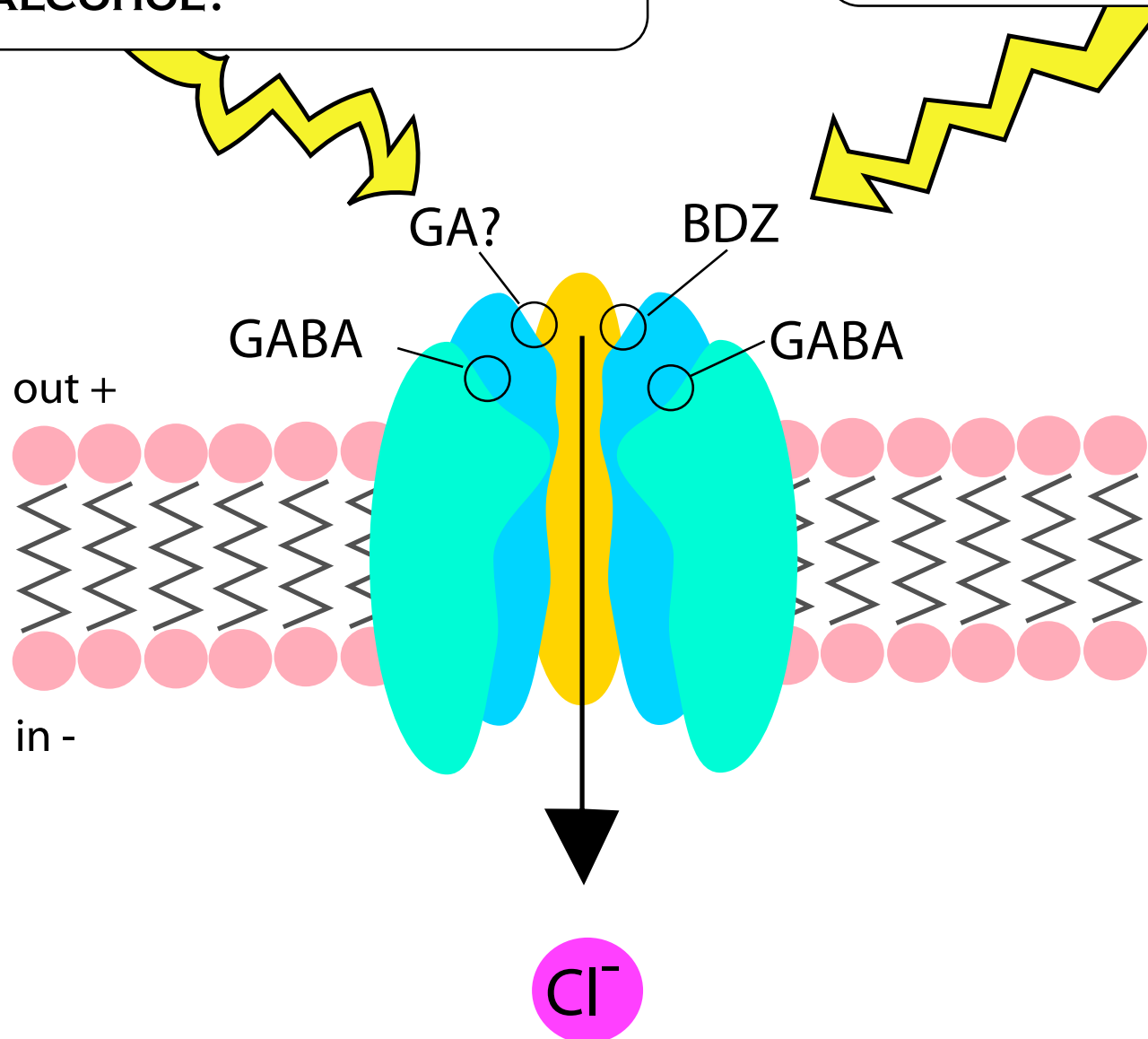
partial agonist

- a drug which occupies a receptor and produces a response which is smaller than that of a full agonist
 - ie it has low efficacy



BARBITURATES
OTHER INJECTION ANAESTHETICS?
INHALATION ANAESTHETICS?
ALCOHOL?

agonist **DIAZEPAM**
antagonist **FLUMAZENIL**
inverse agonist **βCARBOLINE**



affinity

- The tendency of a drug to bind to receptors

$$K_A = \frac{1}{K_D}$$

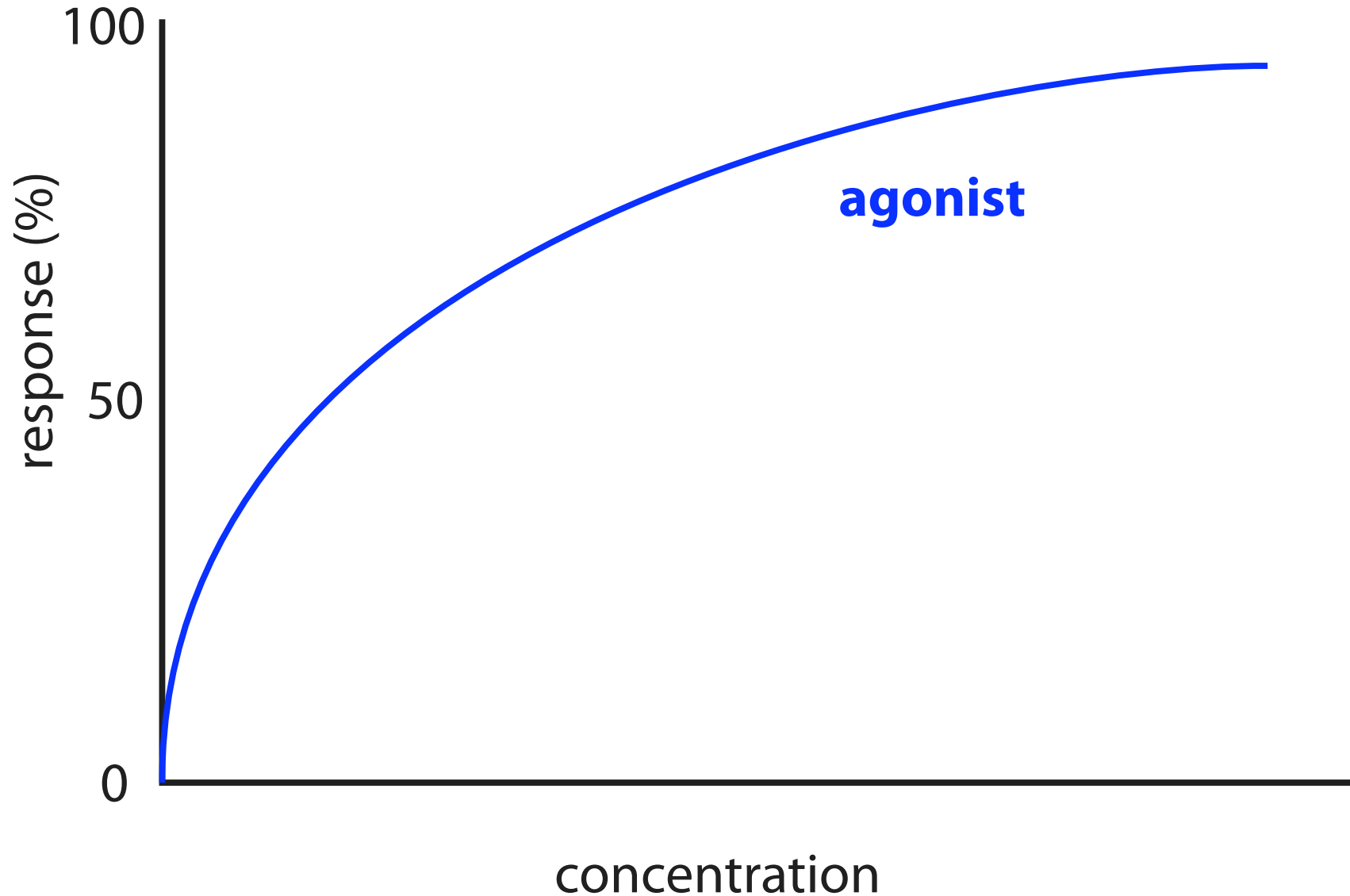
K_D

A red mushroom with white spots is centered in the background of the slide. The mushroom has a bright red cap with numerous small, irregular white patches. It is growing in a field of dry, yellowish-brown grass. The overall image has a dark, semi-transparent overlay to make the text stand out.

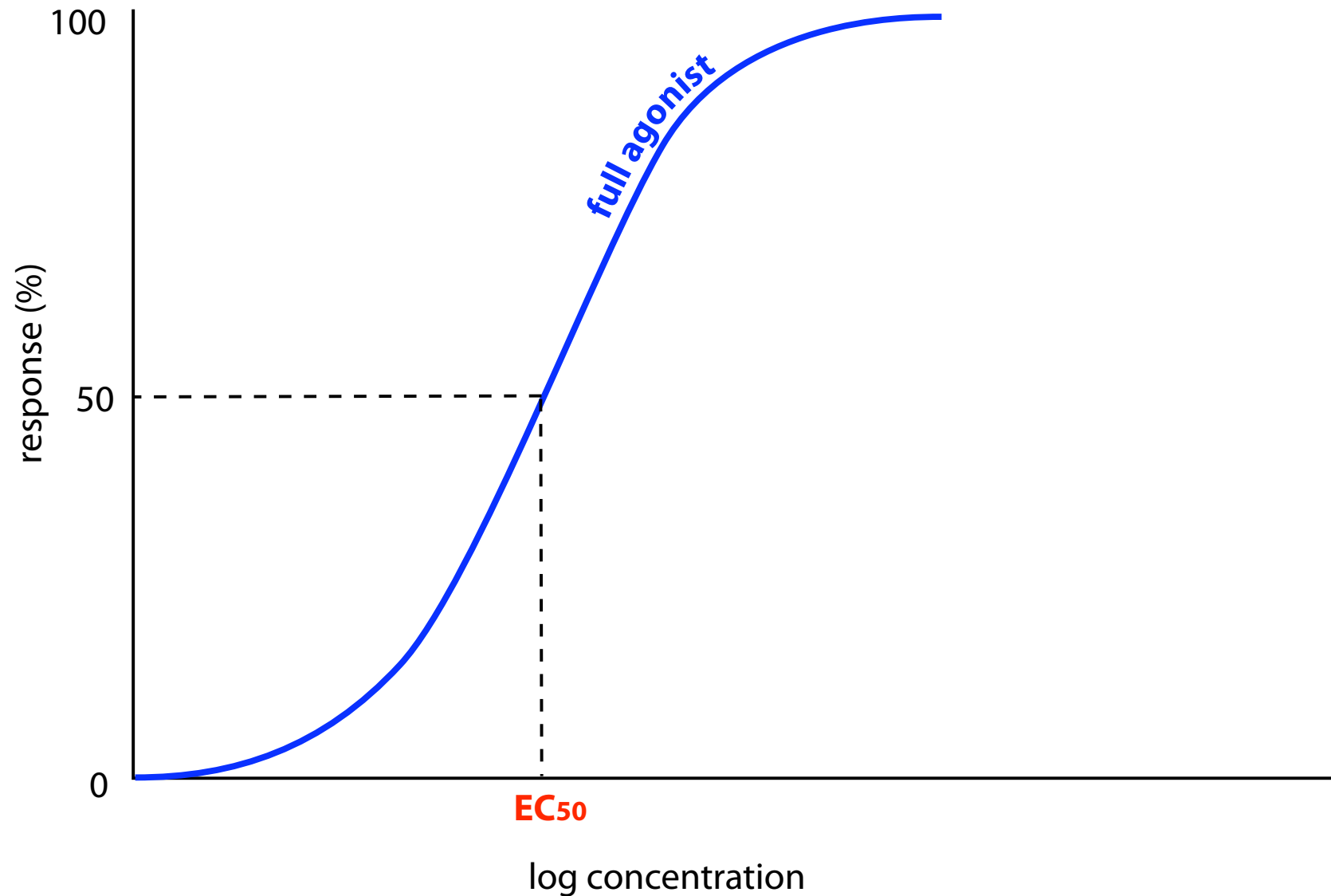
affinity

- **high affinity drug**
 - **high occupancy at low concentration**
- **low affinity drug**
 - **high occupancy at high concentration**

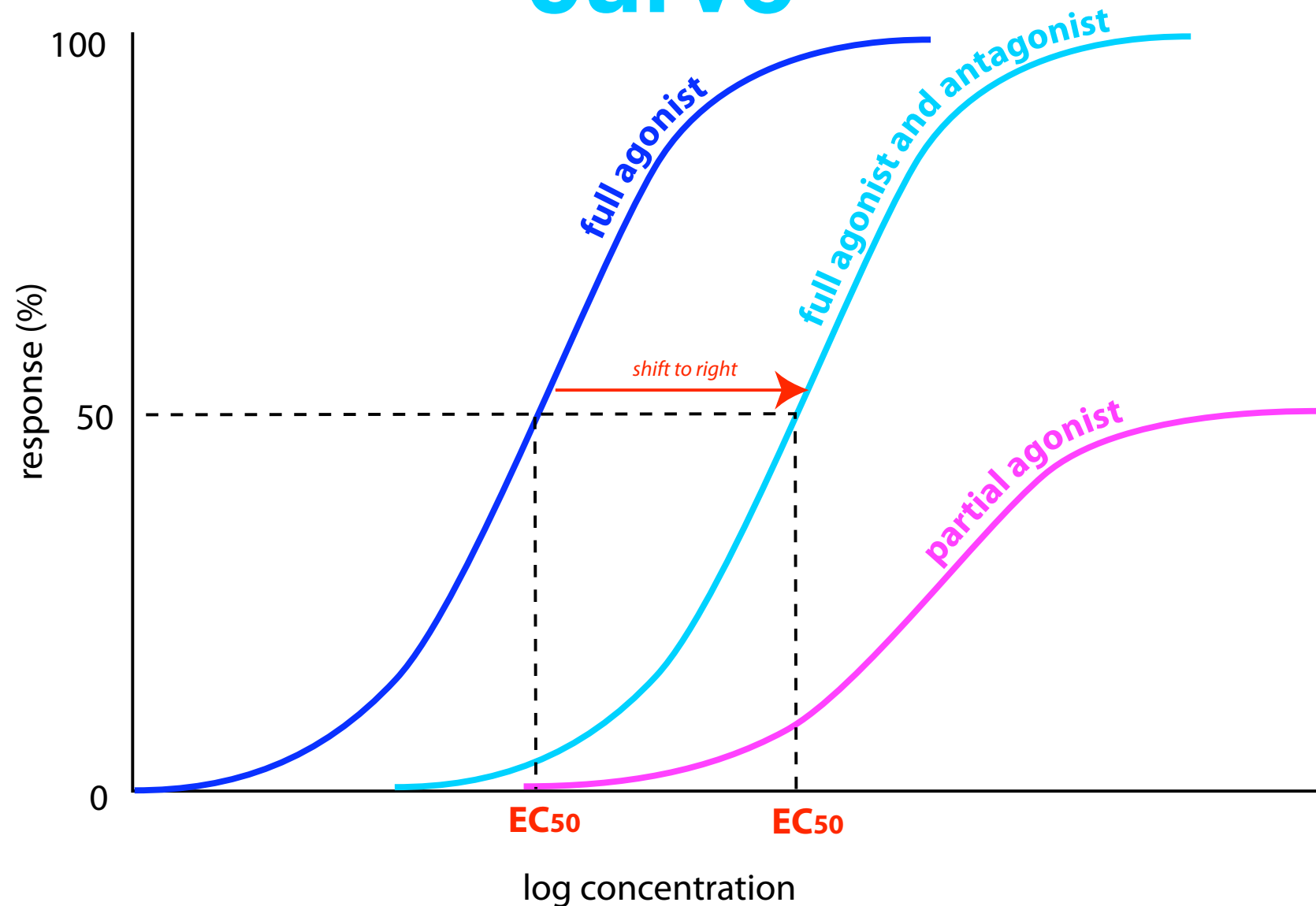
concentration response curves



log concentration response curve



log concentration response curve

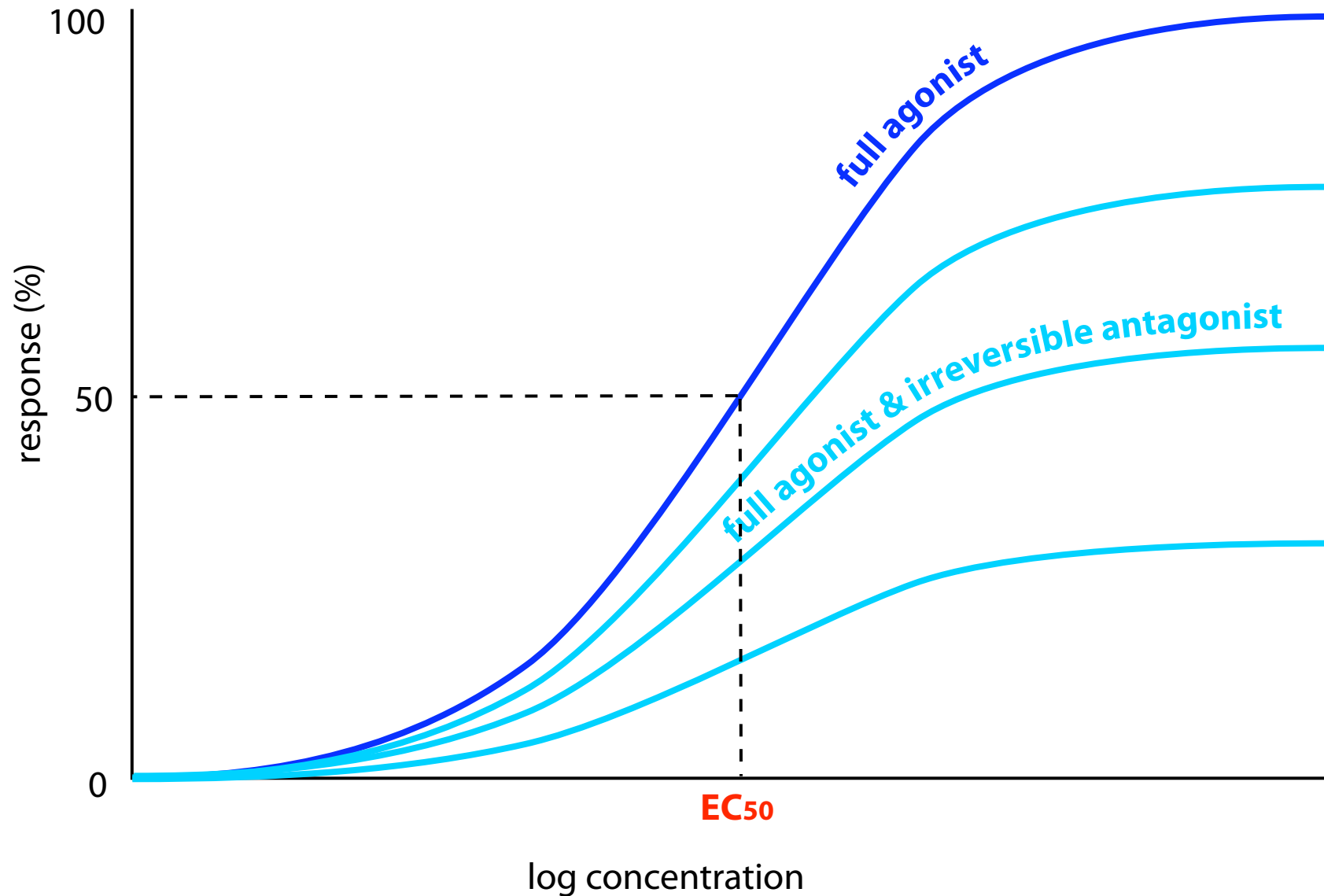


antagonism

A red mushroom with white spots, likely a Amanita muscaria, is the central visual element. It is positioned in the upper right quadrant of the slide, partially overlapping the title and the list. The background is a dark, textured field of dry grass or straw, which is slightly blurred to emphasize the mushroom.

- **competitive**
 - reversible
 - irreversible
- **non-competitive**
 - usually channel blockers
- **physiological**
- **chemical**
- **pharmacokinetic**

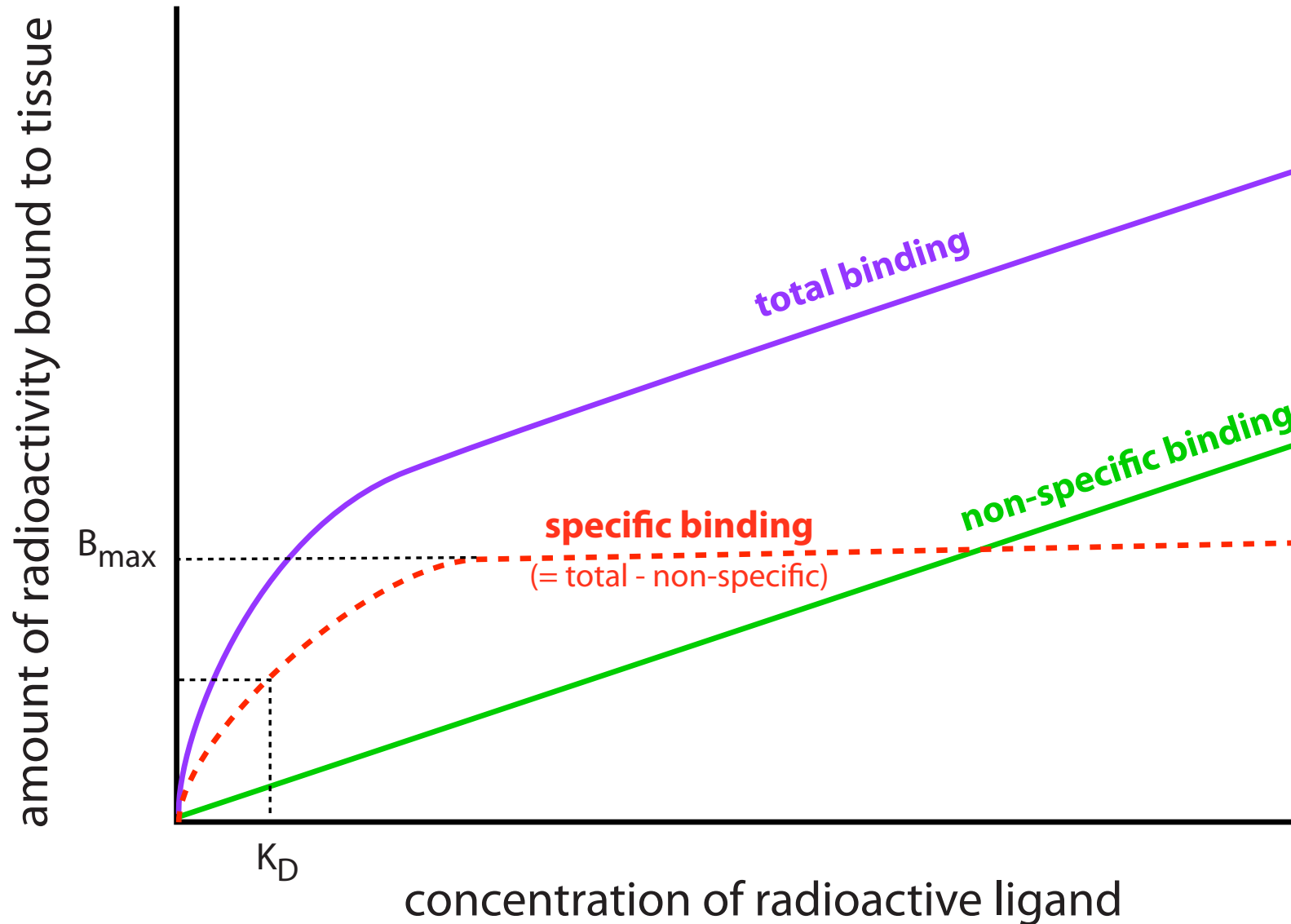
irreversible antagonist



binding assays

- tissues homogenised
- cell membranes collected
- incubated with radioligand
- recovered by filtration & washed
- radioactivity measured
- K_D and B_{max} calculated

binding assays

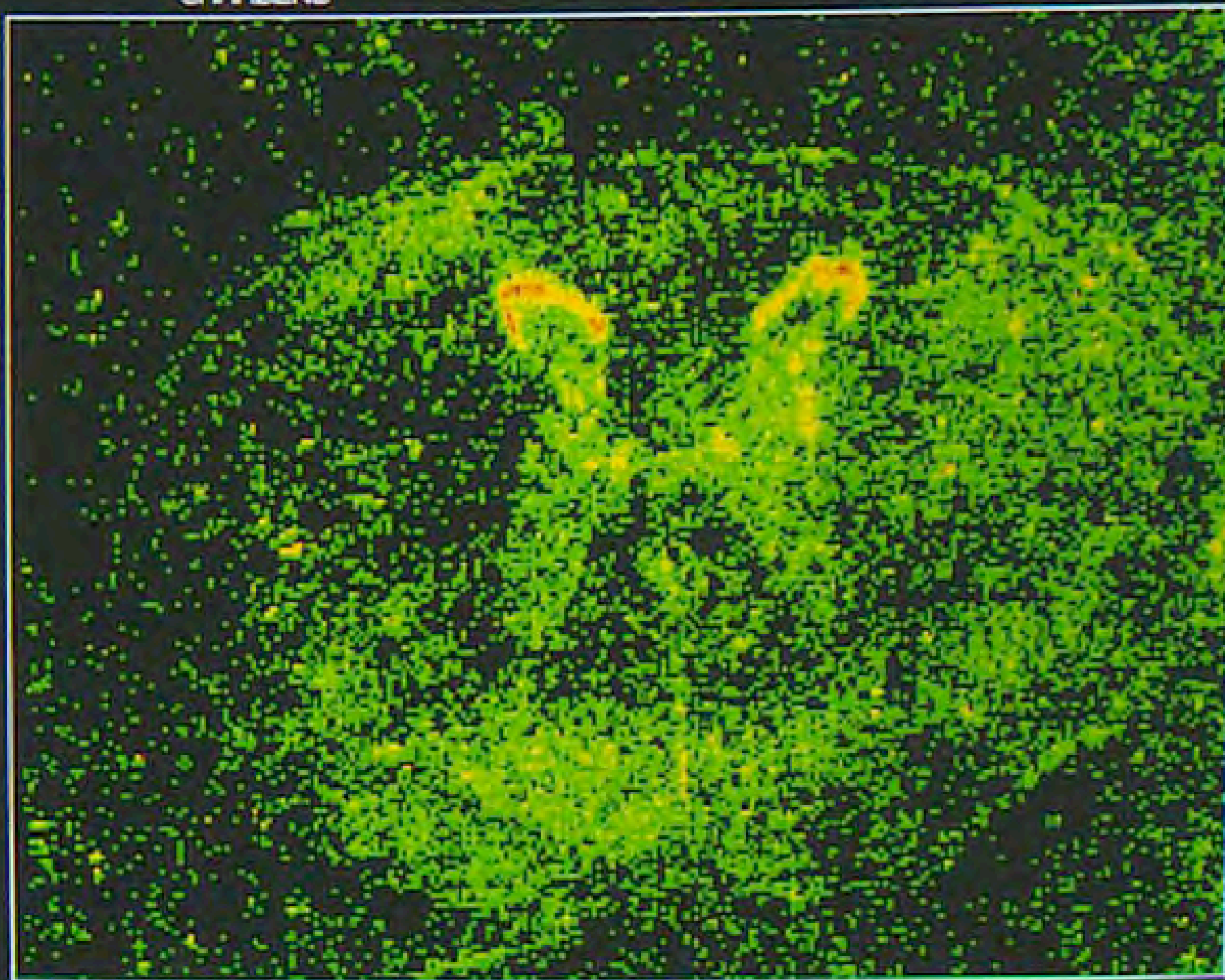
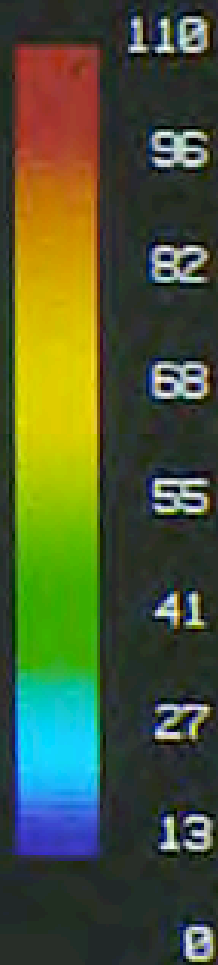


autoradiography



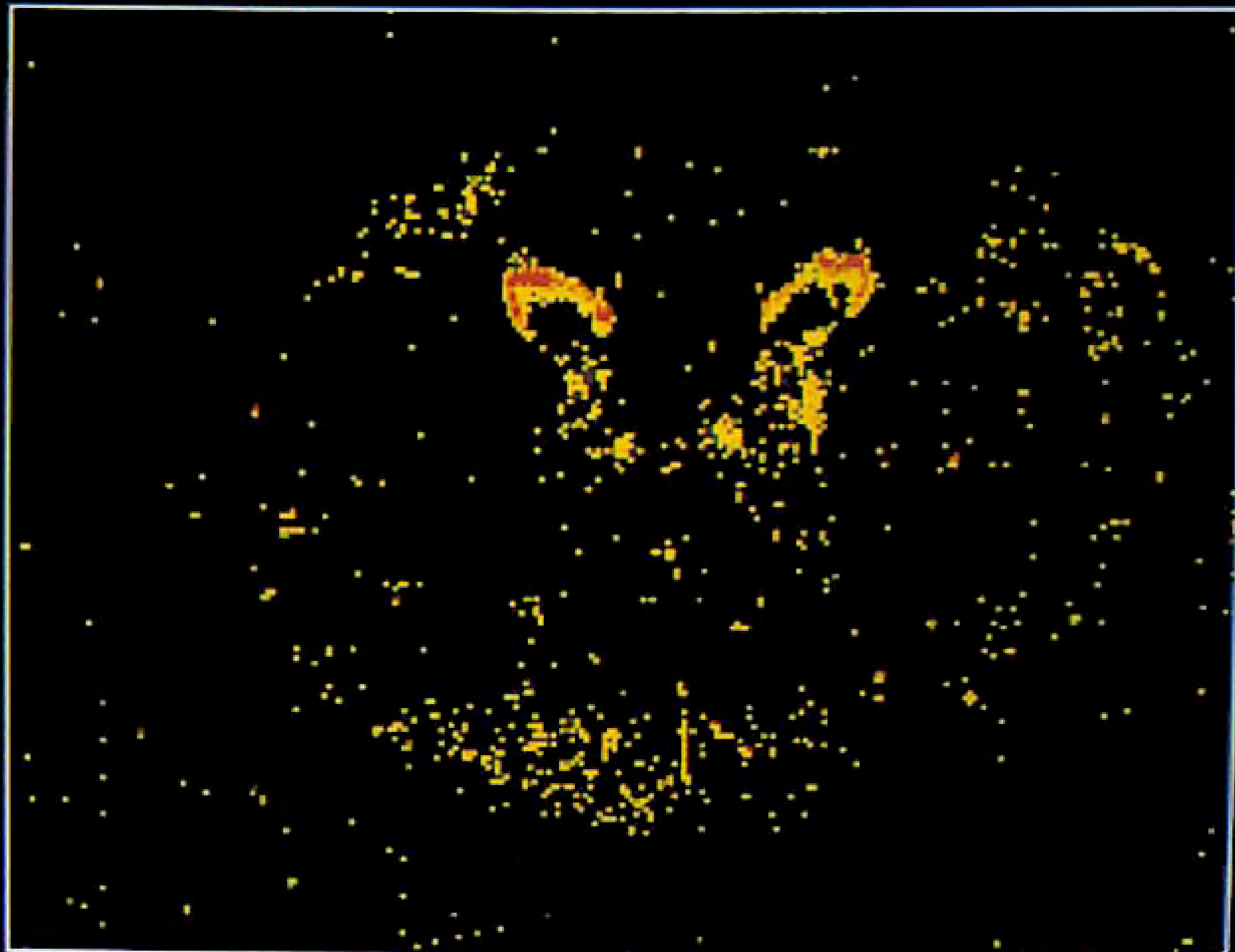
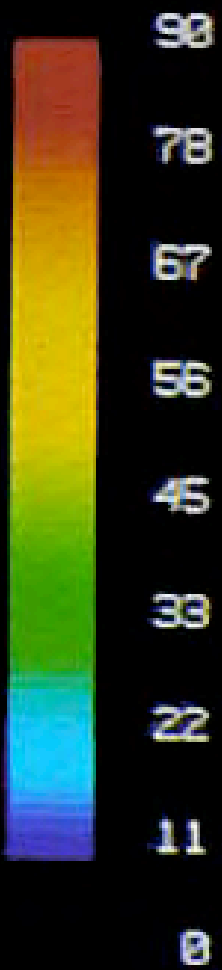
QUANTITATIVE AUTORADIOGRAPHY
ALAN
CHAMBERS

TOTAL
BINDING
fmol/mg

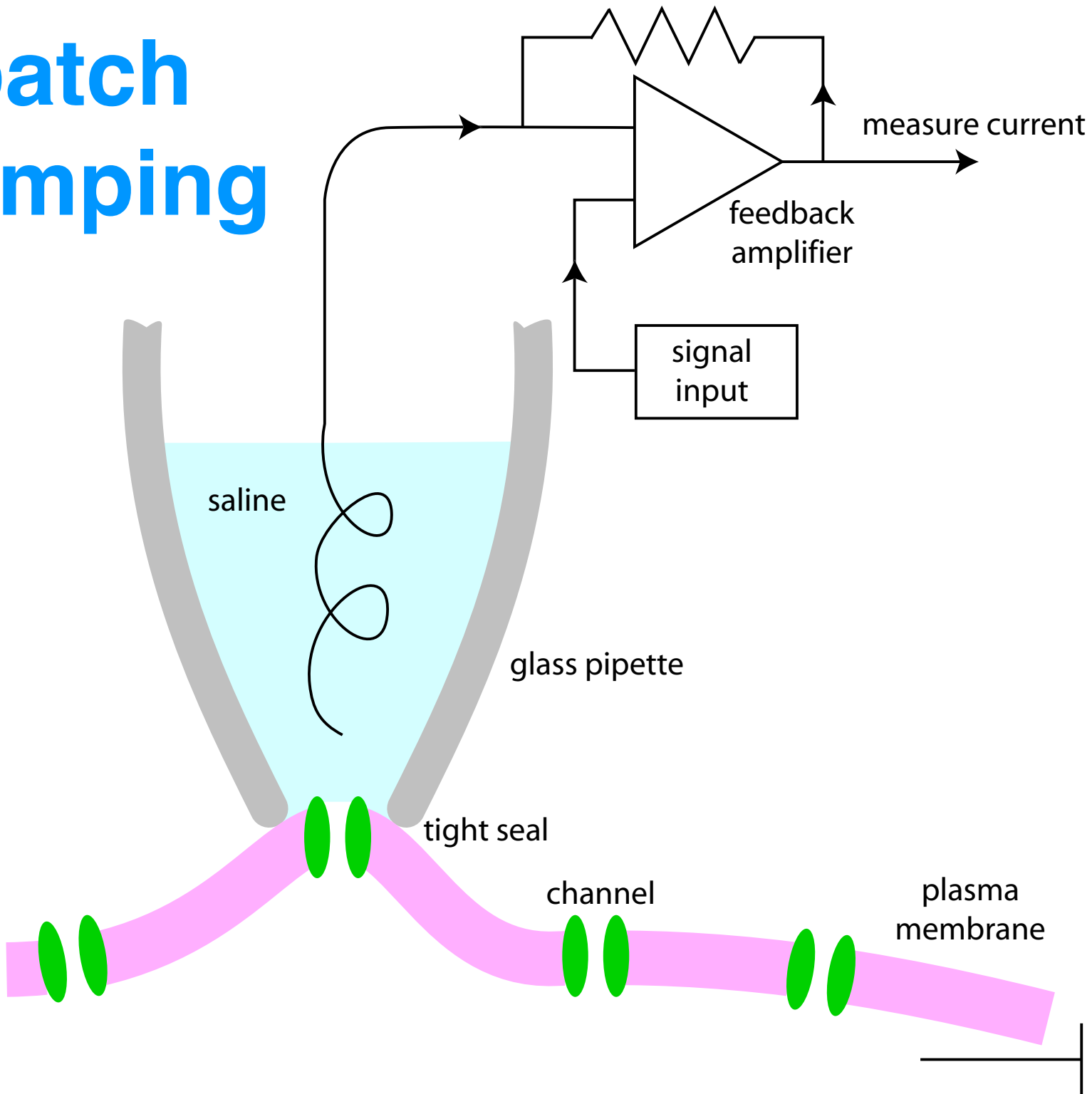


ALAN
CHAMBERS

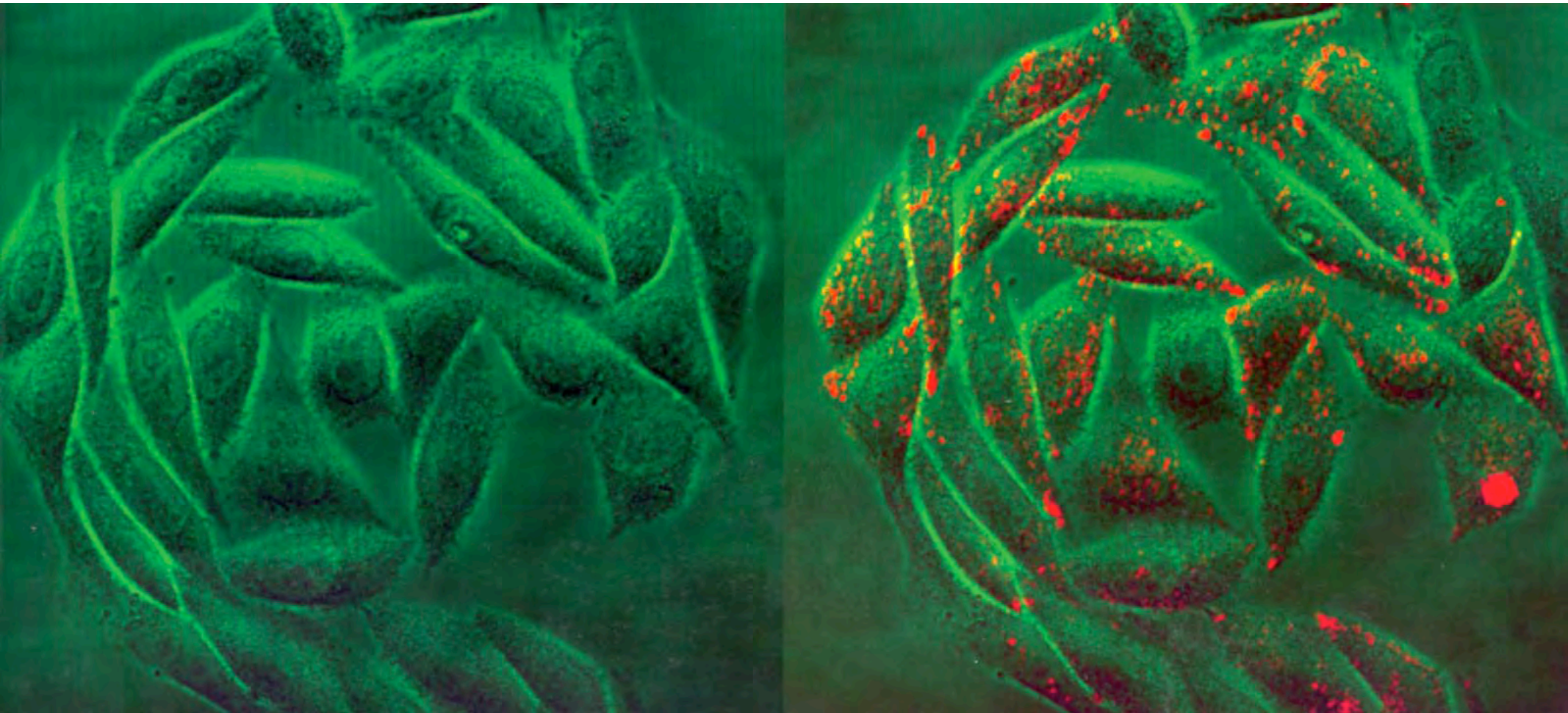
TOTAL
BINDING
fmol/mg



patch clamping



receptor activation assays



receptor numbers

- change with use
- up and down regulation



receptor reserve

- = spare receptors
- more receptors in tissue than required for full response
- partial agonists may produce a full response in a tissue with many spare receptors
- common in smooth muscle

desensitisation / tachyphylaxis (receptors)

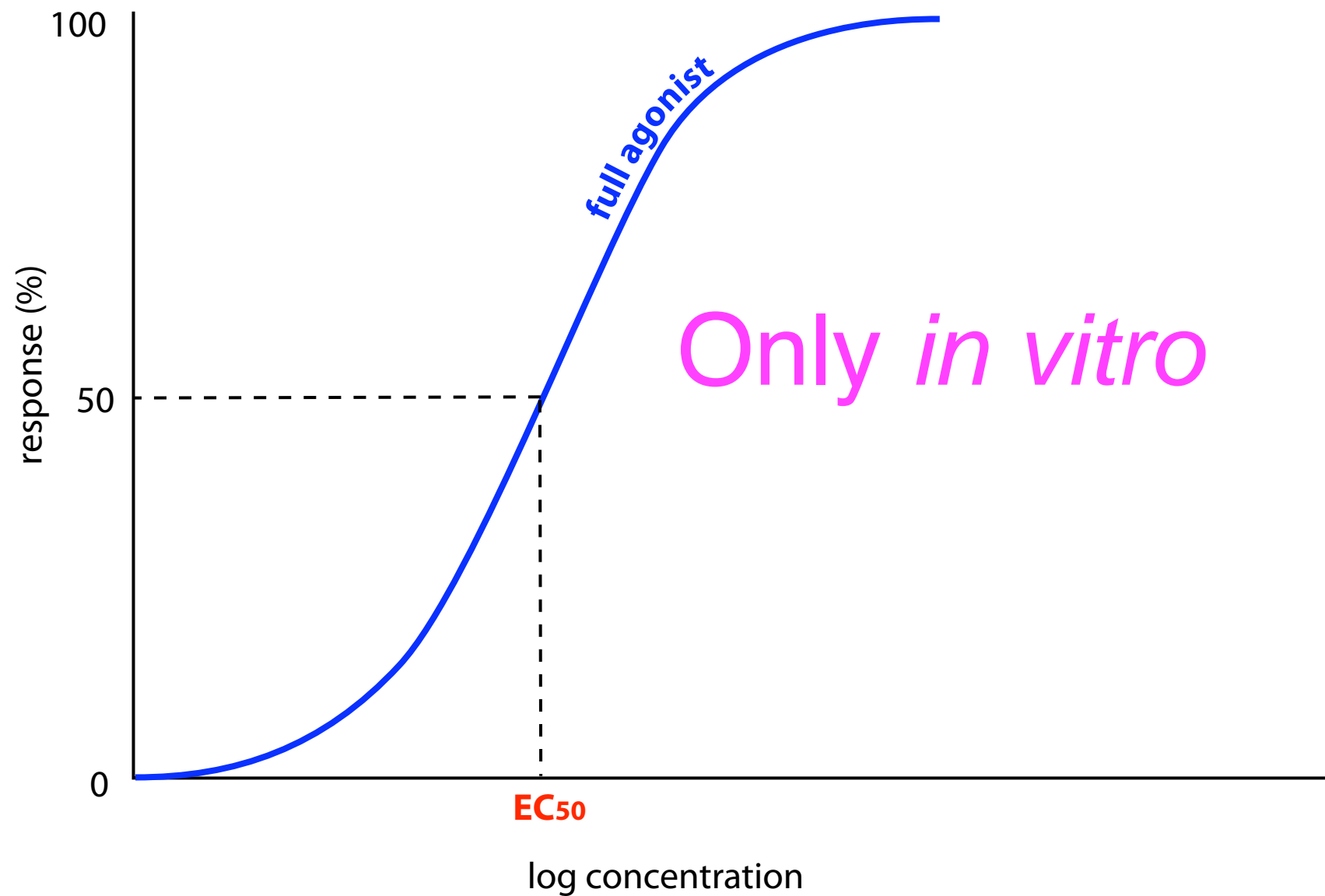
- **receptor down regulation**
- **conformation changes**
- **transducer changes**
- **mediator depletion**

A red mushroom with white spots growing in grass. The mushroom is the central focus, with its cap showing a pattern of white spots on a red background. The stem is white and slightly thick. The background is a dense field of dry, yellowish-brown grass.

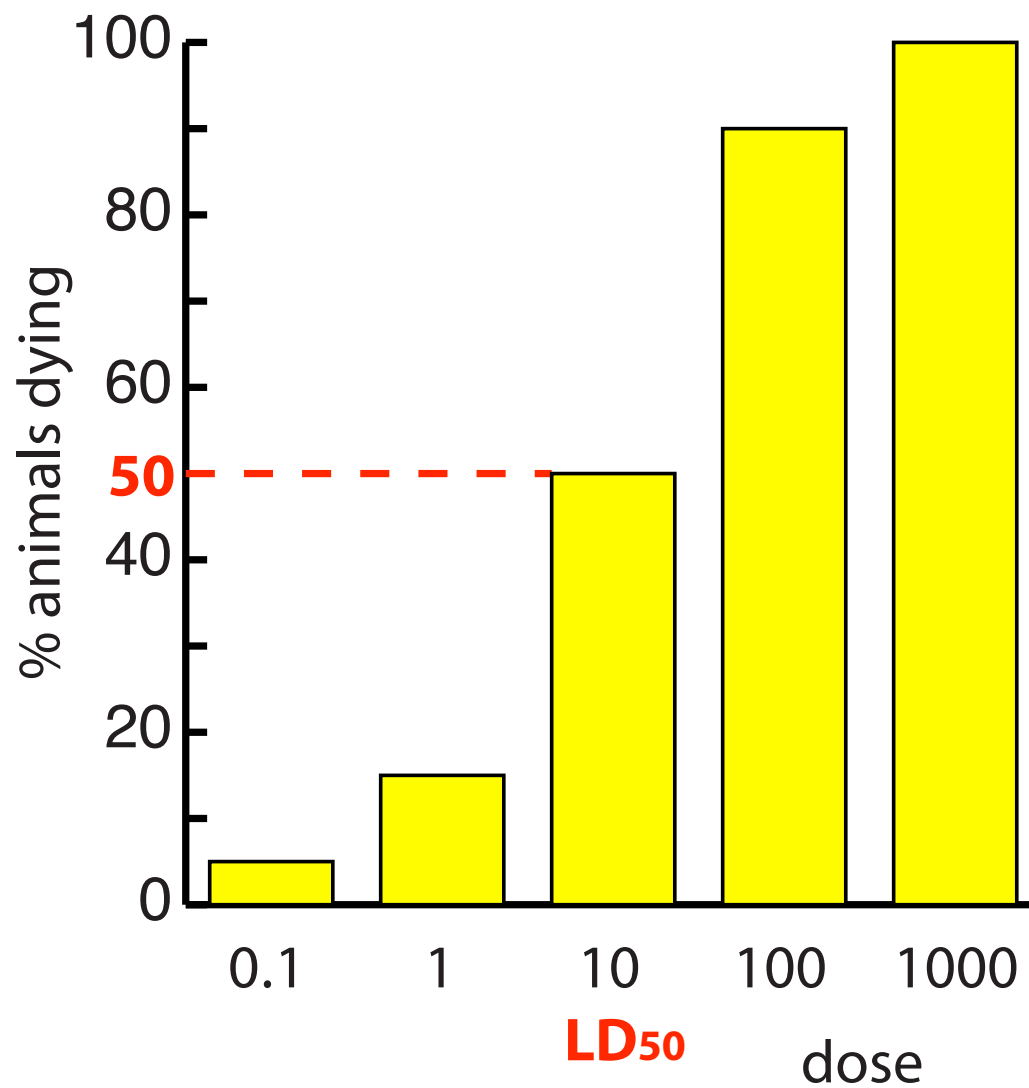
tolerance (animals)

- **increased metabolism**
- **adaptation**
 - **progession of disease**
- **drugs pumped out**

EC₅₀



ED₅₀



therapeutic ratio

- an index of a drug's safety

$$= \frac{LD_{50}}{ED_{50}}$$

therapeutic ratio

- difference between effective dose and dose which produces side effects is clinically important
- LD₅₀ ethically unacceptable

What would you do?

- thoracotomy
- premed:
buprenorphine
(partial agonist)
- intra-op: fentanyl
(full agonist)
- recovery: naloxone
(antagonist)
- post op analgesia?



drug receptor interactions

- agonists produce an effect
- competitive antagonists block the effect but the blockade can be overcome by increasing the agonist concentration
- drugs can be compared using EC_{50} values in vitro and ED_{50} values in vivo
- therapeutic index is a measure of how safe a drug is