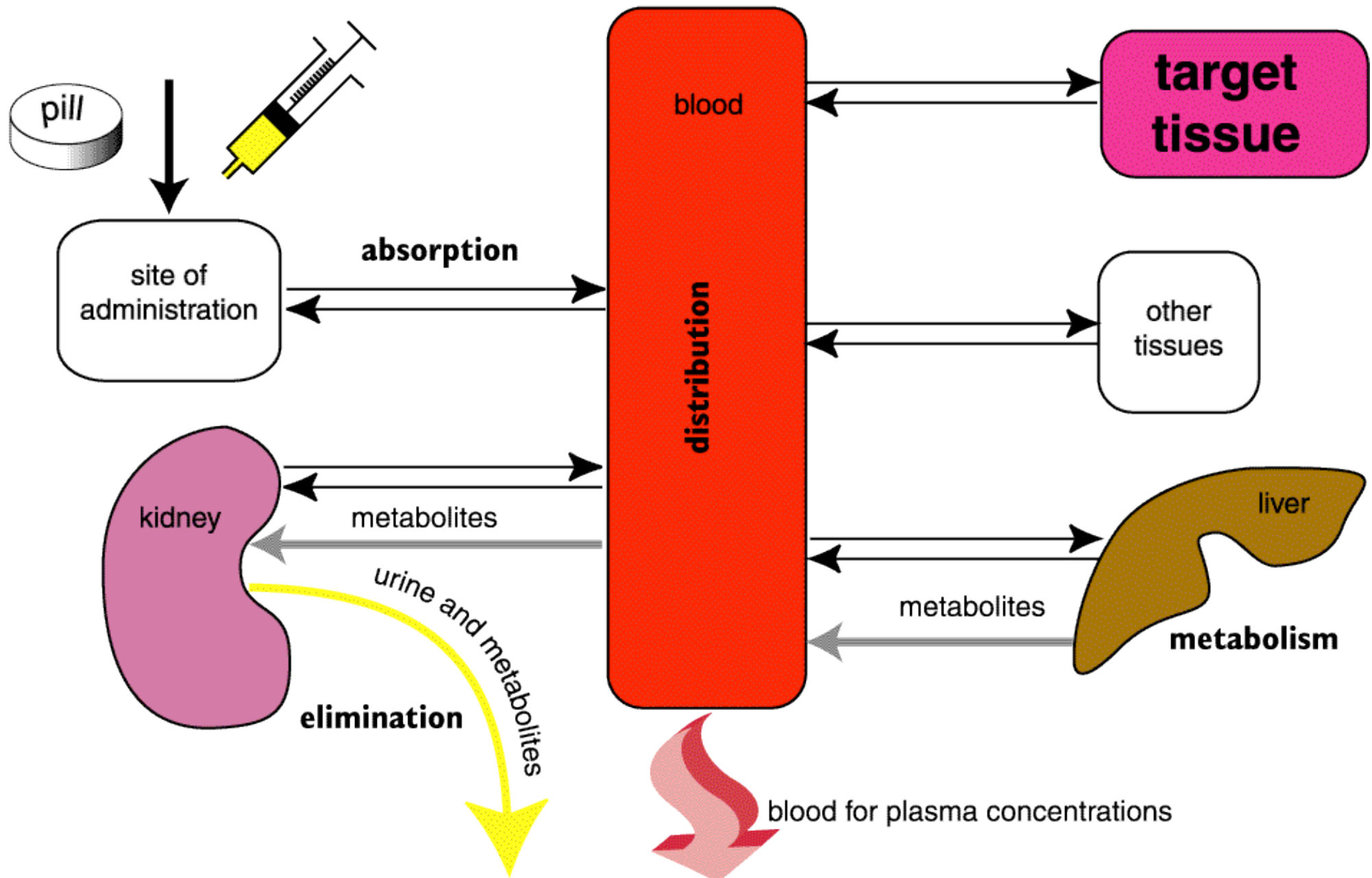


A close-up photograph of a red mushroom with white spots, likely a fly agaric, growing in a field of dry grass. The mushroom has a bright red cap with numerous white, irregular spots. The background is a dense field of dry, yellowish-brown grass.

Pharmacokinetics

Distribution

pharmacokinetics



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.

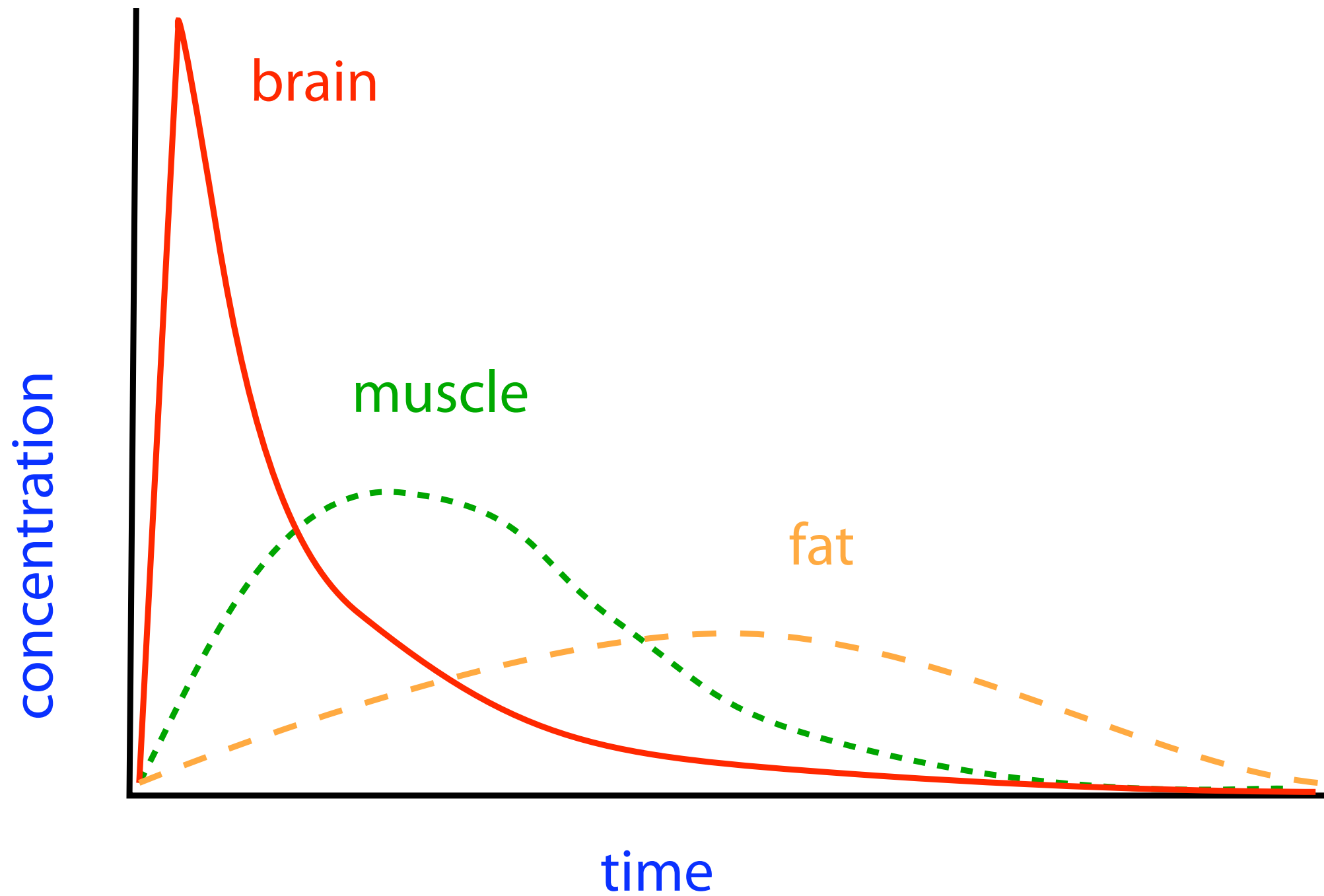
distribution

- the movement of drug from the circulation to the tissues and back

A red mushroom with white spots, likely a fly agaric, is the central visual element. It is positioned in the upper right quadrant of the slide. The background is a dense field of dry, yellowish-brown grass. The text is overlaid on the left side of the image.

distribution

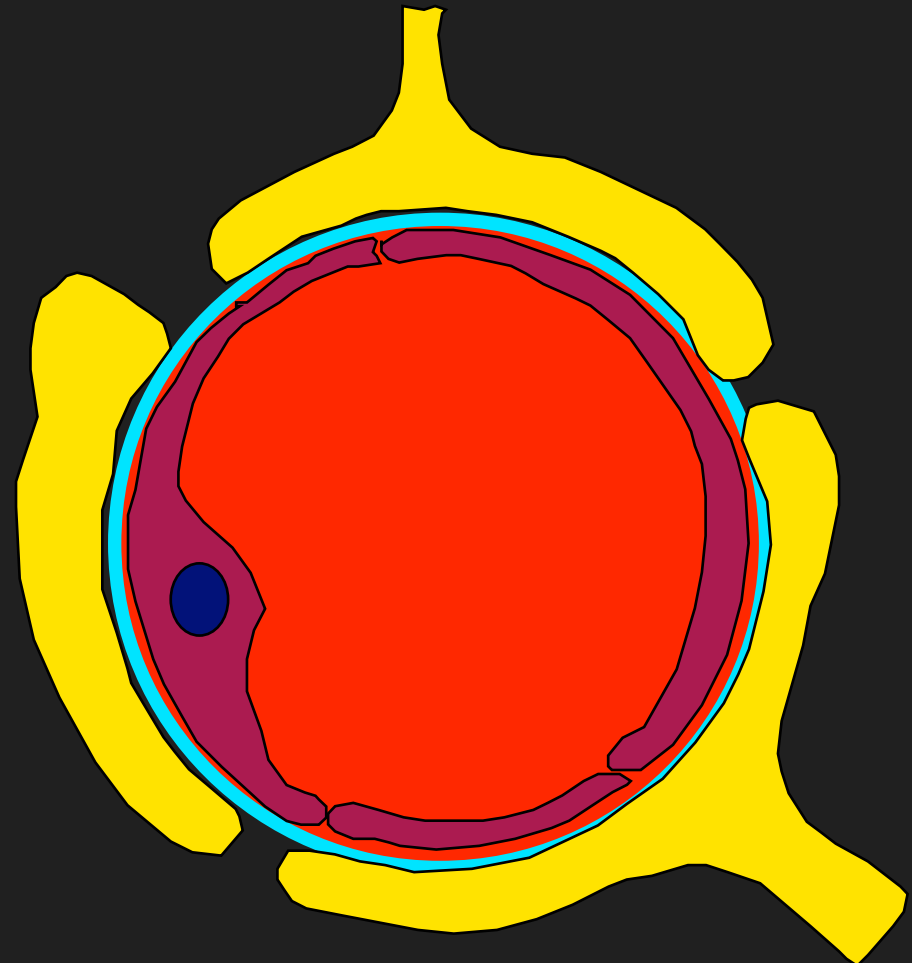
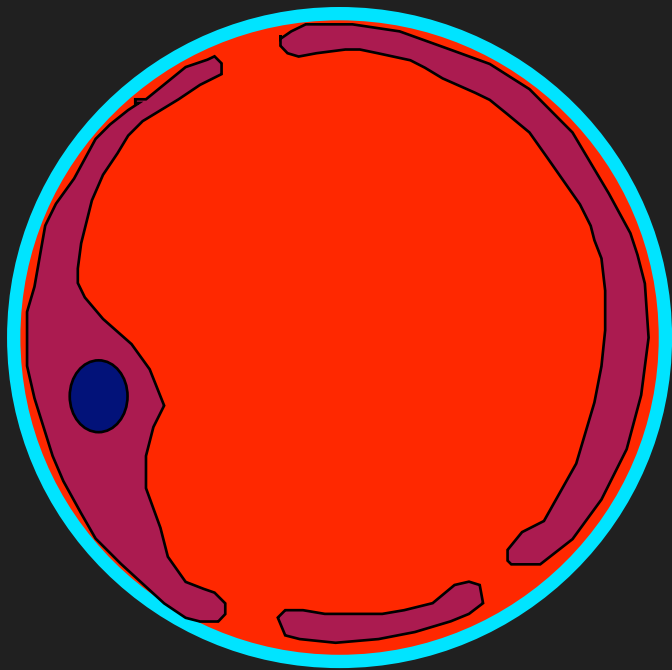
- **blood flow**
- **capillary permeability**
 - **capillary structure**
 - **drug structure**
 - **carrier proteins (efflux pumps)**
- **protein binding**



capillary structure

brain capillary

normal capillary



blood brain barrier

- no access for ionised drugs
 - aminoglycosides
 - penicillins
- lipid soluble drugs rapidly equilibrate and rapidly redistribute
 - anaesthetics
- P glycoprotein pumps many drugs out
 - also cancer cells
 - also bacteria

drug structure

- **size**
 - most drugs c 200Da
 - peptides c 5,000Da
 - proteins c 50,000 Da
- **lipid solubility**
 - oil / water partition coefficients

distribution

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 stem is thick and white. The background is a dense field of dry, yellowish-brown grass.

- **blood flow**
- **capillary permeability**
- **protein binding**

protein binding

- many drugs are bound to albumin
- keeps drugs in circulation
- free drug concentration low
 - only free drug is active

factors affecting protein binding

- other drugs
 - there are usually more binding sites than drug molecules, but if two highly bound drugs are given together, one drug may displace the other resulting in more free (active) drug than expected
 - sulphonamides often saturate binding sites
- hypoproteinaemia
- (body temperature)
- (pH)



protein binding

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.

- needs phenylbutazone
- may be on warfarin
- may also need surgery
 - thiopentone

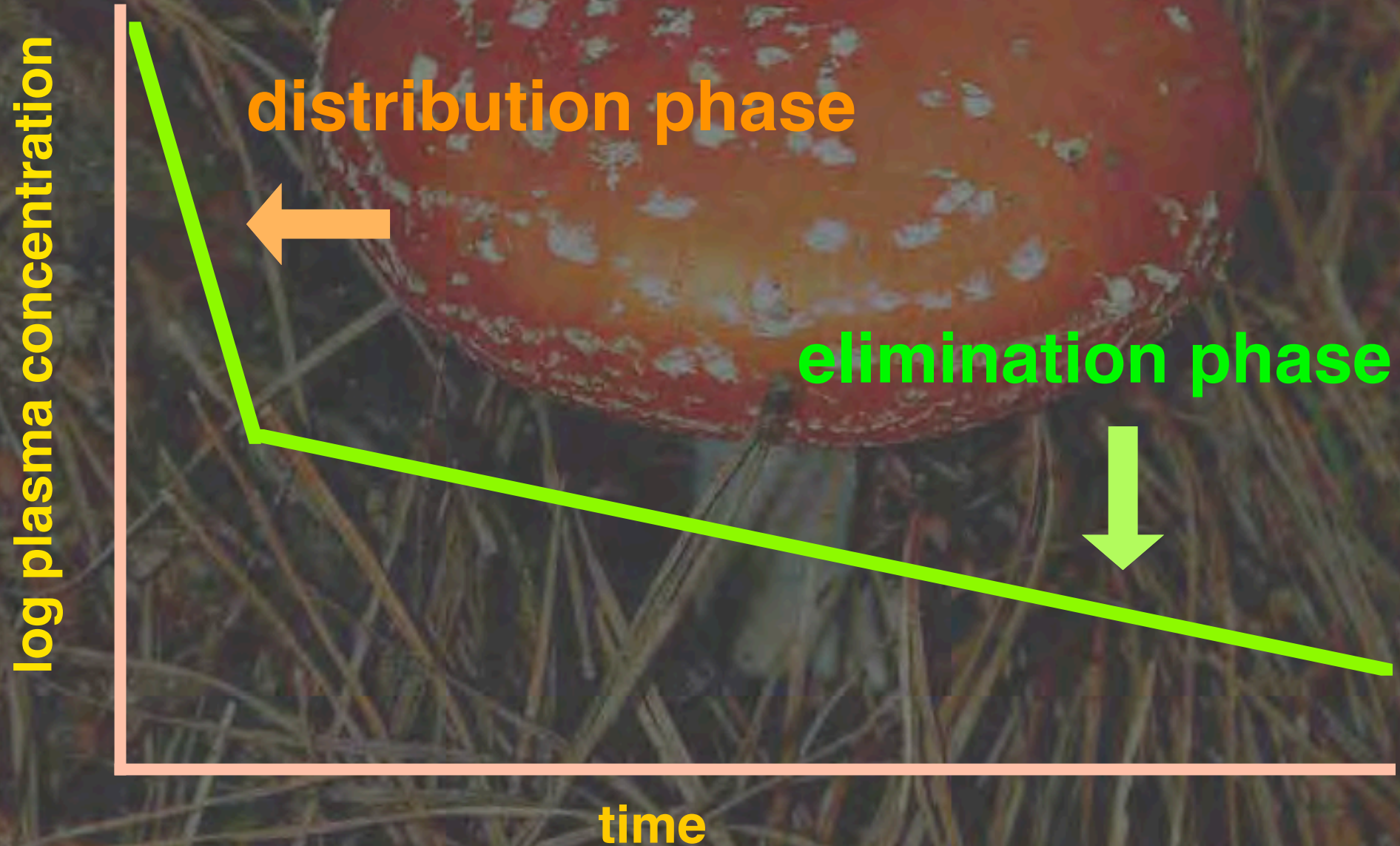
drug distribution

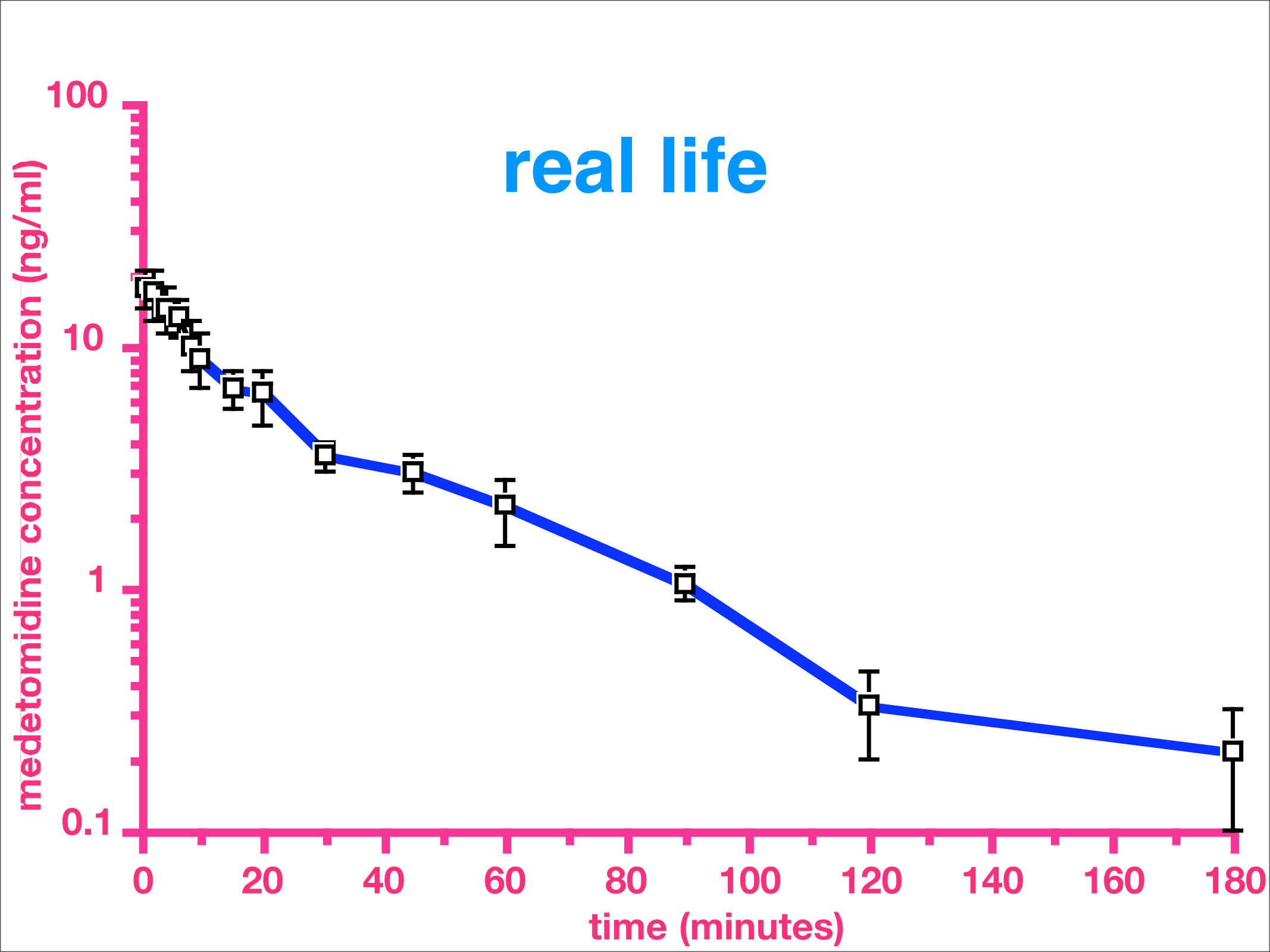
plasma concentration

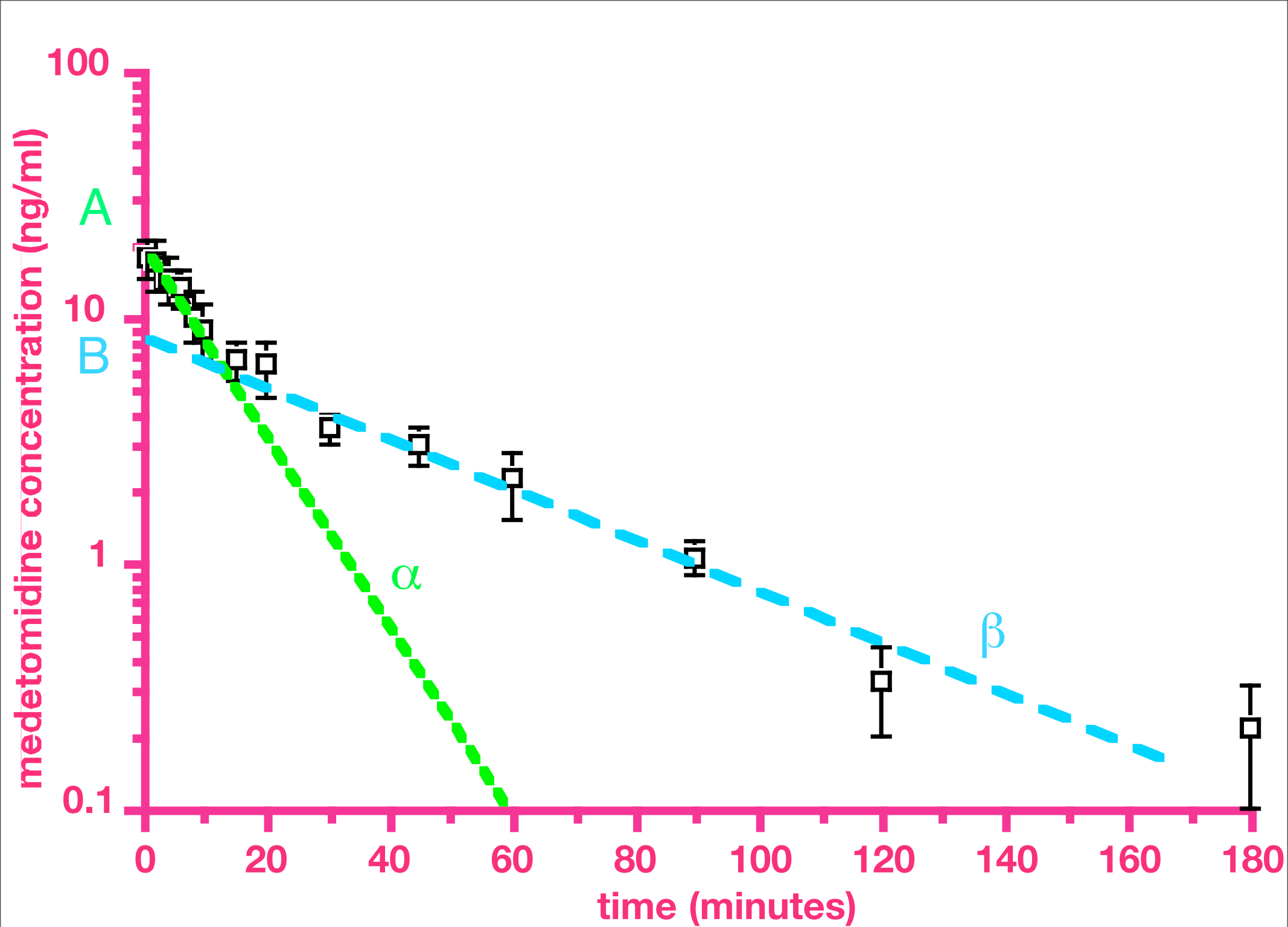


time

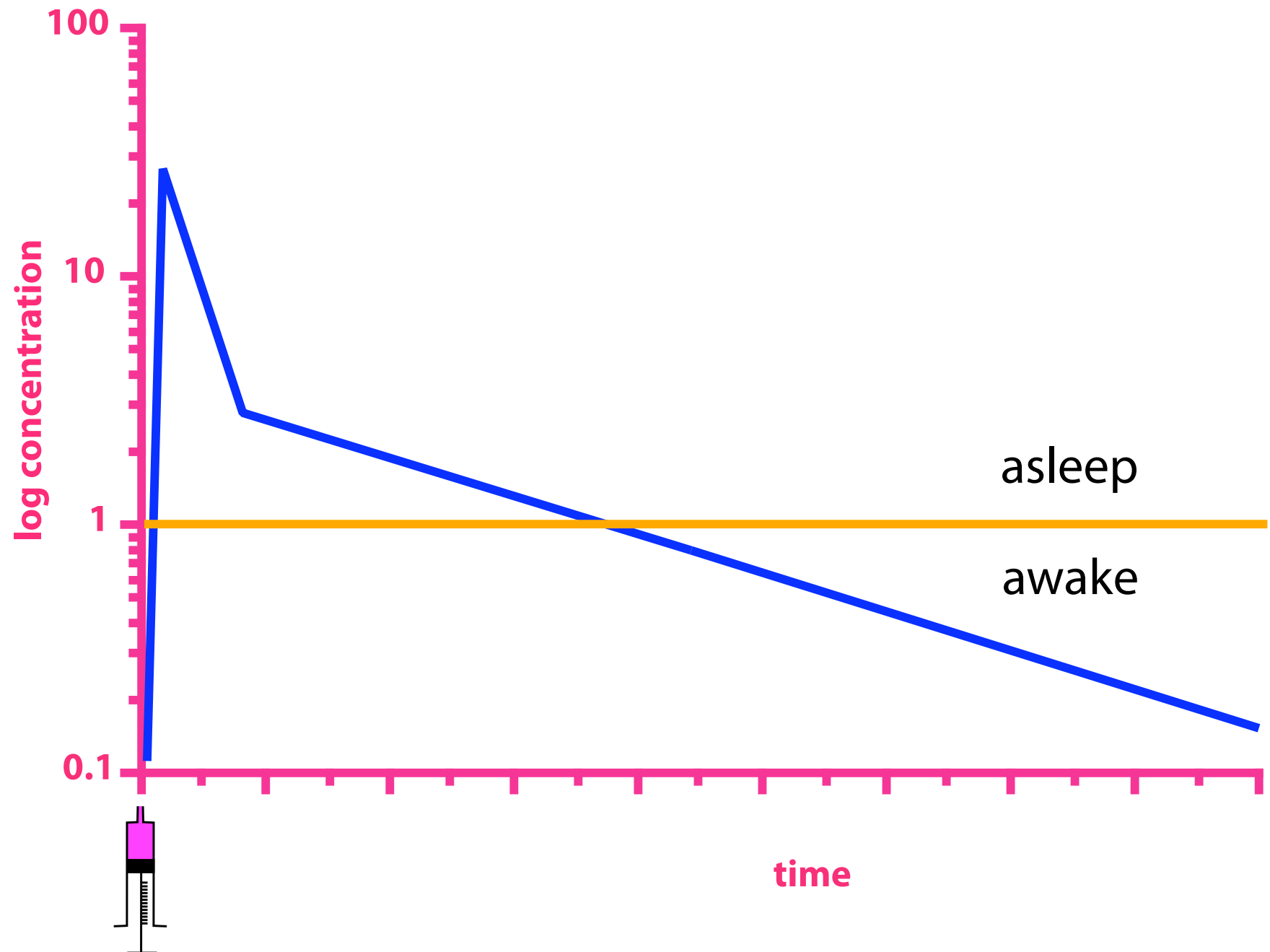
drug distribution



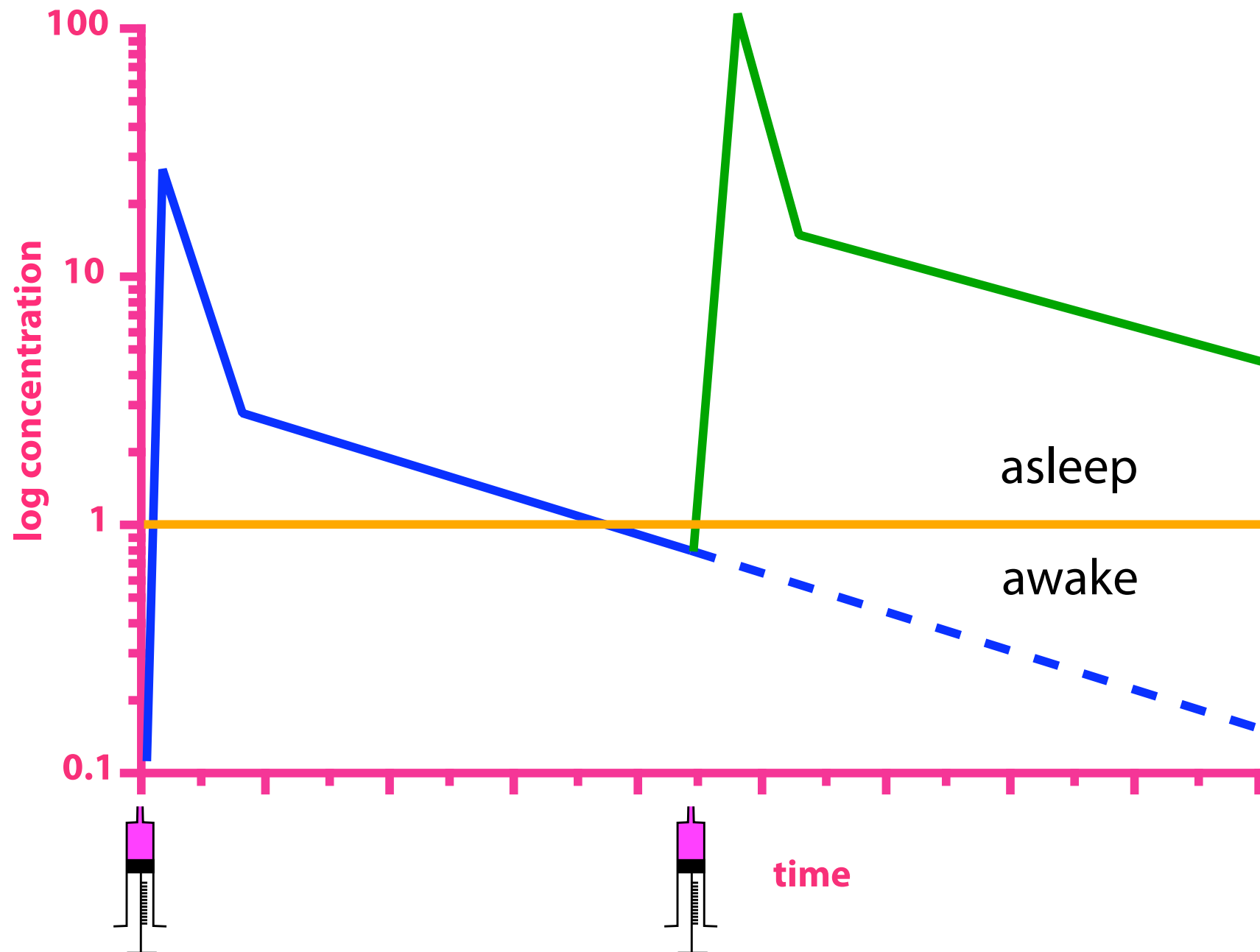


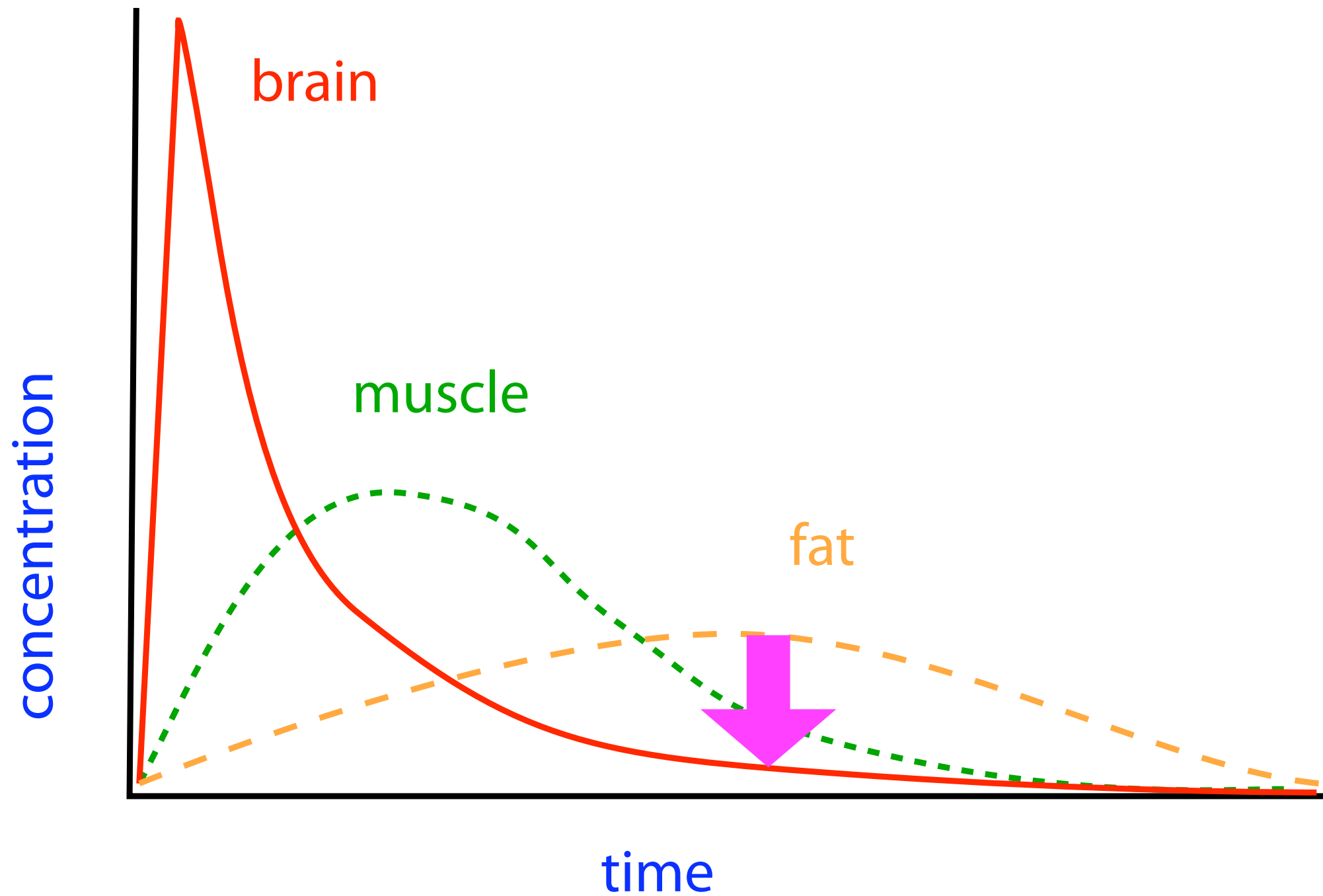


effective plasma levels

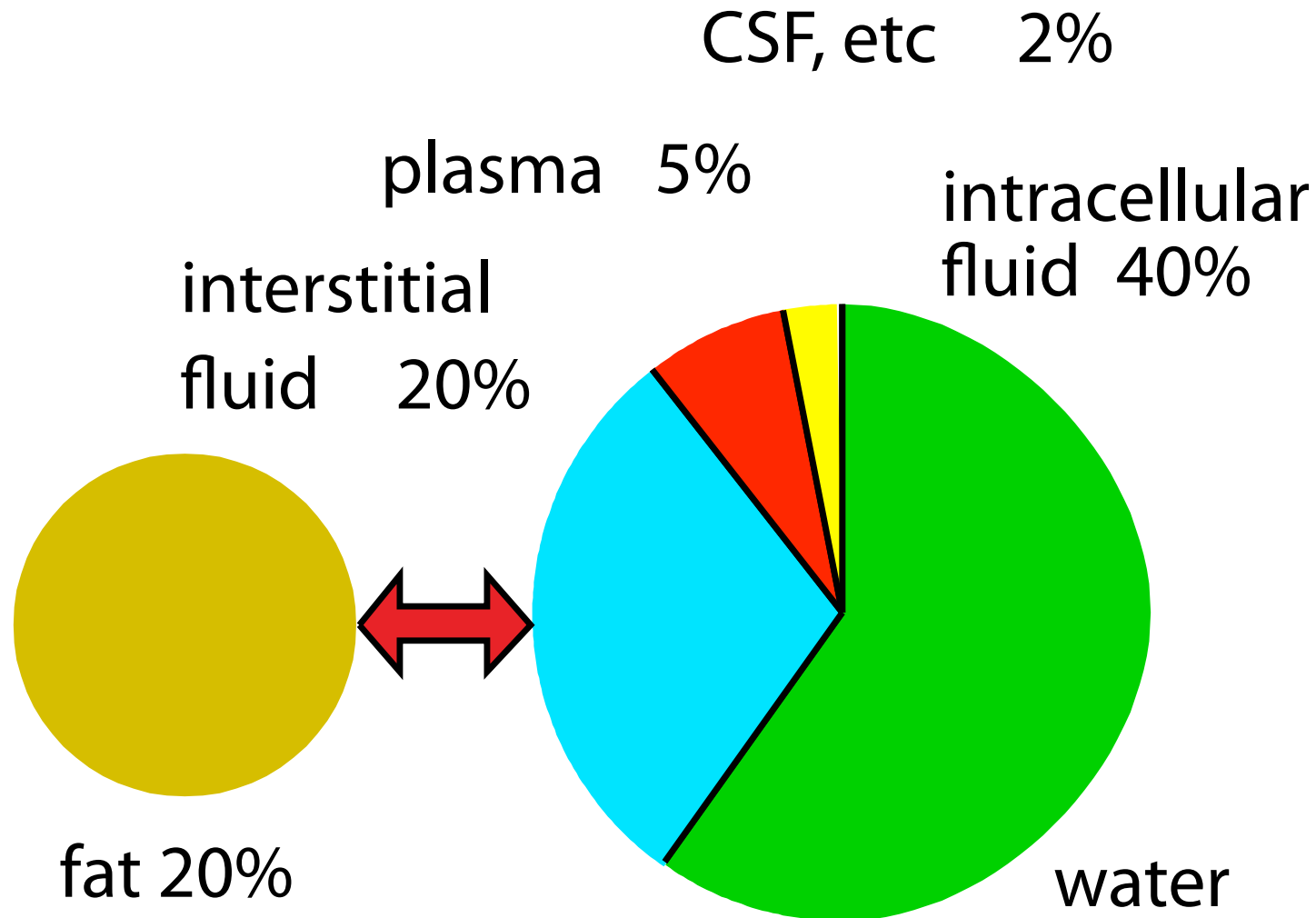


effective plasma levels



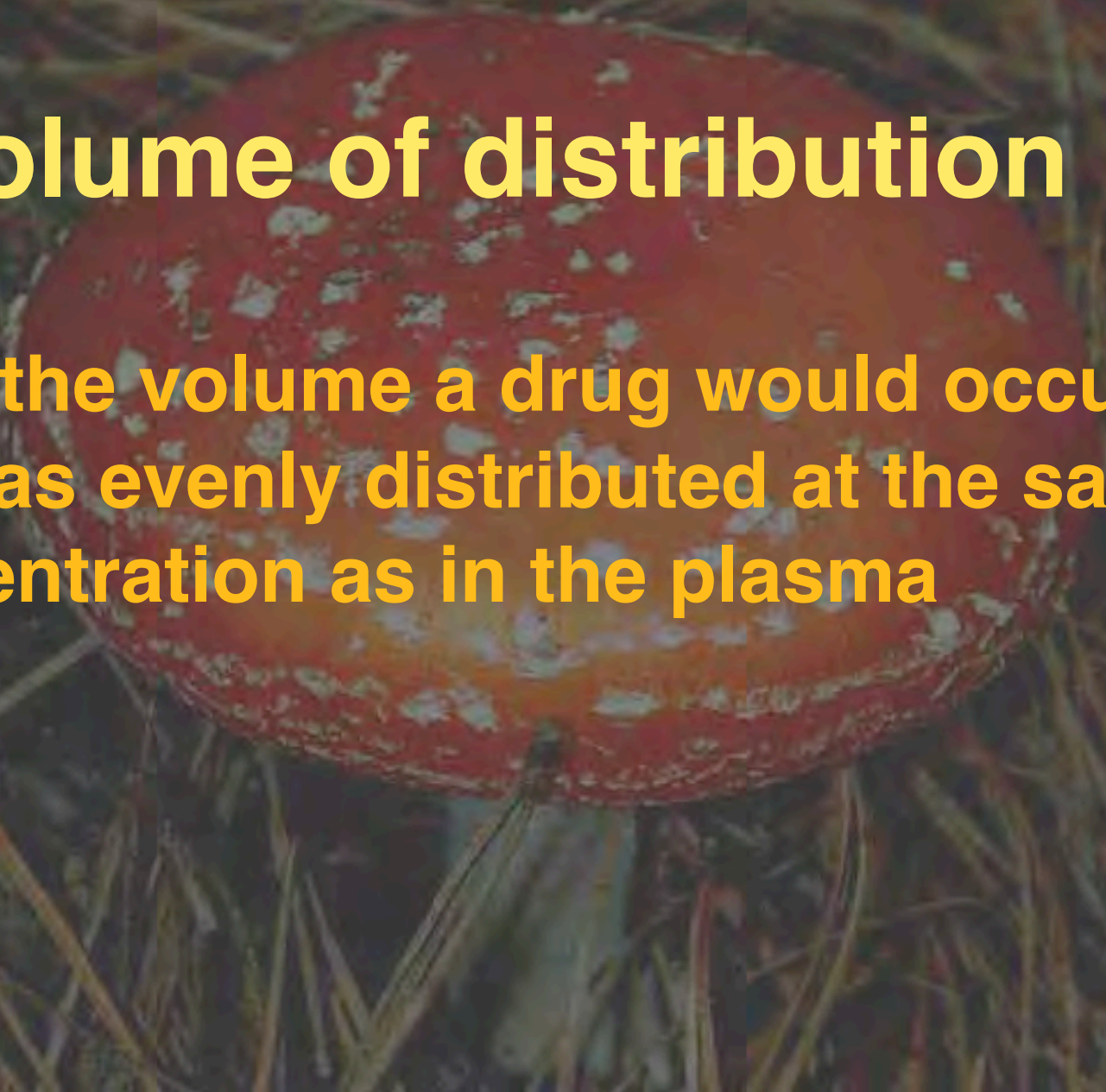


fluid compartments



volume of distribution

- V_d is the volume a drug would occupy if it was evenly distributed at the same concentration as in the plasma



A red mushroom with white spots is centered in the background. The text is overlaid on this image.

V_d

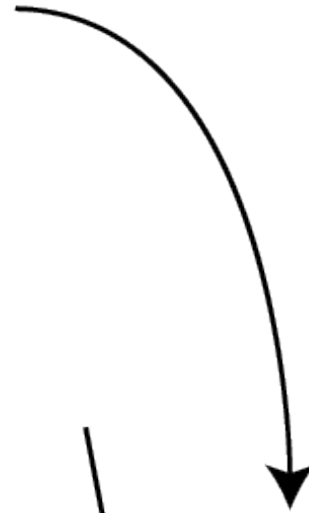
$$V_d = \frac{Q}{C_p}$$

If 25mg of drug results in a plasma concentration of 1mg/L then $V_d = 25/1 = 25L$

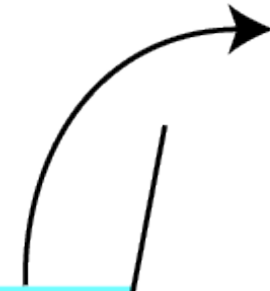
Vd



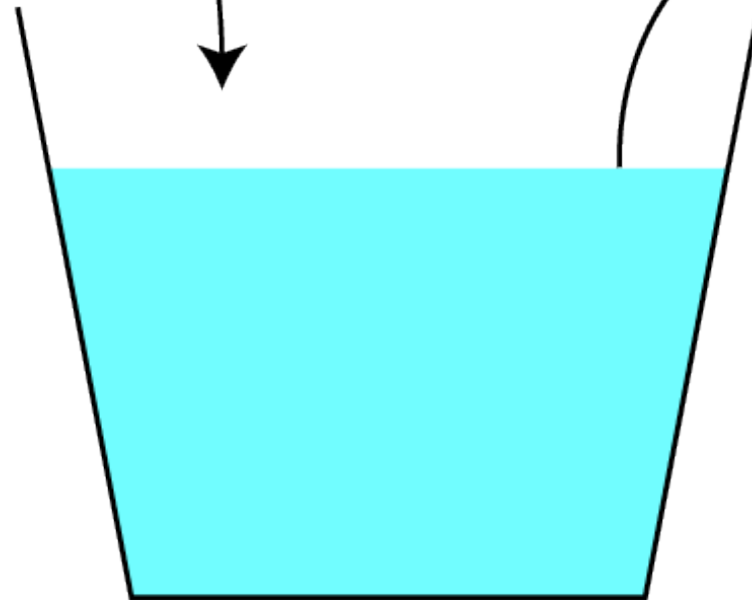
25mg



sample
1mg/L



- animals are more complicated than a bucket of water!



bucket containing unknown quantity of water

A red mushroom with white spots is centered in the image, resting on a bed of dry, brown grass. The mushroom has a rounded, slightly flattened top and a thick, textured stem. The background is a dense layer of dry grass, creating a natural, earthy setting.

V_d

$$V_d C_p = Q$$

**If V_d = 25L and plasma
concentration = 1mg/L,
then dose = 25mg**

Vd

- **Vd does not correspond to any anatomical or physiological compartment**
- **but - can provide some information on where drug goes**

Vd

- heparin - 50 mL/kg ~ plasma volume
- gentamicin - 250 mL/kg ~ ECF volume
- diazepam - 650 mL/kg ~ total body water
- morphine 5 L/kg ~ ?

Vd

- a large Vd implies that the drug is preferentially distributed somewhere - usually to fat - and is unavailable

A red mushroom with white spots, likely a fly agaric, is the central focus of the image. It is growing in a field of dry, brown grass. The mushroom has a bright red cap with numerous white, irregular spots. The background is a dense field of dry grass, creating a textured, brownish-green environment. The overall lighting is soft, and the colors are somewhat muted, giving it a naturalistic feel.

V_d

- used to calculate doses to achieve target plasma levels
- but
 - individual variation
 - pathology

What would you do?



- epileptic
- fits twice a week
- on phenobarbitone
- 20kg

phenobarbitone

- effective plasma levels $25 - 35\mu\text{g/mL} = \sim 30\text{mg/L}$
- comes as 30 & 60mg tablets
- completely bioavailable
- $V_d 0.75\text{L/kg}$
- dose?

phenobarbitone dose

$$V_d C_p = Q$$

- $V_d = 0.75 \times 20 = 15L$
- $C_p = 30mg/L$
- $Q = 30 \times 15 = 450mg$ or $22.5mg/kg$
- nb. frequency of dosing depends on how quickly the dog gets rid of the drug!!

distribution

- **drugs are usually distributed out of the blood to their site of action**
- **many drugs bind to plasma proteins and are unavailable for action or metabolism**
- **drugs are not distributed evenly throughout the body - each has a volume of distribution**