

A close-up photograph of a red mushroom with white spots, likely an Amanita muscaria, growing in a field of dry grass. The mushroom has a bright red cap with numerous white, irregular spots. The stem is white and appears to have a fine, hair-like texture. The background is a dense field of dry, yellowish-brown grass.

Pharmacokinetics

pharmacokinetics

A red mushroom with white spots, likely an Amanita muscaria, is growing in a field of dry, yellowish-brown grass. The mushroom has a bright red cap with numerous white, irregular spots and a thick, white, fuzzy ring around the base of the stem. The background is a dense field of dry grass, creating a textured, natural setting.

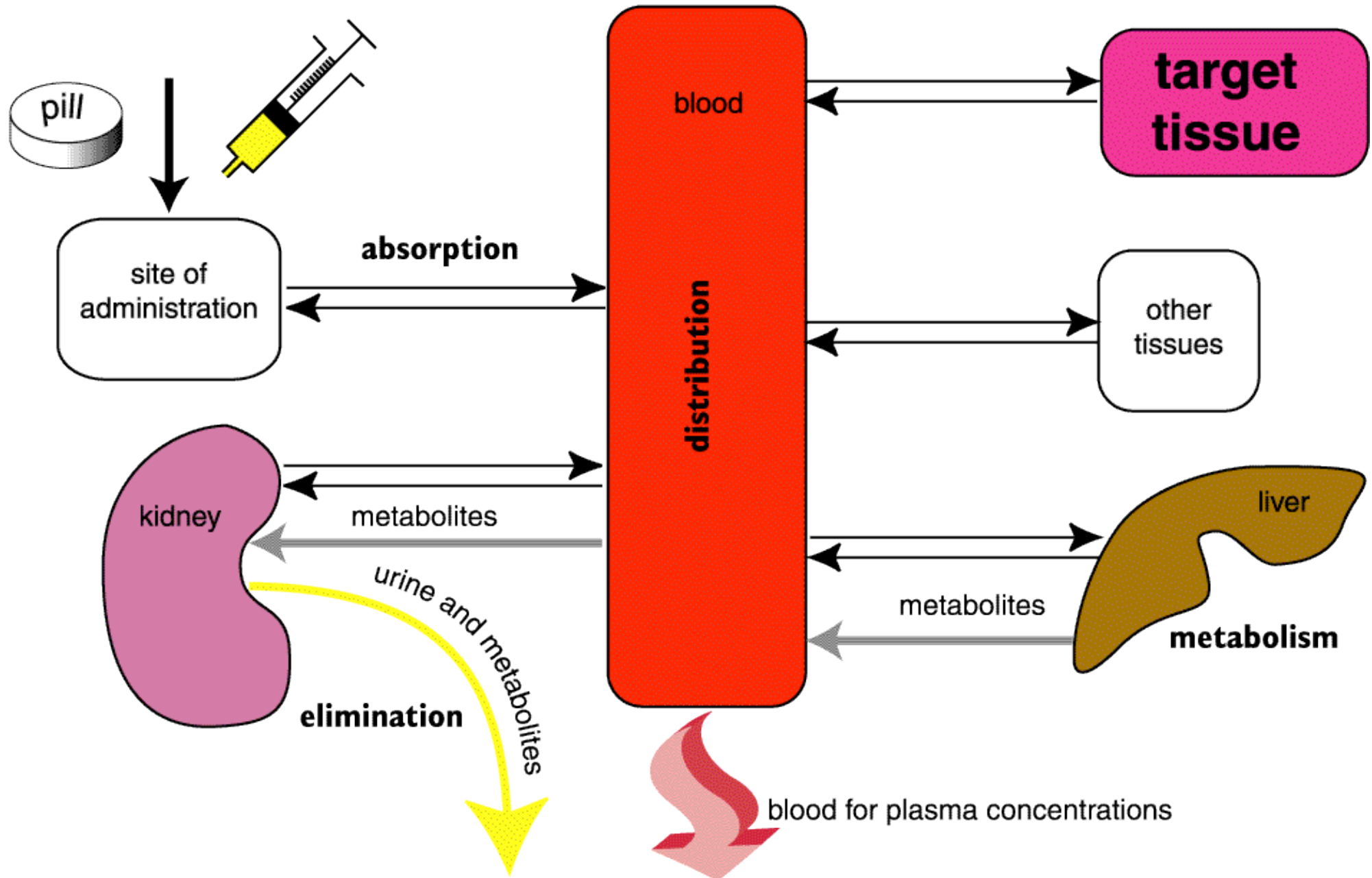
- What the animal does to the drug
- Movement of the drug in the body

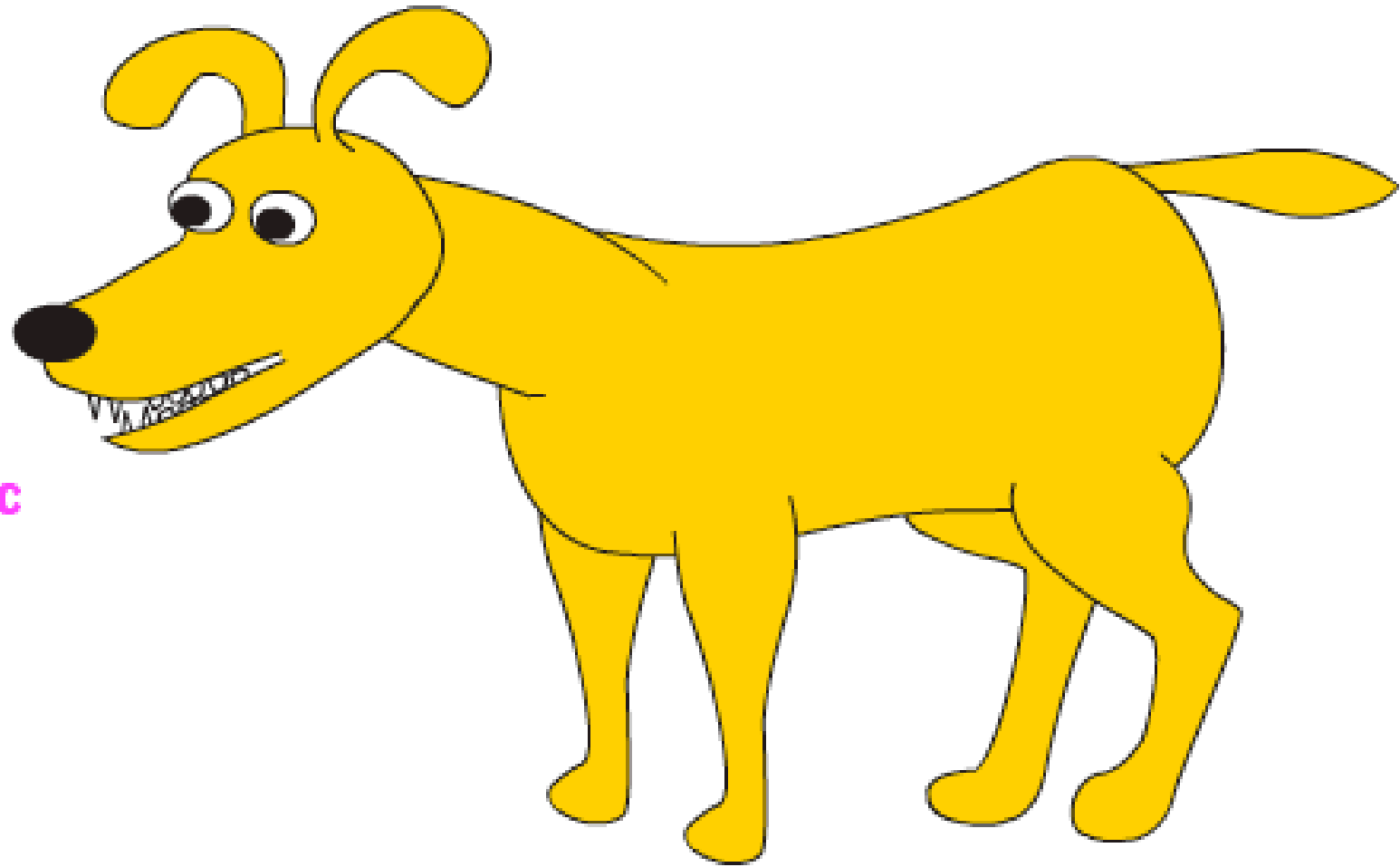
pharmacokinetics

A red mushroom with white spots, likely a fly agaric, 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.

- **absorption**
- **distribution**
- **metabolism**
- **elimination**

pharmacokinetics





Antibiotic

basic assumptions

- drugs must cross membranes to get to target
- actions are proportional to plasma concentrations

routes of administration

- enteral
 - via the gut
- parenteral
 - by injection
- other



routes of administration

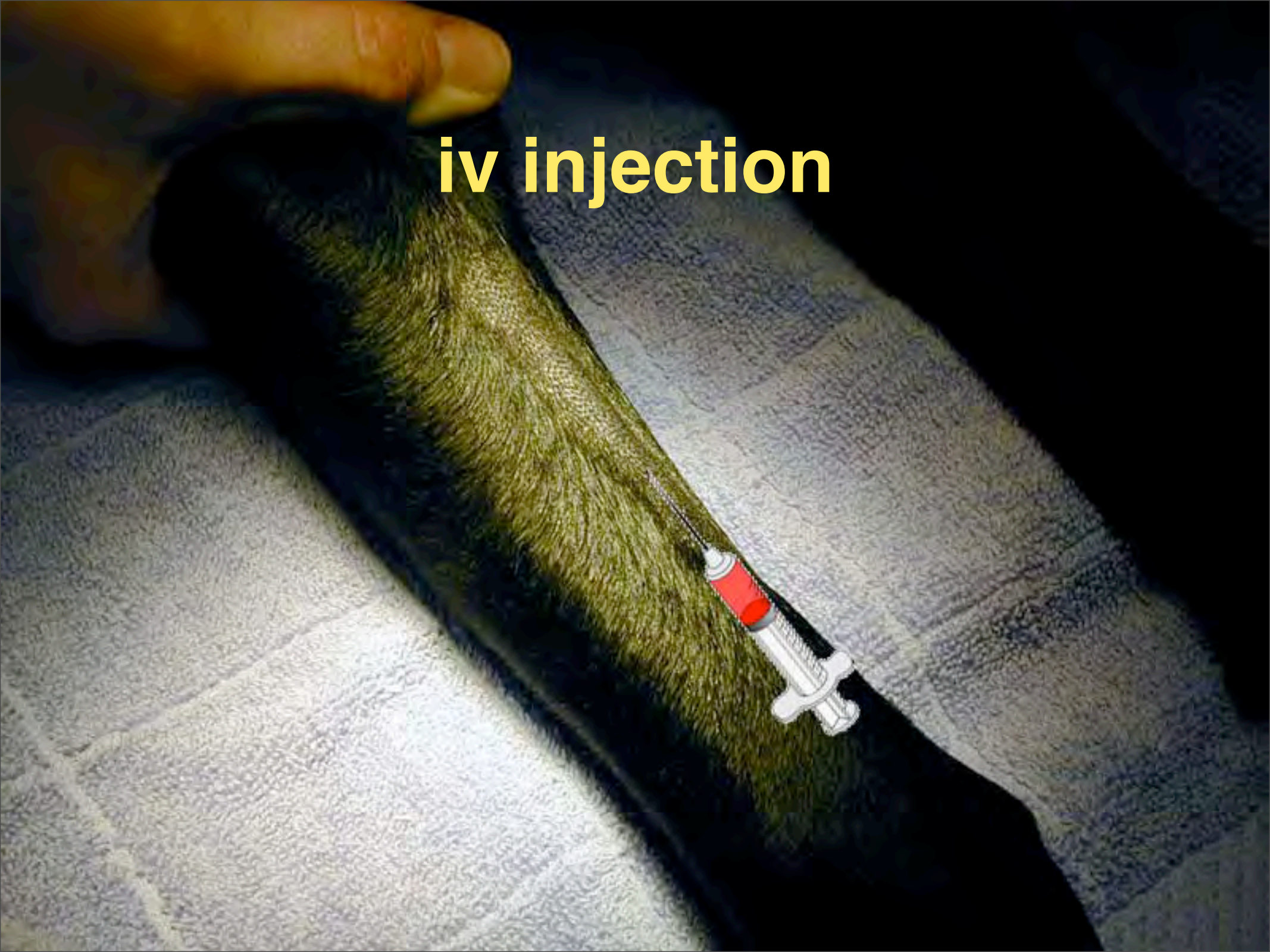
A red mushroom with white spots, resembling a fly agaric, is growing in a field of dry grass. The mushroom has a bright red cap with numerous white, irregular spots. Its stem is thick and appears to have a white, possibly poisonous, base. The background is a dense field of dry, yellowish-brown grass.

- enteral
 - oral (po = *per os*)
 - sublingual
 - rectal

routes of administration

- **parenteral**
 - intravenous (iv)
 - intramuscular (im)
 - **nb muscle becomes meat in food animals!**
 - **subcutaneous (sc or SQ)**
 - **intraperitoneal (ip)**

iv injection



im injection



routes of administration

- **parenteral**
 - intravenous (iv)
 - intramuscular (im)
 - **nb muscle becomes meat in food animals!**
 - **subcutaneous (sc or SQ)**
 - **intraperitoneal (ip)**

routes of administration

A red mushroom with white spots, resembling a fly agaric, is the central visual element. It is positioned in the upper right quadrant of the slide. The background is a dark, textured field of dry grass or straw, which is slightly blurred to emphasize the mushroom. The overall color palette is muted, with the red of the mushroom providing a strong contrast against the dark background.

- inhalation
- topical
 - intramammary
 - intrauterine
 - onto cornea
- transdermal
- nasal
- epidural / intrathecal

absorption

A red mushroom with white spots, likely an Amanita muscaria, is growing in a field of dry grass. The mushroom is the central focus of the image, with its bright red cap and white spots contrasting against the dry, brownish-yellow grass. The background is slightly blurred, emphasizing the mushroom.

- **dissolution**
- **movement out of site of administration**
- **movement into blood vessels**

dissolution

A red mushroom with white spots, likely an Amanita muscaria, is the central visual element. It is positioned in the upper right quadrant of the frame. The background is a dense field of dry, yellowish-brown grass. The entire image has a dark, semi-transparent overlay that serves as a background for the text.

- most drugs must dissolve in water and oil
- ionisation important
 - pH important

dissolution



- **main factors**
 - **pills**
 - **coatings**
 - **disintegrants**
 - **vehicle**
 - **all**
 - **solute**

injection formulation

- **solutions in water**
 - rapid onset of action
- **suspensions of insoluble salts**
 - slower release
 - mixtures of salts can be used
 - **not iv**
- **solutions in oil**
 - slow release
 - **not iv**

injection formulation

- **complexes with soluble carriers**
 - cyclodextrins
 - polyvinyl pyrrolidone (PVP)
 - propylene glycol
- **used to get lipid soluble drugs into aqueous solution**

drug delivery devices

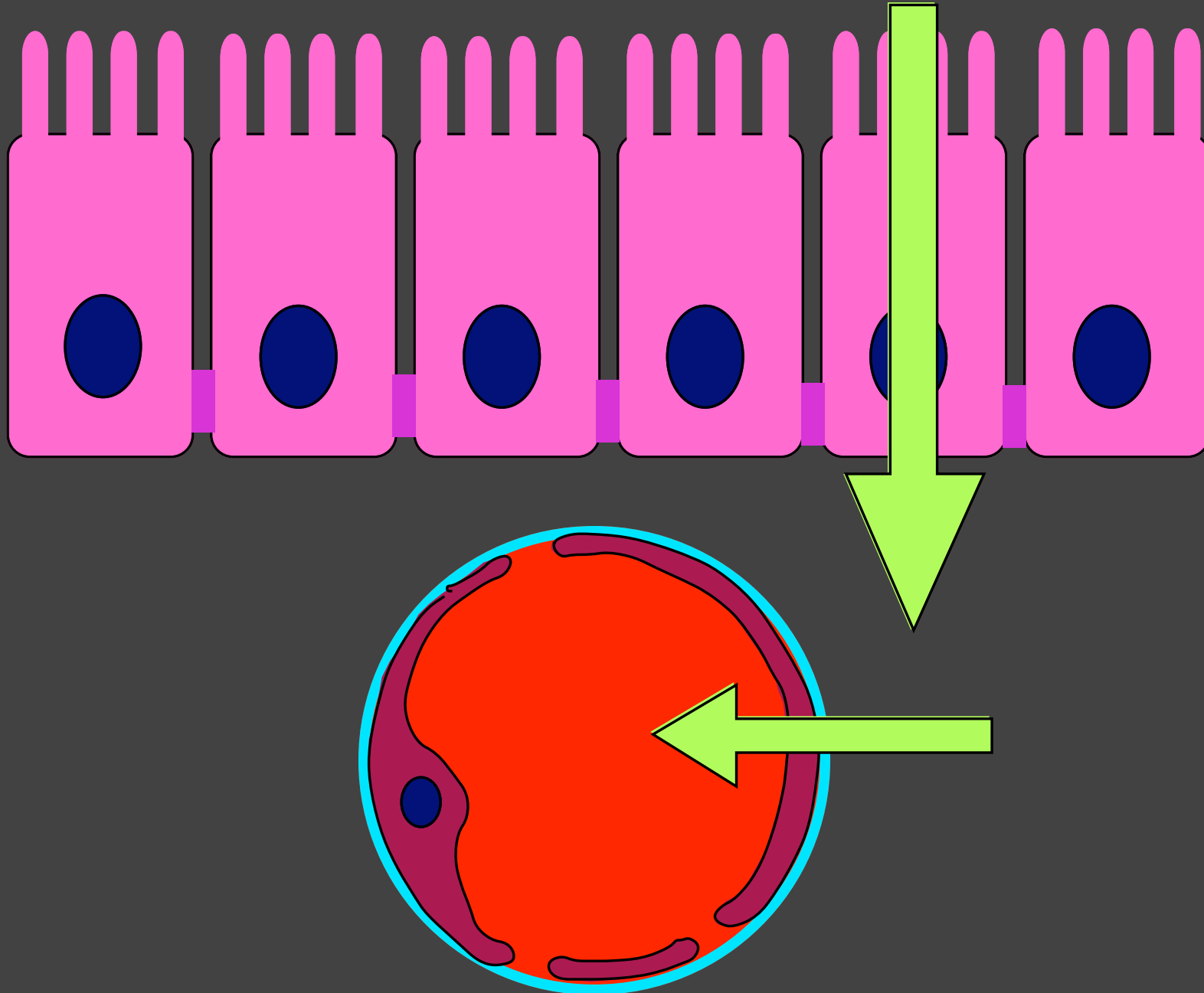
- “solution” in silicone rubber
 - very slow release
- osmotic pumps
 - predictable slow release
- mechanical pumps
 - variable rates of delivery
 - can be computer controlled \pm feedback

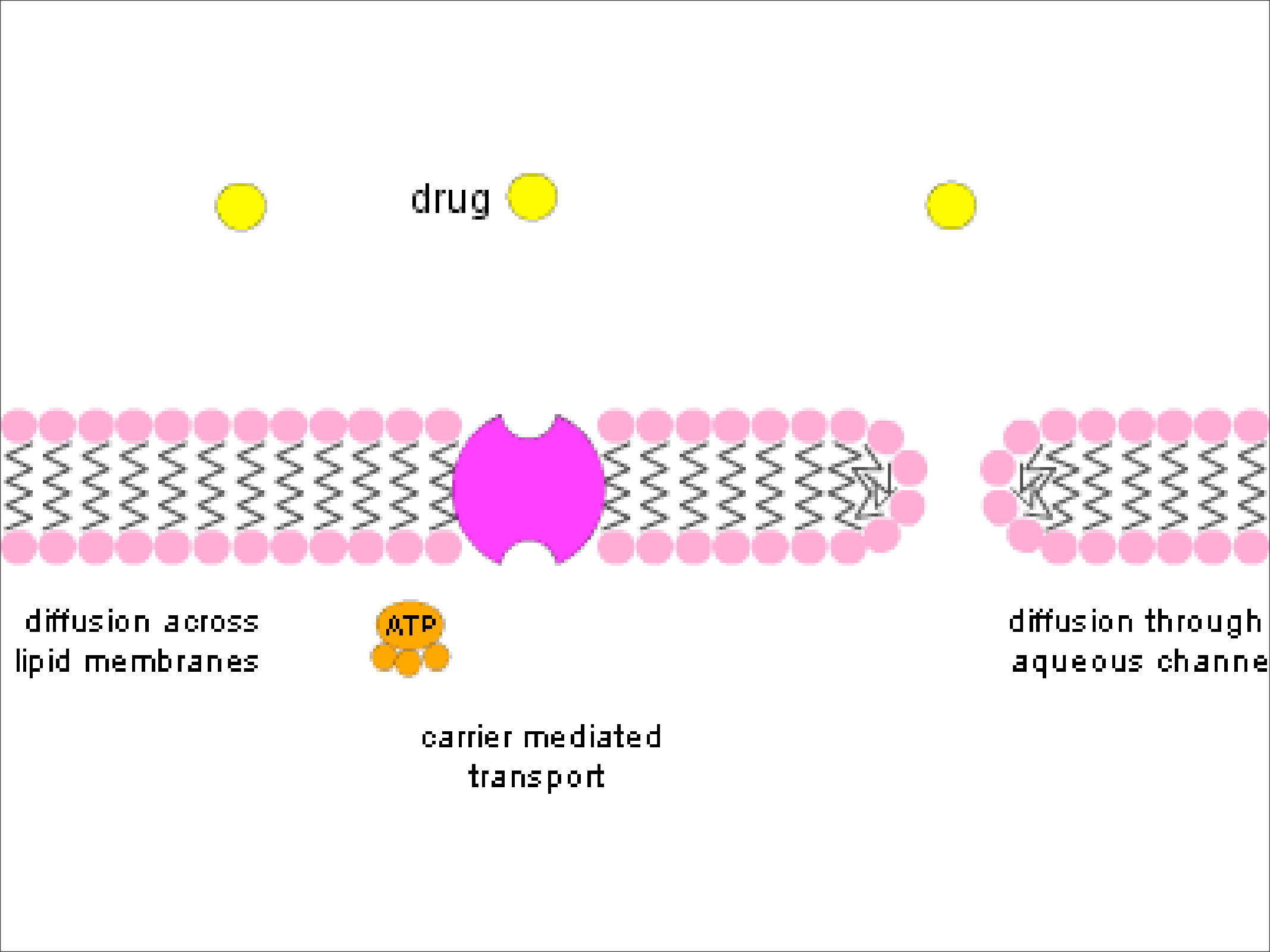


barriers to absorption

- after iv administration
 - none
- after oral administration
 - gastric mucosa
 - endothelium
- after im or sc administration
 - endothelium

drug

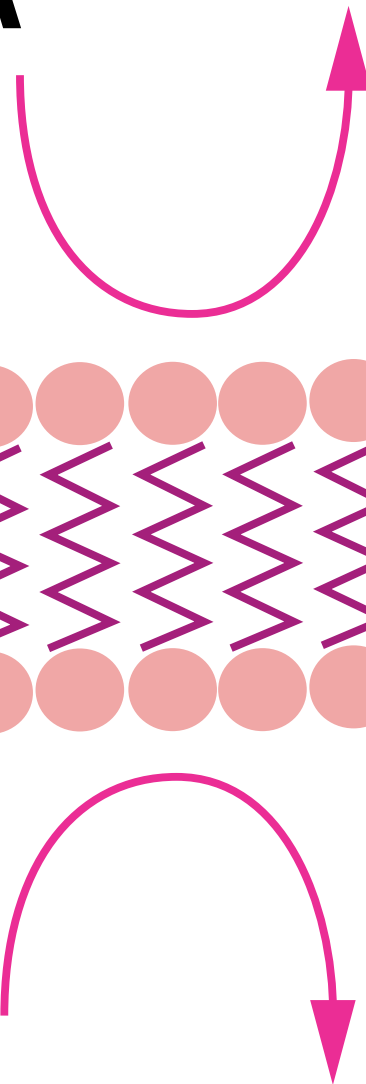
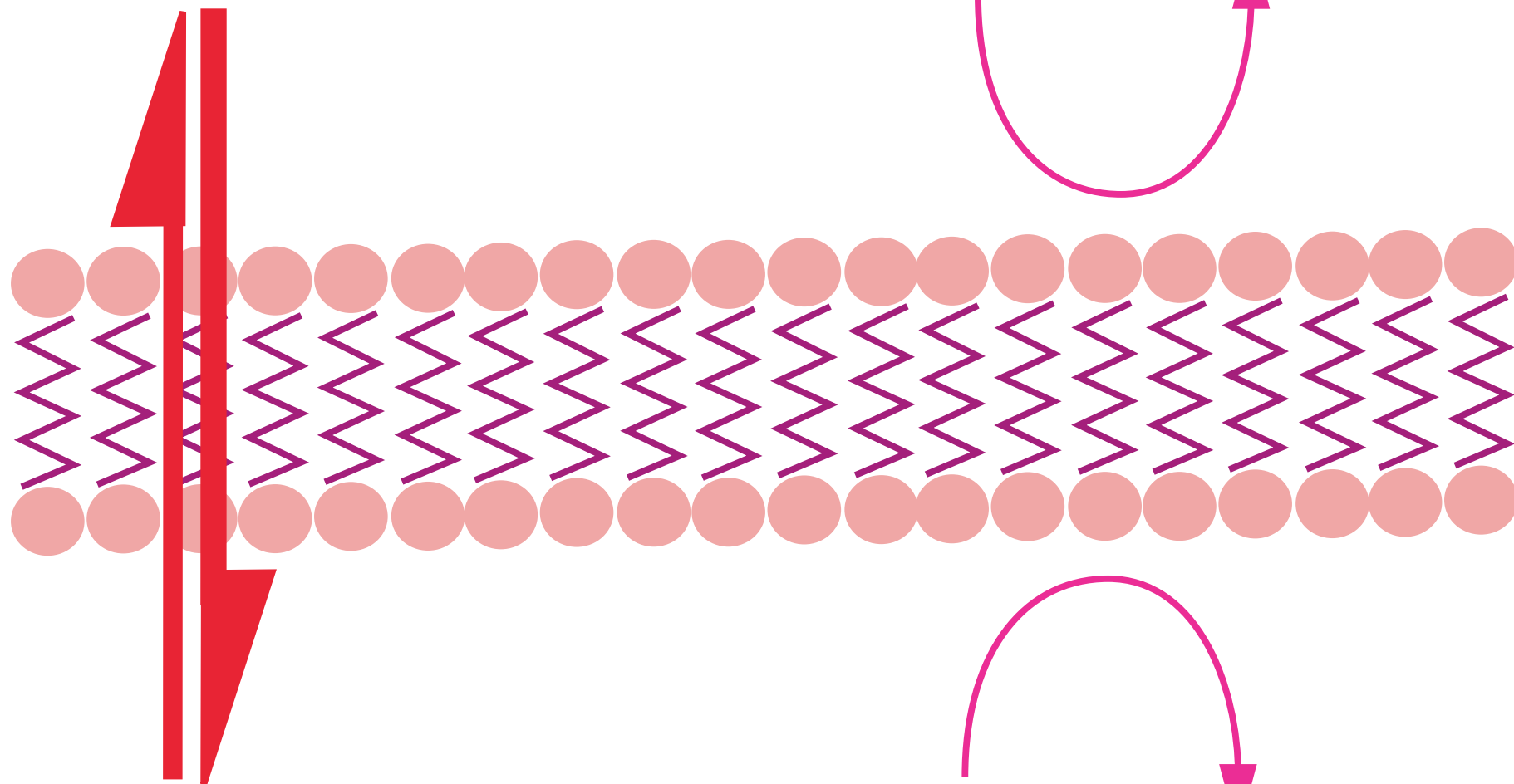


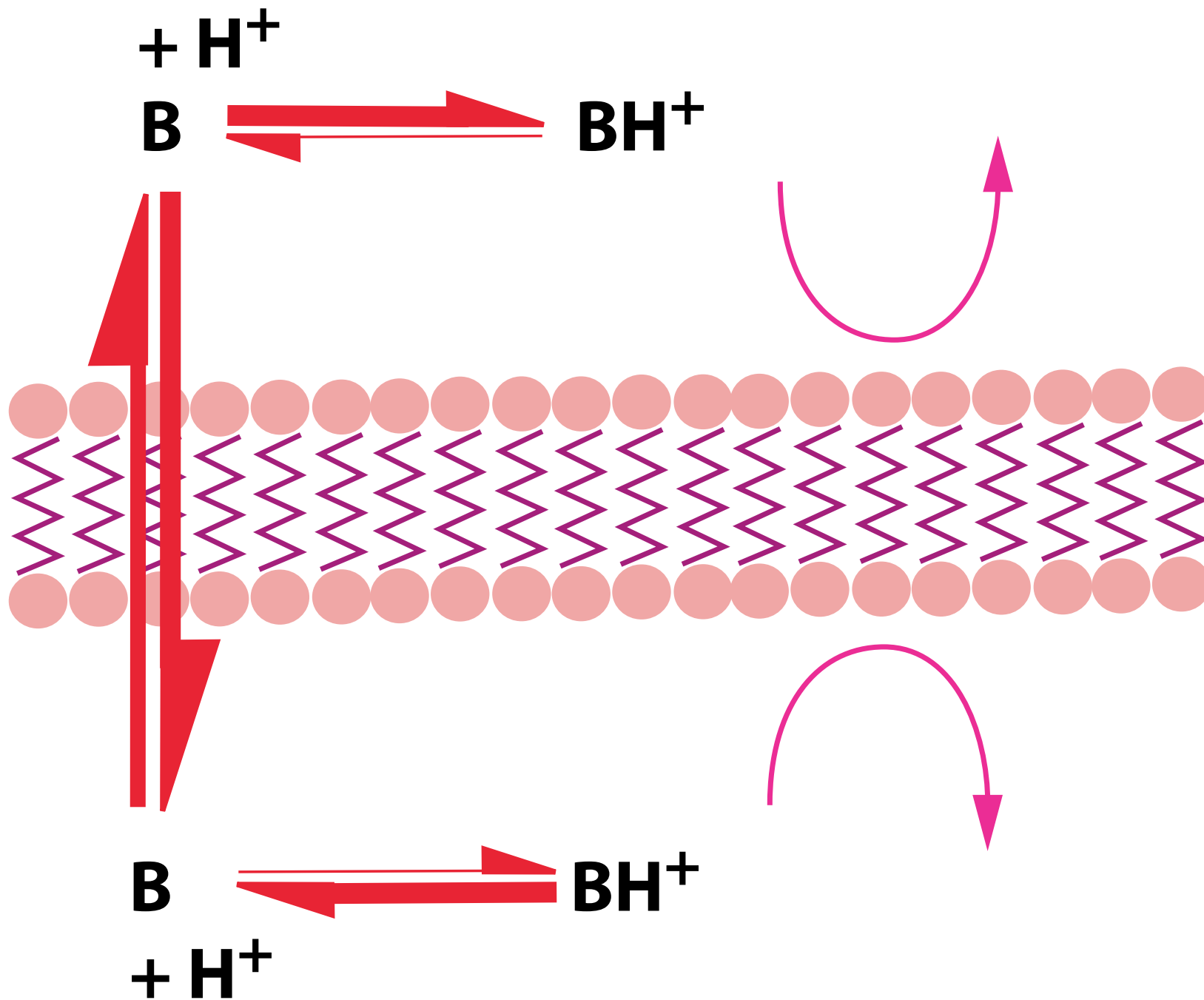


effects of pH

- most drugs are either weak bases or weak acids
- ionised forms are not lipid soluble







Henderson Hasselbach equation

for acids $\text{pH} = \text{pK}_a + \log \frac{\text{A}}{\text{AH}}$

for bases $\text{pH} = \text{pK}_a + \log \frac{\text{B}}{\text{BH}^+}$

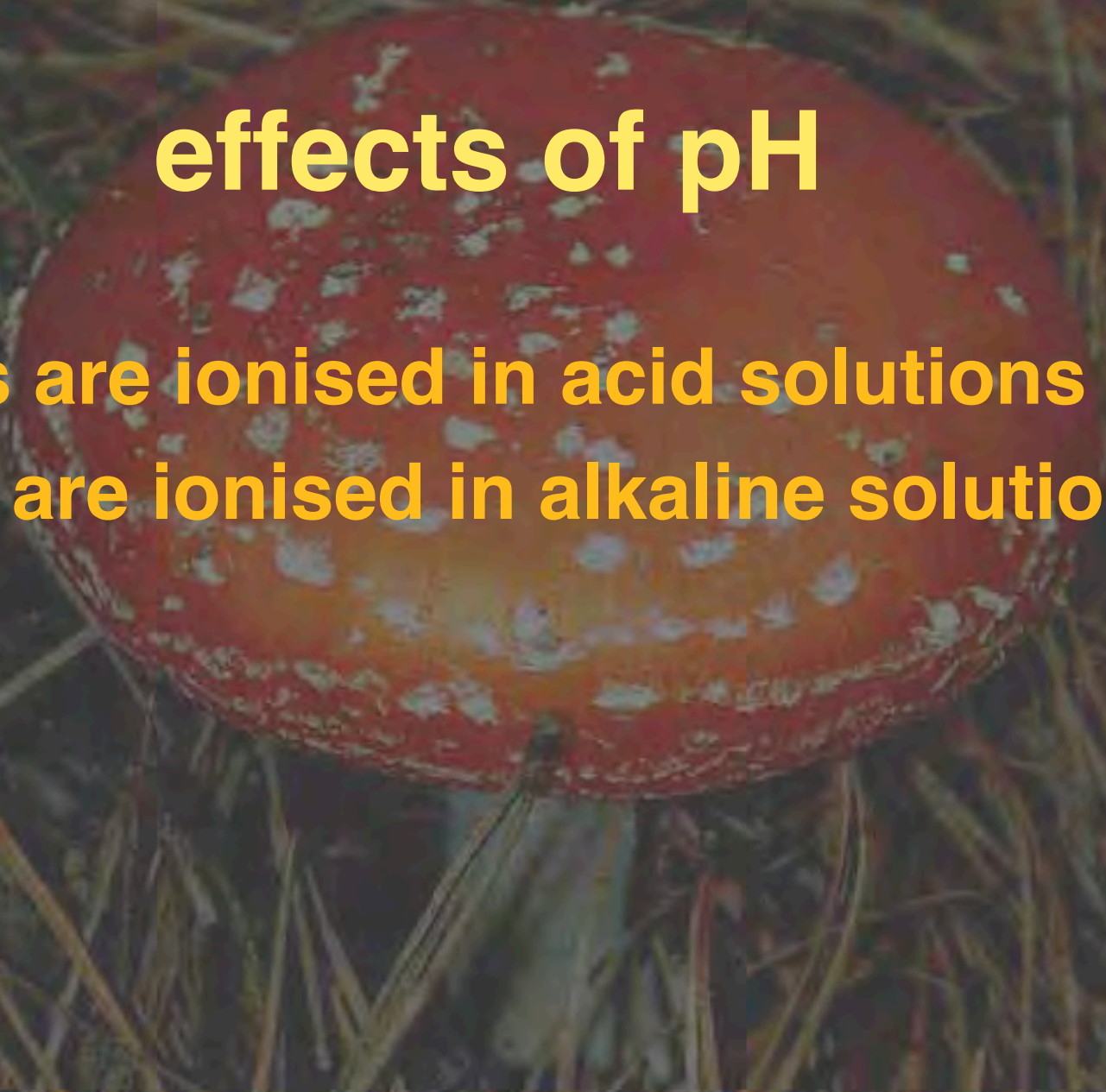
ie, when $\text{pH} = \text{pK}_a$, the drug is 50% ionised

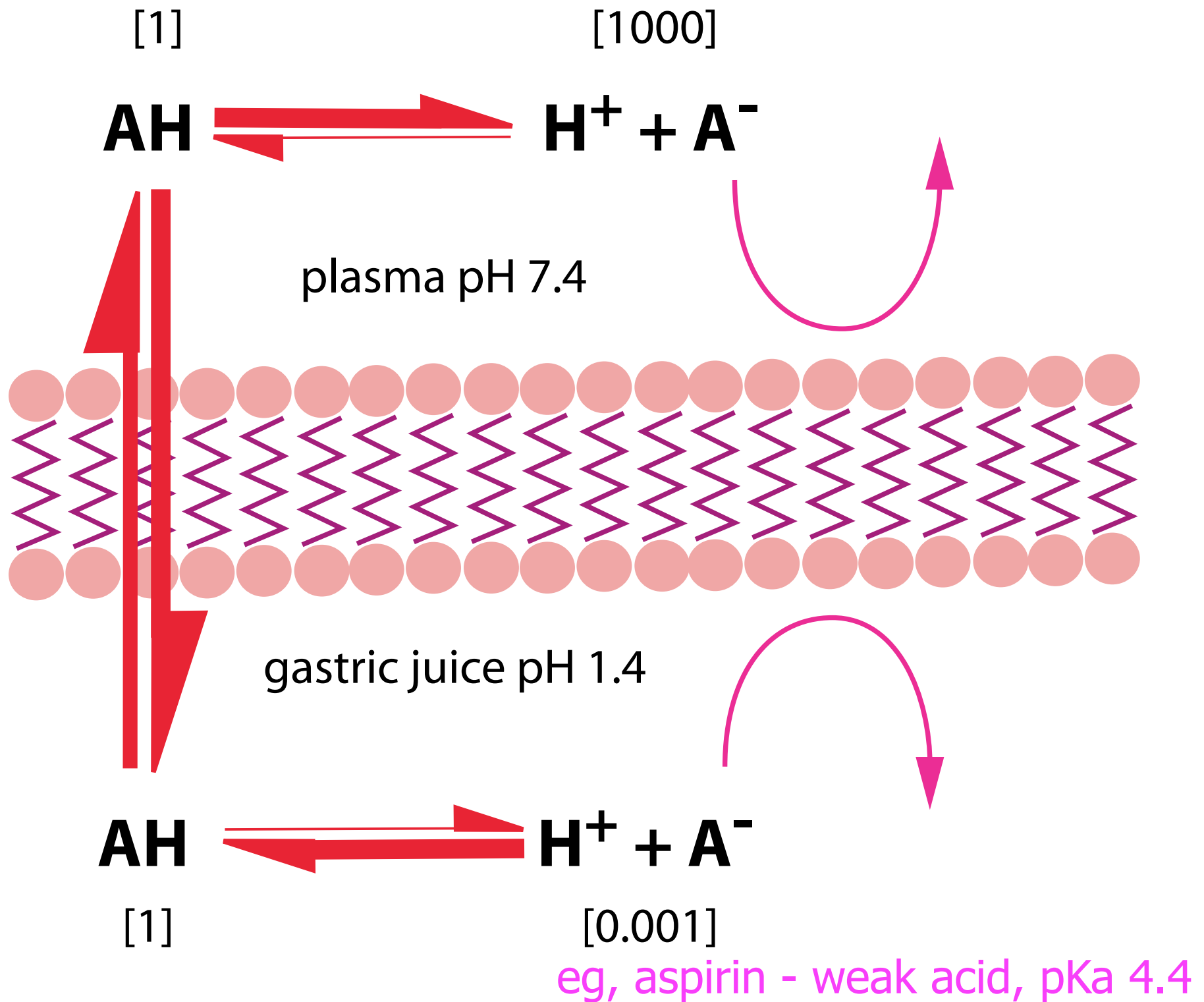
effects of pH

- when $\text{pH} < \text{pK}_a$, more protonated drug exists (AH & BH^+)
- when $\text{pH} > \text{pK}_a$, more unprotonated drug exists (A^- & B)

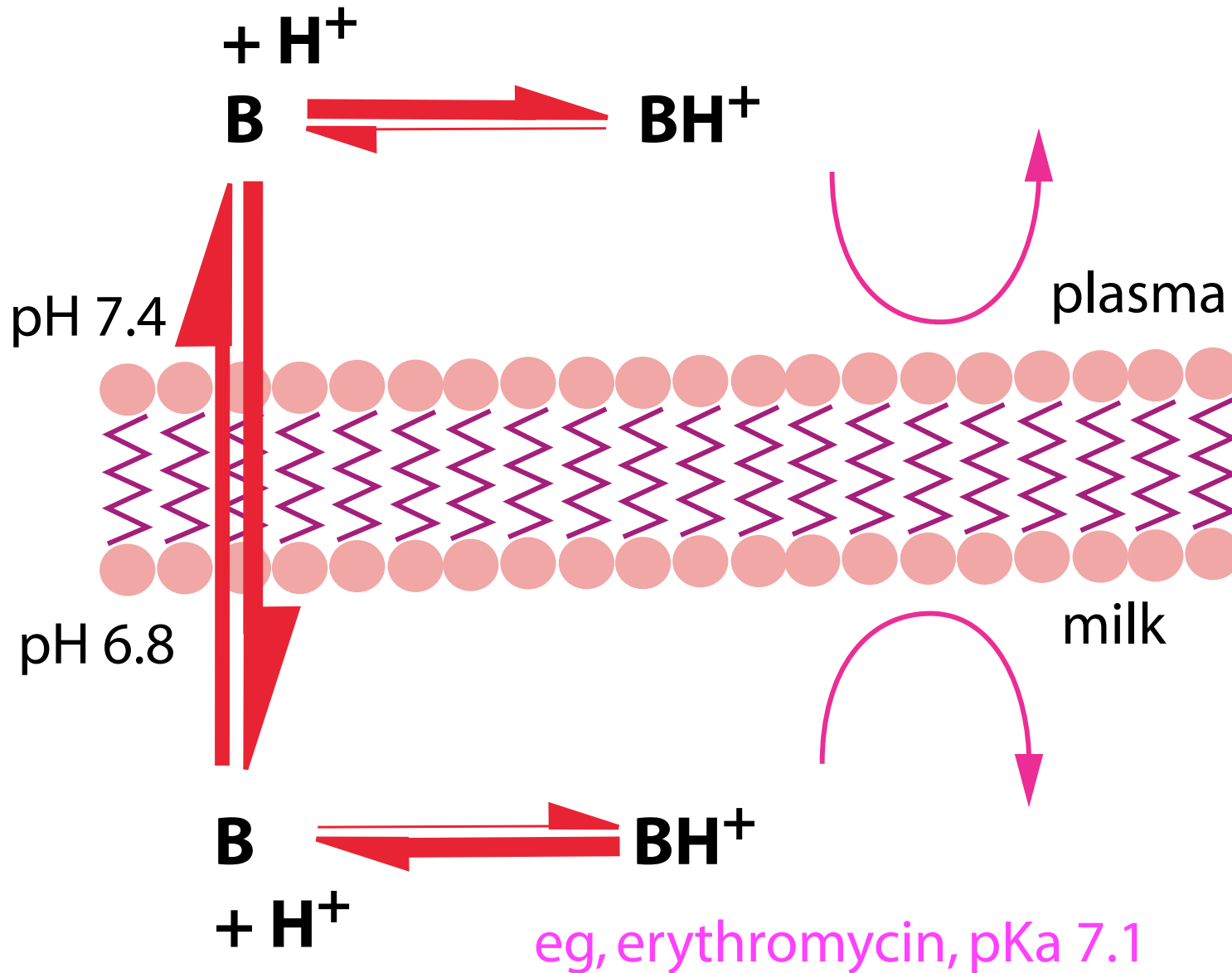
effects of pH

- **bases are ionised in acid solutions**
- **acids are ionised in alkaline solutions**





ion trapping



other factors influencing oral absorption

- **blood flow**
 - reduced in shock
- **surface area**
 - intestine > stomach
- **contact time**
 - reduced in vomiting & diarrhoea
- **food**
 - drugs may bind to food
- **carrier mediated transport**
 - both ways

other factors influencing parenteral absorption

- **blood flow**
 - **im - medium speed**
 - exercise
 - intra-fat rather than im!
 - **sc - slow and variable**
 - ambient temperature
- **pH**
- **inflammation**
- **formulation**

iv "absorption"

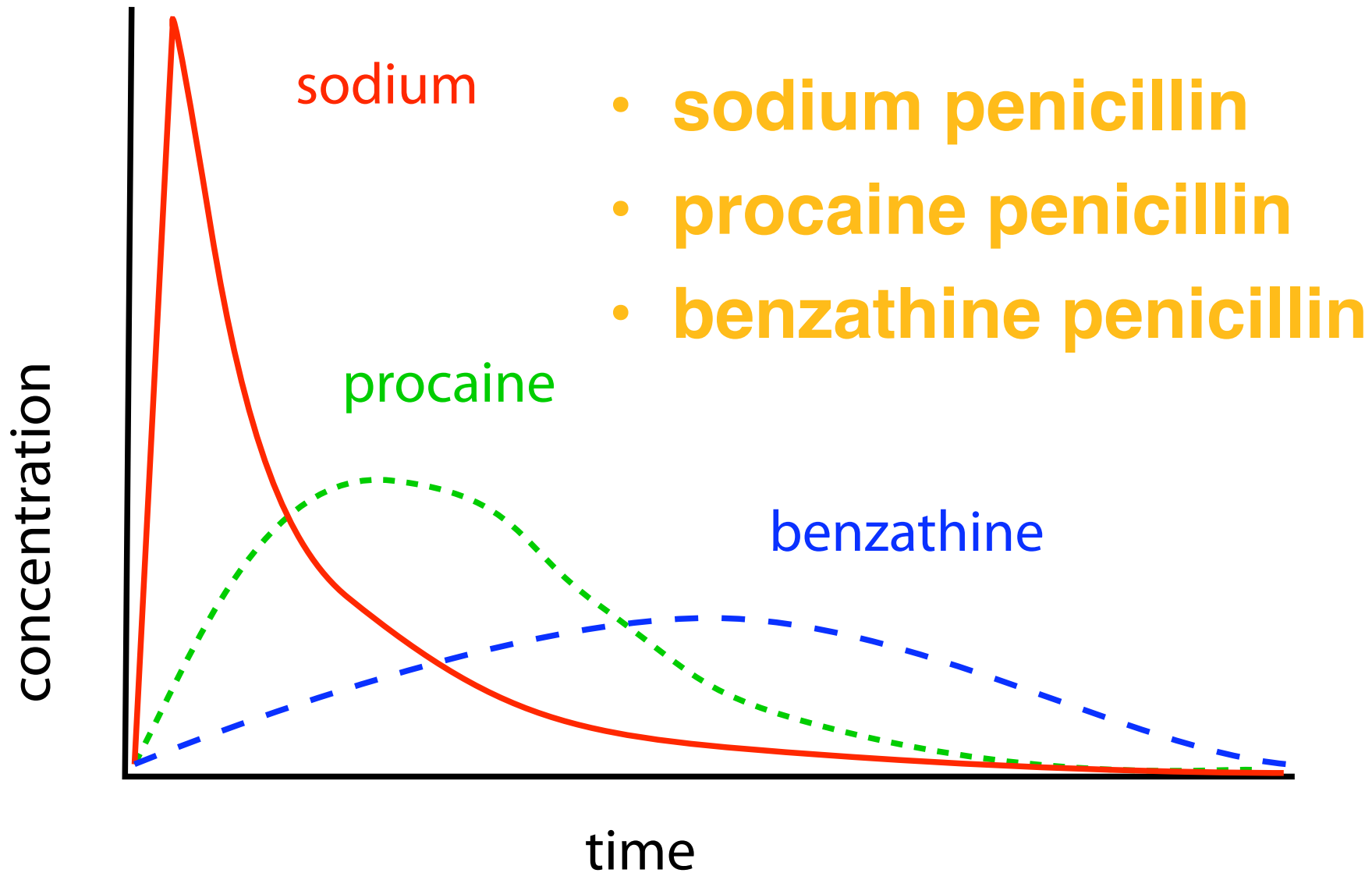
- **absorption is bypassed by iv injection**
- **rate of injection = rate of absorption**
- **if rate of absorption is critical to the patient, iv infusion can be used**

A red mushroom with white spots, likely a fly agaric, growing in a field of dry grass. The mushroom is the central focus of the image, with its bright red cap and white spots contrasting sharply with the dry, brownish grass. The text is overlaid on the upper half of the image.

alterations in rate of absorption can have clinical effects

- **antibiotics**
- **sedatives**

penicillin



penicillin

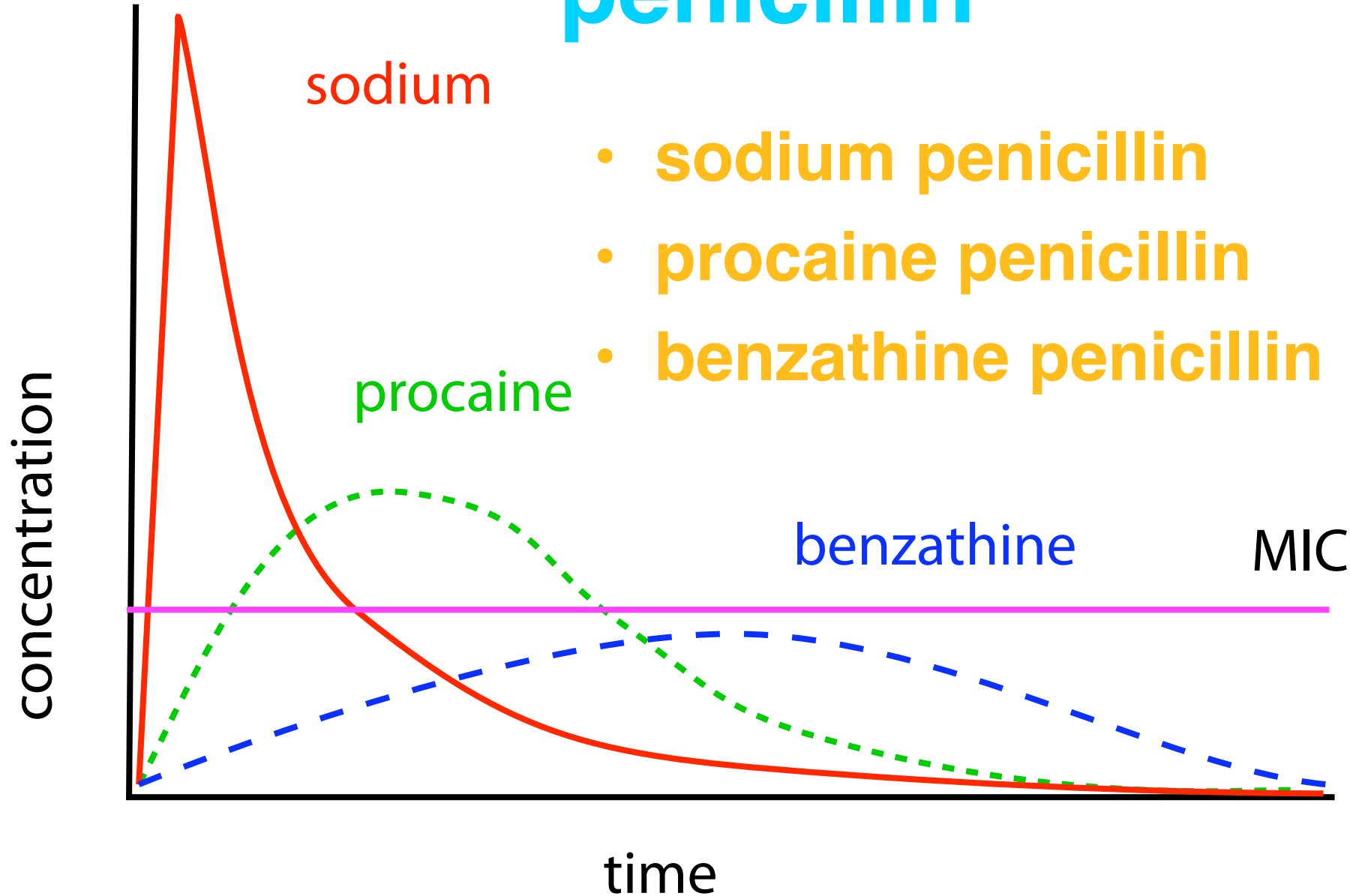
sodium

- sodium penicillin
- procaine penicillin
- benzathine penicillin

procaine

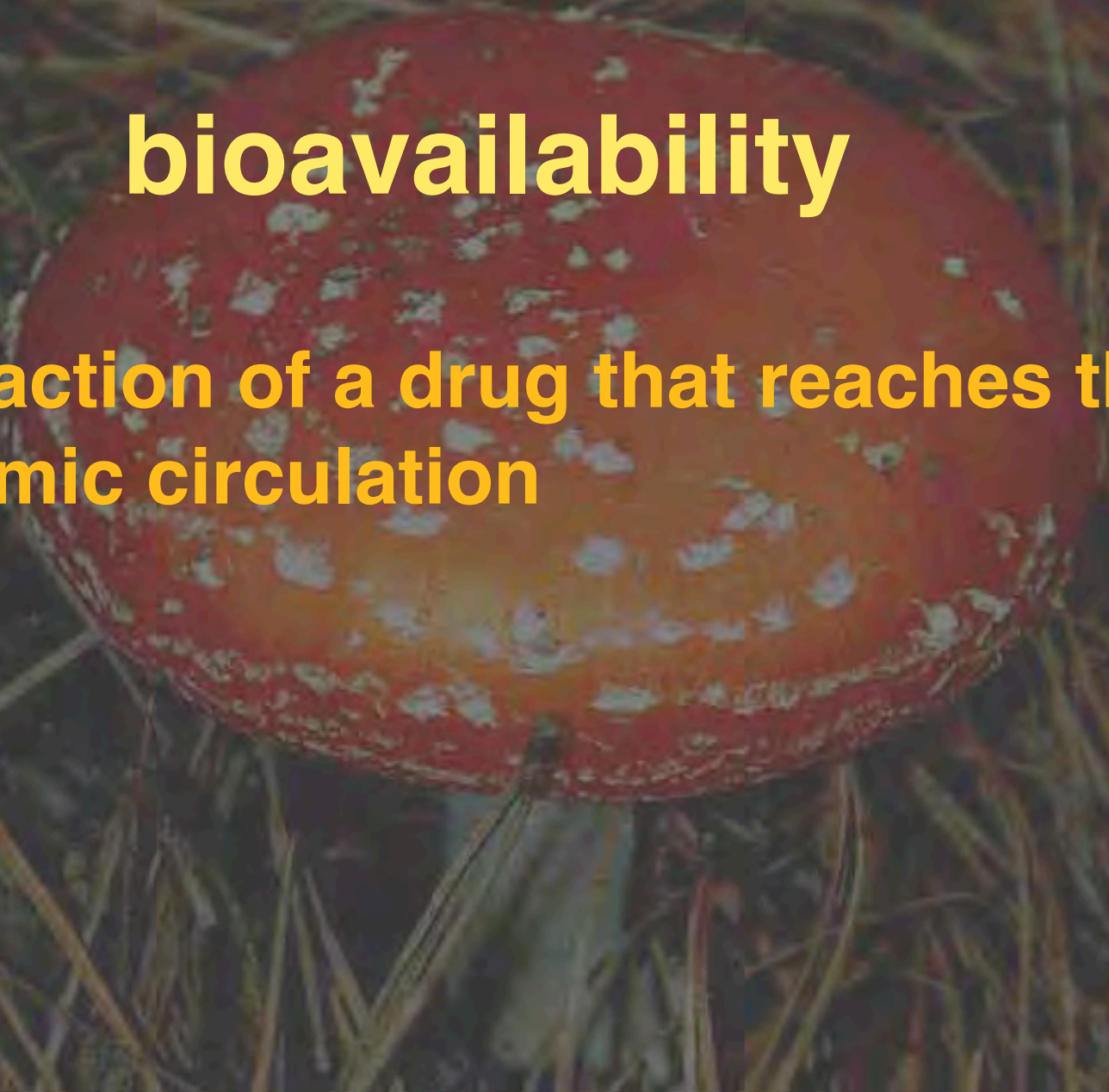
benzathine

MIC

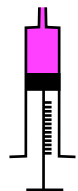


bioavailability

- the fraction of a drug that reaches the systemic circulation

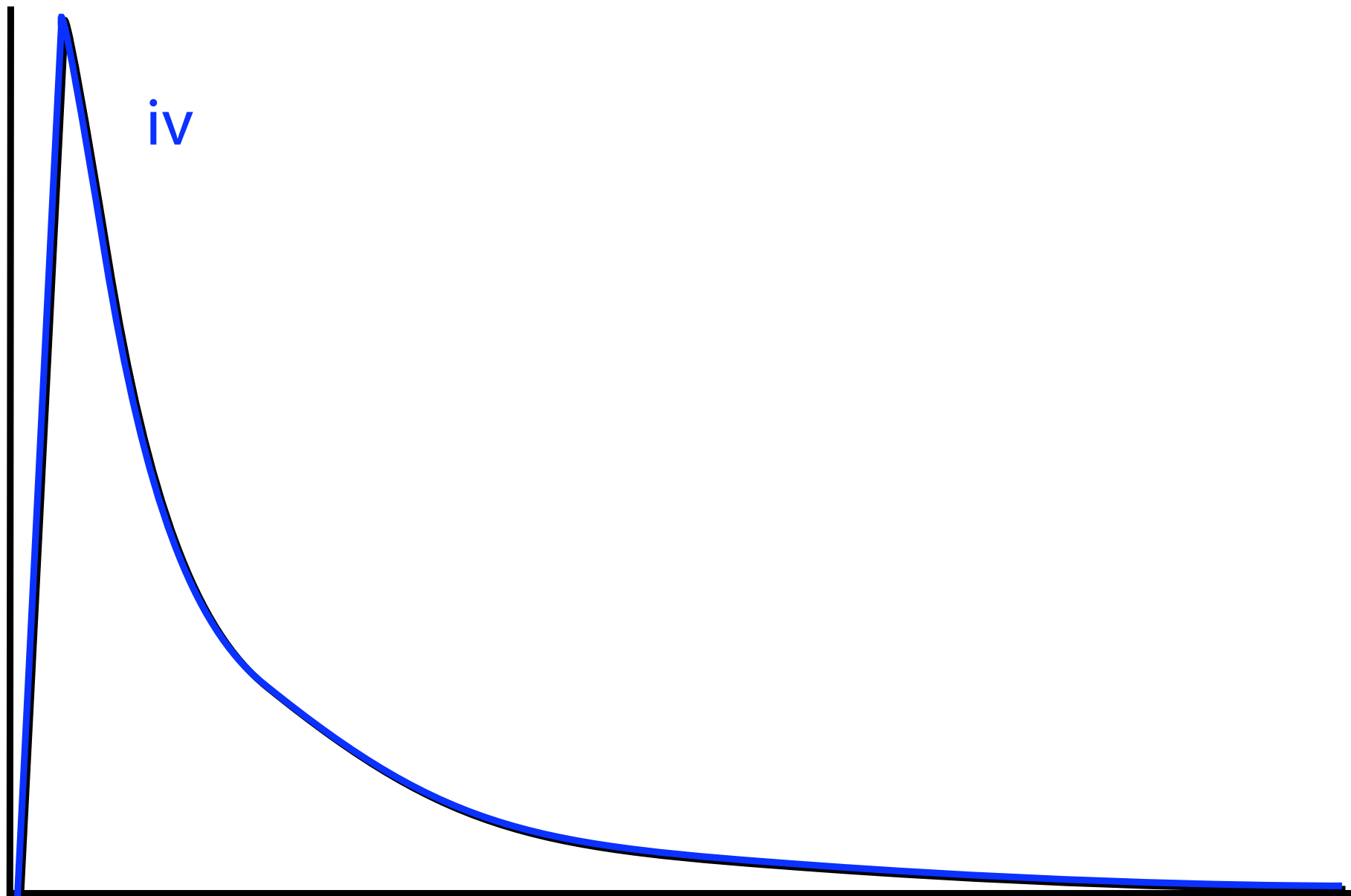


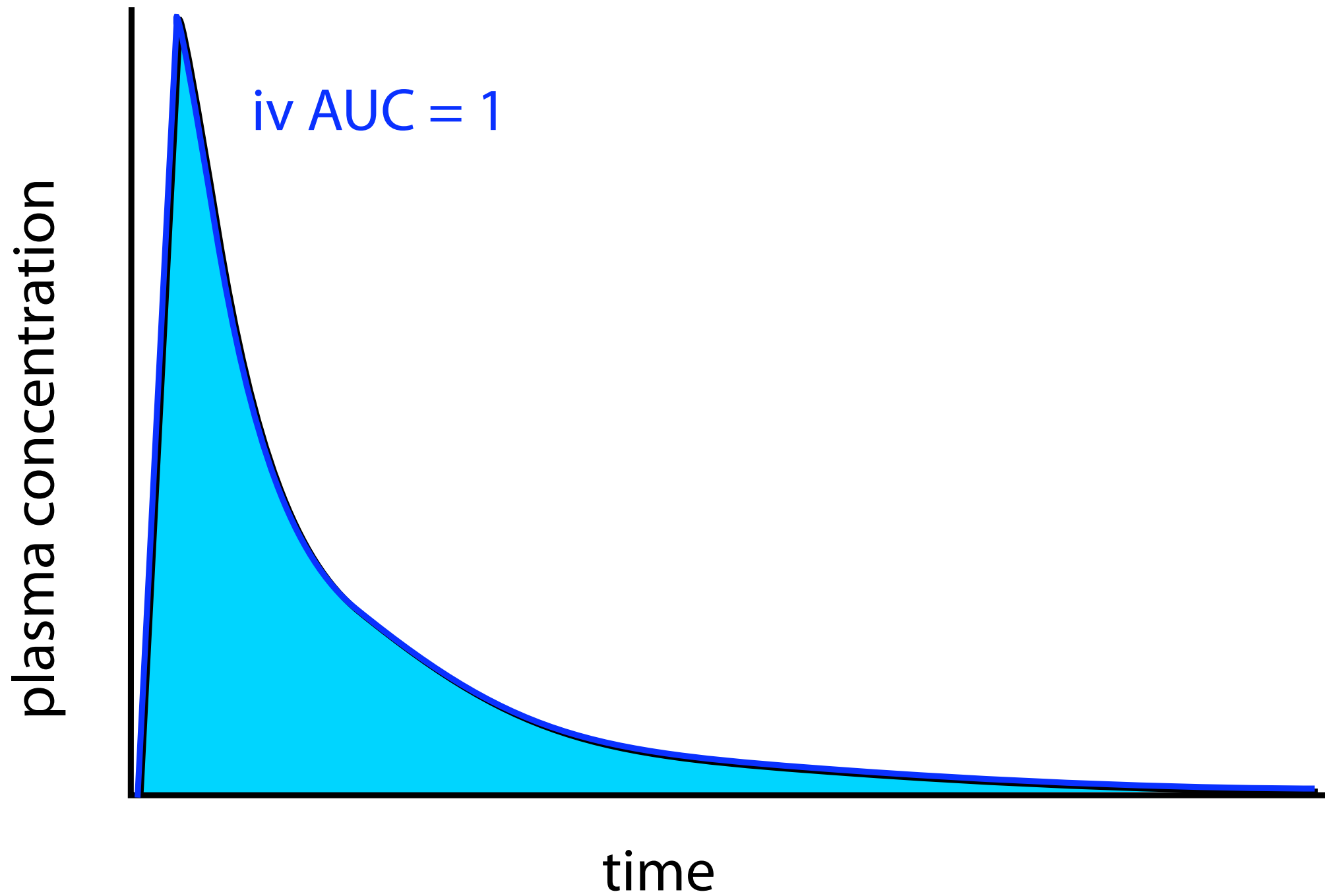
plasma concentration

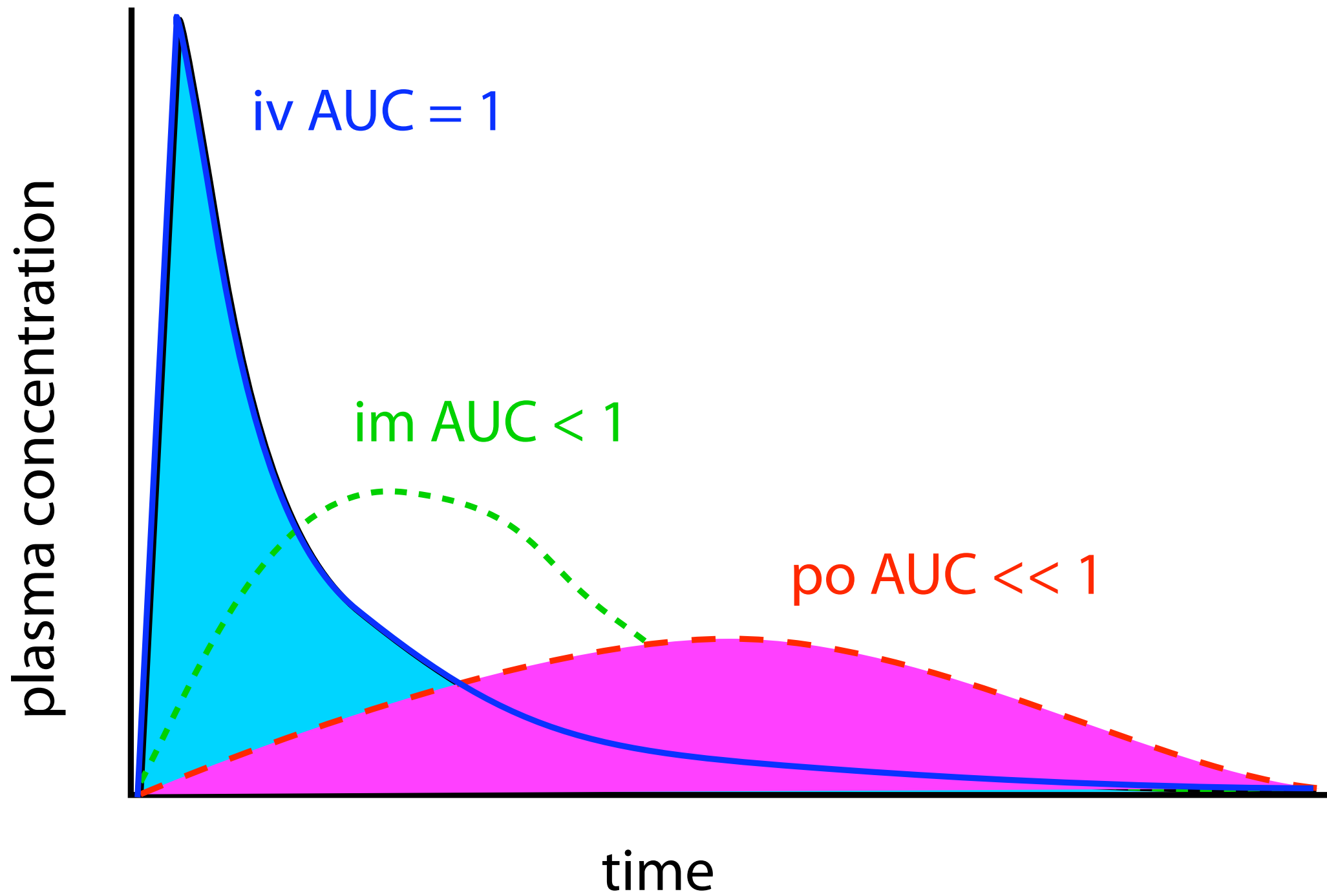


iv

time



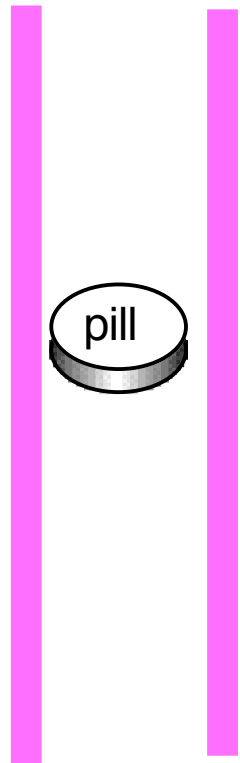




low bioavailability

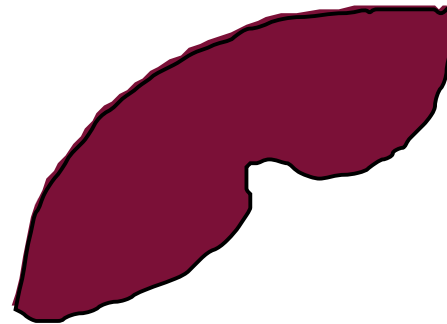
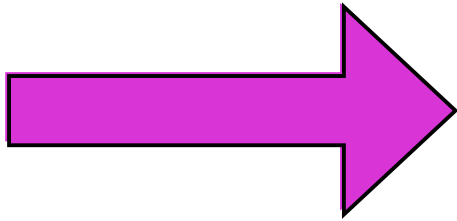
- **poor absorption**
 - very hydrophilic drug
 - chemical instability
 - drug formulation
- **first pass metabolism**

first pass metabolism



gut

portal vein



liver

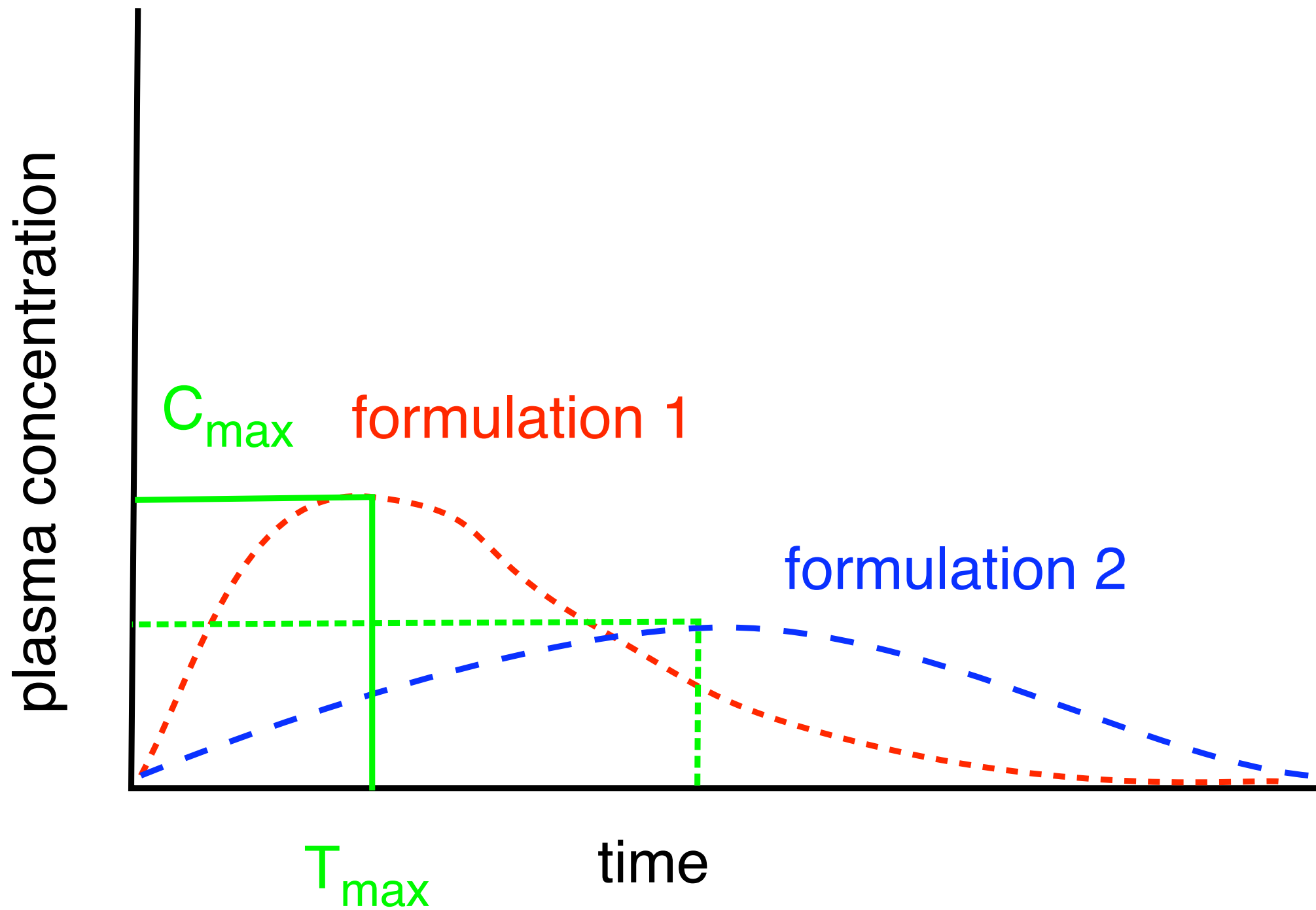
systemic
circulation



target
organ

bioequivalence

- same bioavailability
- AUC
- peak concentration (C_{max})
- time to peak (T_{max})
- same effects





How would you get an antibiotic to here?

absorption

- **most drugs must be absorbed to act**
- **iv administration bypasses absorption**
- **absorption depends on lipid solubility and ionisation**
- **drugs are often formulated to provide delayed absorption**